Gabriel Hortobagyi, M.D.

Interview #29

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Interview Profile

Interview Information:

Five interview sessions: 30 November 2012, 7 January 2013, 23 January 2013, 28 January 2013, 15 March 2013
Total approximate duration: 8 hours 45 minutes
Interviewer: Tacey A. Rosolowski, Ph.D.

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About the Interview Subject:

Gabriel Hortobagyi, M.D. (b. summer 1946, Sarvoc, Hungary) came to MD Anderson in 1974 as a Fellow in the Department of Developmental Therapeutics. He joined the faculty of the Breast Medical Service in 1976. Dr. Hortobagyi's research has focused on multimodality and adjuvant and neoadjuvant treatments for breast cancer, as well as personalized therapies and gene therapy. He served as chair of the Department of Breast Medical Oncology until 2012. He is a professor in that department and heads the Breast Cancer Research Program.

Major Topics Covered:

Personal and educational background

The Department of Developmental Therapeutics; Emil J Freireich, MD

Research: FAC metastatic breast cancer, locally advanced breast cancer, LABC treatment; shift to translational research projects and gene therapy; angiogenesis blocker;

Breast cancer treatments and service: evolution at MD Anderson

Overview of breast medical oncology: as a field; history of at MD Anderson

The Department of Breast Medical Oncology; history and evolution of at MD Anderson

The Breast Center; history of

Multi-disciplinary teams, evolution of at MD Anderson

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Leadership and mentoring experiences and principles

Educating breast medical oncologists

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University of Texas MD Anderson Cancer Center
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Original Interview Profile #29: Gabriel Hortobagyi, M.D.

Submitted by: Tacey A. Rosolowski, Ph.D.
Date revised: 3 July 2014

This interview of Gabriel Hortobagyi, M.D. (b. summer 1946, Sarvoc, Hungary), a leader in breast medical oncology, is conducted in five sessions (approximately 8 hours 45 minutes total duration) in 2012-2013. Dr. Hortobagyi came to MD Anderson in 1974 as a Fellow in the Department of Developmental Therapeutics: he joined the faculty in 1976. He served as chair of the Department of Breast Medical Oncology until 2012. He is currently a professor in that department and holds the Nellie B. Connelly Chair in Breast Cancer. He also heads the Breast Cancer Research Program. The interview sessions take place in Dr. Hortobagyi's office in the Department of Breast Medical Oncology in the Cancer Prevention Building on the Main Campus of MD Anderson. Tacey A. Rosolowski, Ph.D. is the interviewer.

Born in Hungary, Dr. Hortobagyi's family escaped as refugees to Bogota, where Dr. Hortobagyi was educated. He received the equivalent of the B.S. in 1963 from the Colegio Helvetia in Bogota, and his M.D. in 1970 from the Universidad Nacional de Colombia, Bogota. He served as a Rotating Intern at the Hospital San Juan de Dios, Bogota (69-70). He decided to continue his education in the United States, and secured a position as a Clinical Resident in Internal Med at St. Luke's Hospital in Cleveland, Ohio ('71 – '74). In 1974, he came to MD Anderson for his Fellowship in Developmental Therapeutics, continuing with a Clinical Fellowship in Medical Oncology from '75-'76. He joined the faculty as a Faculty Associate in the Breast Medical Servie in 1977, advancing to Assistant Professor in '79. He became full professor in 1985. Dr. Hortobagyi has been instrumental in building the Breast Medical Oncology service at MD Anderson since his arrival. He became Chief of the Section in 1984 and assumed the role of Department Chair in 1992, when the section was restructured as a Department under Dr. Charles LeMaistre. He actively built the Breast Cancer Research Group at MD Anderson and has been active in Breast Cancer and Breast Medical Oncology groups worldwide. His research has influenced Standards of Care in breast cancer treatments: he initiated regimen that used anthracycline as backbone of adjuvant chemotherapy (20 yrs later became standard of care for primary breast cancer) and he was the first to prove the value of paclitaxel for front line and adjuvant therapy. He developed combination drug strategy for preoperative chemotherapy followed by surgery and radiation, now considered standard for most primary breast cancers. He developed a neoadjuvant modality allowed surgery for many inoperable tumors and advanced multidisciplinary research efforts to design personalized therapies and clinical trials to test gene therapy. In 2013 Dr. Hortobagyi received the Jill Rose Award for outstanding research excellence from the Breast Cancer Research Foundation and the Bob Pinedo Cancer Care Prize from the Society for Translational Oncology in 2011. In 2004 he was the first recipient of the Umberto Veronese Award for the Future Fight Against Breast Cancer. He is a Chevalier of the Order of the Legion of Honor, France (received 2001). In 2009 he received the John Mendelsohn Lifetime Achievement Award from MD Anderson.

In this interview, Dr. Hortobagyi gives an overview of his career and commitments. He sketches his childhood experiences as a refugee and his formative medical training in Bogota. He details the many dimensions of his research. (His discussion covers the ongoing debates about clinical trials that were taking place at MD Anderson into the eighties.) He also speaks at length about what was required to establish multi-disciplinary and patient centered breast cancer service at the institution, as well as tracing the evolution of Breast Medical Oncology. Dr. Hortobagyi comments on leadership both within the institution and in the field of Breast Medical Oncology as an international endeavor. Dr. Hortobagyi sets events in an historical perspective, and this interview consequently includes many snapshots of the development of oncology, of research, of the design of clinical trials, as well as vignettes of leadership, mentoring, and MD Anderson at many phases of its evolution.

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Segment Summaries

Interview Session One: 30 November 2012

Segment 00A
Interview Identifier

Segment 01
A Family Escapes to Colombia
A: Personal Background

Story Codes
A: Personal Background
A: Character, Values, Beliefs, Talents

In this segment Dr. Hortobagyi describes his childhood Hungary after WW II: the Hortobagyi family was interred in a concentration camp and Dr. Hortobagyi's father sentenced to three years of hard labor for political differences with the government. (Dr. Hortobagyi explains that he was assigned to work for a townsman collecting manure for fertilizer.) When Josef Stalin died in 1953, the family was granted amnesty and released, and Dr. Hortobagyi next explains how in 1954 the family escaped to Colombia, first walking across the Hungarian border to Austria and settling in a refugee camp, then traveling to Genoa, Italy where the family was able to secure passage to South America as refugees from Genoa. They arrived in Colombia on May 10th, 1957, where Dr. Hortobagyi's father opened a business in Bogota.

Segment 02
Becoming a Doctor
A: Educational Path

Story Codes
A: Character, Values, Beliefs, Talents
A: Personal Background
A: Professional Path
A: Inspirations to Practice Science/Medicine
A: Influences from People and Life Experiences
A: Professional Values, Ethics, Purpose
C: Professional Practice
C: The Professional at Work
C: Formative Experiences

Here Dr. Hortobagyi sketches his scientific and medical education, beginning with the observation that he never thought of any other profession than medicine even as young person.

Dr. Hortobagyi observes that his mother wanted to be a doctor, but couldn't because of limits on women's choices at the time. She had an impact on his own choice of profession because she gave him books on science and medicine when he was young.

Dr. Hortobagyi then notes that he had very good science teachers in middle school and, under the Colombian educational system, had made a commitment to his profession by his senior year in high school. He talks about his medical education at the Universidad Nacional de Colombia, Bogota (M.D. conferred in 1970). The Colombian system gave Dr. Hortobagyi an accelerated medical education. By the time he was a college freshman, he had the equivalent of a clerkship at the University hospital –the only charity hospital in the city and the only one with a real emergency room. It was a very busy hospital, and during his clerkship in ob/gyn, the delivery room sometimes handled a hundred babies a day. (At times there were two women in a bed.) By the time he received his M.D., Dr. Hortobagyi had delivered 80-110 babies. Dr. Hortobagyi also explains that surgery attracted him and that he has a "type A" personality, which is perfect for a surgeon. He describes his emergency room rotations: 24 hours on, 12 hours off for ten weeks, a system that gave very intensive hands-on training.

Segment 03
A Small Town Offers Good Training
A: Professional Path

Story Codes
A: Character, Values, Beliefs, Talents
A: Personal Background
A: Professional Path
A: Inspirations to Practice Science/Medicine
A: Influences from People and Life Experiences
C: Evolution of Career
A: Professional Values, Ethics, Purpose
C: Professional Practice
C: The Professional at Work
C: Formative Experiences

Dr. Hortobagyi begins this segment with a brief description of some of the rotations he completed at the University Hospital, then describes his year serving as a doctor to the small town of Pacho to repay the government for tuition support. (Dr. Hortobagyi describes how the State assessed tuition based on need and merit: by his second year, Dr. Hortobagyi's tuition was fully covered because of his exemplary performance.) Pacho is located in the Andes and the tiny town has a 100-bed hospital. Dr. Hortobagyi saw the results of violent conflict between gangs of emerald smugglers. He describes treating the victim of a murder attempt.
Dr. Hortobagyi describes treating a woman who was continuously pregnant for eighteen years and had sixteen children.

Dr. Hortobagyi explains that the experiences in Pacho taught him that medicine is an art, not a science. He gives other examples of caring for patients and describes the organization of the hospital in Pacho, where the generator was turned off at night so Dr. Hortobagyi had to study by candlelight.

Dr. Hortobagyi describes how he fit into the social life of the small town and how he came to understand how this situation could be comfortable, but ultimately limiting to his professional and intellectual growth.

Segment 04
Choosing to Focus on Cancer
A: Joining MD Anderson/Coming to Texas

Story Codes
A: Character, Values, Beliefs, Talents
A: Personal Background
A: Professional Path
A: Inspirations to Practice Science/Medicine
A: Influences from People and Life Experiences
C: Discovery and Success
C: Human Stories
C: Offering Care, Compassion, Help
C: Patients
C: Cancer and Disease
C: Professional Practice
C: The Professional at Work
C: Evolution of Career
C: Formative Experiences
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care

Dr. Hortobagyi explains that once he felt the limitations of small-town medical practice, he applied for residencies in the U.S., first going to Case Western Reserve University to serve at Saint Luke's Hospital Cleveland, Ohio (1971-'74). (He chose Cleveland because of the large Hungarian community, where Hungarian was even spoken at the MacDonald's.) At this time he left surgery for a more intellectually stimulating, and began thinking about oncology. He also notes that on recognizing the more generous resources and education available in the U.S., he had a crisis about whether or not to return to Colombia.

Dr. Hortobagyi describes how oncology was the "wild west of medicine" and offered a field where he could bring together his thinking on hematology and immunology. He recalls that, during rounds in the early seventies at Saint Luke's Hospital, physicians would by-pass rooms of patients with solid tumors. He tells an anecdote about two women with advanced breast cancer who were treated only with morphine. He found an article on chemotherapy and once he began treating women with chemotherapy, they lived.

Segment 05
Inspired by Dr. J Freireich
A: Joining MD Anderson/Coming to Texas

Story Codes
C: Portraits
A: Joining MD Anderson

A: Personal Background
A: Professional Path
A: Inspirations to Practice Science/Medicine
A: Influences from People and Life Experiences
C: Funny Stories
A: Character, Values, Beliefs, Talents

Dr. Hortobagyi recounts how, early in his second year of his residency, he attended an American Cancer Society conference in Columbus, Ohio, where he heard Dr. Emil (J) Freireich give a talk. Dr. Hortobagyi notes that no one was talking about curing cancer in the early seventies, and he describes how inspiring it was to hear Dr. J Freireich state that he believed it was possible to cure the disease.

Dr. Hortobagyi explains that hearing this talk inspired him to apply for a fellowship at MD Anderson. He wrote to J Freireich, who approved hired him without even speaking with him.

Dr. Hortobagyi confesses his love of automobiles and tells an anecdote about buying his first car –a blue Dodge Challenger-- with no money and no credit.

Dr. Hortobagyi tells how he loaded his belongings in his car and drove down to Houston, despite the fact that everyone told him, “Nobody goes to Texas.” On arriving, he immediately went to the hospital and introduced himself to the head of the Breast Service, George Blumenschein.

Segment 06
Developmental Therapeutics in 1974
B: An Institutional Unit

Story Codes
B: MD Anderson History
B: Institutional Politics
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
C: Understanding the Institution
A: Personal background
A: Character, Values, Beliefs, Talents
A: Personal Background
A: The Researcher
C: Understanding the Institution
B: MD Anderson Culture
C: Evolution of Career
C: This is MD Anderson
C: Education at MD Anderson
D: On Research and Researchers
D: On Education

Dr. Hortobagyi talks about his fellowship in Developmental Therapeutics (DT, ’74 – ’75), beginning with a discussion of the “serious political split” between the Division of Medicine, which focused on patient care to the near-complete exclusion of research, and Developmental Therapeutics, which focused closely on research. Though Dr. Hortobagyi was interested in breast cancer, Developmental Therapeutics had no access to breast cancer patients, handled

via the Division of Medicine, and the head of the Fellowship Program, Ken McCready, assigned him to the leukemia service. Dr. Hortobagyi describes his busy days on this service, then recounts how he was assigned to Developmental Therapeutics' Outpatient Service. Dr. Hortobagyi describes the influence of Anthony Burgess (head of the Outpatient Clinic) and Jeffrey Gottlieb (Chief of Solid Tumors in Developmental Therapeutics).

Dr. Hortobagyi describes his interest in singing. He sang with the Cleveland Symphony while living in Ohio and he auditioned for the Houston Symphony Chorale and sang with them until 1979. He then explains that he was married in 1976 to Agnes, whom he met on a date arranged by his sister.

Dr. Hortobagyi describes some of the research he conducted while in the Department of Developmental Therapeutics. Dr. Jordan Gutterman recruited him to work on immunotherapy research using BCG (Bacillus Calmette-Guérin). He describes DT as a "tornado of intellectual activity" that nonetheless left him little time for innovation and creative thinking.

Dr. Hortobagyi states that his Fellowship in Developmental Therapeutics prepared him with the basic concepts of clinical research. He describes specific lessons he learned and compares his experience with the more structured training programs offered today.

Segment 07
Building Knowledge of Breast Cancer in the Division of Medicine
B: An Institutional Unit

Story Codes
A: The Researcher
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care
B: MD Anderson History
C: Mentoring
C: Leadership
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
C: Discovery, Creativity and Innovation
C: Professional Practice
C: The Professional at Work
C: Personal Reflections, Memories of MD Anderson
C: MD Anderson Past
A: The Researcher
B: Understanding the Institution
B: Multi-disciplinary Approaches
B: Institutional Mission and Values
C: MD Anderson Past
C: This is MD Anderson

Dr. Hortobagyi explains that he was focused almost exclusively on breast cancer when he finished the first year of his fellowship in Developmental Therapeutics, at which point he shifted to the Division of Medicine ('75 – '76). He sketches his research projects: preoperative chemotherapy for breast cancer; clinical trials for adjuvant treatment of breast cancer; developing a database of breast cancer patients. He also describes the vacuum of knowledge

about breast cancer among the four leaders of the breast service at that time, noting the main question in his mind, “Who was I going to learn from?”

Dr. Hortobagyi provides background on how George Blumenschein became head of the breast service, though he knew little about breast cancer, then provides a sketch of Blumenschein and of Nylene Eckles [M.D., Ph.D), who headed the service for many years.

Dr. Hortobagyi lists other individuals connected to the breast service who did teach him about breast cancer, despite the lack of immediate mentorship. Dr. Hortobagyi then describes how he organized biweekly case-review meetings for everyone involved in breast cancer to “bring together the discipline.” He explains that it took ten to fifteen years before everyone felt there was a benefit to this multi-disciplinary review of cases. He also describes the process required to encourage specialists to open up to other specialists. He also reflects on what enabled him to get people to work together.

Interview Session Two: 7 January 2013

Segment 00B
Interview Identifier

Segment 08
Discovering the FAC Regimen for Metastatic Breast Cancer
A: The Researcher

Story Codes
A: The Researcher
B: MD Anderson History
A: The Researcher
C: Discovery and Success
C: Patients
C: Cancer and Disease
C: This is MD Anderson
B: Understanding the Institution
B: Institutional Mission and Values
C: Healing, Hope, and the Promise of Research
A: Overview
A: Definitions, Explanations, Translations
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care

In this segment, Dr. Hortobagyi describes his research into drug combinations for the treatment of breast cancer. He begins by stating that no one discovers anything new in science, but rather integrates and builds on knowledge created by others.

Dr. Hortobagyi says MD Anderson was an exciting place when he arrived in 1974, and the field was progressing. He also notes that the original pioneers were at the peaks of their careers or retiring, making room for new researchers. He summarizes philosophical differences between

the Division of Medicine and Developmental Therapeutics, noting that the latter had visionary leaders who provided a unique environment for innovation. “Cancer was no longer a disease with no hope.“

Dr. Hortobagyi sets the context for his research by explaining that, at the time, important drugs had been discovered and needed a champion. His mentors were looking at chemotherapeutic agents, and he put them together and explored what would become the FAC combination treatment. Dr. Hortobagyi provides an overview of the drugs included in the regimen (Fluororacil, Adriamycin, Cyclophosphamide) and explains how they were selected and why that combination proved effective. The FAC regimen is still one of the most effective treatments against metastatic breast cancer.

Segment 09
Treatment for Locally Advanced Breast Cancer
A: The Researcher

Story Codes
A: The Researcher
C: Discovery and Success
C: Patients
C: Cancer and Disease
C: This is MD Anderson
B: Understanding the Institution
B: Institutional Mission and Values
C: Healing, Hope, and the Promise of Research
A: Overview
A: Definitions, Explanations, Translations
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care

Dr. Hortobagyi explains that at the same time that he was working on the FAC regimen (Fluorouracil, Adriamycin, Cyclophosphamide), he was also influenced by one of his mentors, Jordan Gutterman, who was experimenting with immunotherapy. Dr. Hortobagyi added BCG (Bacillus Calmette-Guérin) to the FAC regiment. Though unsuccessful, this study opened a new path, as it revealed that a patient’s baseline immune status determined her responsiveness to chemotherapy. Dr. Hortobagyi explains how this observation led him to look at locally advanced breast cancer (LABC), a disease that required extensive surgery and radiation for little effect on patient survival. (MD Anderson was seeing 300-400 cases per year and still sees many more cases than other cancer institutes: Dr. Hortobagyi explains what causes this disease and why it is so much more prevalent in the South.) Dr. Hortobagyi also observes that medical oncology was not respected in the seventies, but in the case of LABC, they relented. Studies were begun using the FAC regimen for LABC and also inflammatory breast cancer. The multidisciplinary regimen involved the drug regimen, surgery, then chemo therapy. Dr. Hortobagyi explains that 90% of patients had an objective response, with 10% showing a complete response. Patients were less disfigured and showed a much greater survival rate.

Segment 10
A Great Step for MD Anderson: Building Multidisciplinary Teams
B: Building the Institution

Story Codes
B: Critical Perspectives on MD Anderson
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
B: Institutional Mission and Values
C: MD Anderson Past
B: Controversy
D: On Research and Researchers
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care
C: Professional Practice
C: The Professional at Work
C: Collaborations
A: The Administrator
D: On Research and Researchers
D: The Healthcare Industry
D: Fiscal Realities in Healthcare
B: Beyond the Institution
D: Global Issues –Cancer, Health, Medicine

Dr. Hortobagyi begins this segment by stating that, in 1975, he was disillusioned by the lack of collegiality at MD Anderson, and so he invited individuals from many disciplines (including Developmental Therapeutics) to discuss cases, explain, their different perspectives on treatment, and collectively determine the best combination and order of measures. Slowly, he notes, they were able to build mutually respectful teams. He describes some of the clinical trials that emerged from the collaborations. Dr. Hortobagyi affirms that this interdisciplinary work represents one of the greatest steps forward at the institution, one that created team work twenty years before the creation of the official multidisciplinary breast center.

Dr. Hortobagyi next explains that, in the seventies some leaders at MD Anderson considered randomized clinical trials immoral because they would withhold from some patients therapies believed to be more effective than what was in existence. Dr. Hortobagyi himself believes that clinical trials are an important tool for medical science. He sketches the development of thought regarding ethics and randomized trials and explains other reasons why physicians do not believe that randomized trials are necessary. He observes that that oncology is “light years ahead” of the rest of medicine in accepting their value. He tells a story that demonstrates how radiology does not see the benefit; he also notes that there are no controlled trials comparing, for example, proton therapy to conventional electron beam therapy. He sees a similar situation with the treatment options for prostate cancer, and states that it is “tragic” that there is a lack of evidence-based information for major decisions. Dr. Hortobagyi then compares the laboratory research scenario to the complex challenges characterizing clinical investigation of living human systems. He states that much of what physicians do has no basis in fact. He goes on to talk about the economic impact that such decisions can have. He compares the $1000 one might spend on adjuvant therapy to the $200,000 one can spend on a full regimen of neoadjuvant treatment, surgery, and chemo, noting that his group has done cost-benefit studies to insure the money on these treatments is well spent.

Dr. Hortobagyi points out that very expensive treatments cannot always be exported to other institutions. Randomized trials provide a way of determining how effective treatments are at each cost level and therefore provide a logical way of seeing incremental benefit. This provides

a sound basis for making decisions on which treatment methods to adopt for the greatest public benefit.

Dr. Hortobagyi explains that he is not a “purist” who insists that every point be demonstrated through randomized trials. He advocates the identification of basic questions and treatment options in each specialty and a strategy of comparing them via Comparative Effectiveness Research methods.

Segment 11
Adapting LABC Treatment for Stages 2 and 3 Breast Cancers
A: The Researcher

Story Codes
A: The Researcher
C: Discovery and Success
C: Professional Practice
C: The Professional at Work
C: Cancer and Disease
B: Understanding the Institution
B: Controversy
A: Overview
A: Definitions, Explanations, Translations
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care

Dr. Hortobagyi begins by explaining that the LABC (Locally Advanced Breast Cancer) treatment involved six months of chemotherapy, surgery, radiation, and treatment with hormonal Herceptin. His group then decided to expand the regimen to stage two and stage three tumors and they designed a national clinical trial comparing the regimen with a protocol that performed the surgery first. Dr. Hortobagyi explains that new regimen offered advantages even though the effects on the tumor were not statistically greater than with surgery first. He points out that it was not possible to do a randomized trial at MD Anderson in the seventies, and so the process of clearly demonstrating the regimen’s value was greatly prolonged. To explain why surgery was the last to participate in randomized trials, Dr. Hortobagyi mentions that a 1980 conference in Tuscon brought the discussion to a head when Dr. Chuck [Charles] Moertel (a proponent) debated the issue with Dr. J Freireich (an opponent). It was clear that most of the oncology community in the country supported randomized trials and that MD Anderson had to evolve. The NCI became involved and spoke to institution leadership about the need to initiate such trials and the culture of the institution changed accordingly.

Segment 12
From Adriamycin to Molecularly Designed Drugs
A: The Researcher

Story Codes
A: The Researcher
C: Discovery and Success
B: Devices, Drugs, Procedures
C: Discovery, Creativity and Innovation

C: Professional Practice
C: The Professional at Work
D: On Research and Researchers
D: The History of Cancer Research and Care

Dr. Hortobagyi explains that he was the first to introduce Adriamycin into adjuvant therapy, responding to the fact that many patients were referred to the breast service after surgery (though MD Anderson surgeons were not referring patients to them). Adriamycin was combined with the FAC therapy and accepted as a standard of care by the 1990s. MD Anderson was also the first institution to report that Taxol was just as effective as Adriamycin when used in the FAC regimen and it was acceptedas a new standard. His group then worked with Taxotere, which was demonstrated effective. Research in the eighties was frustrating and his group tested about forty drugs, with little to show for it. He talks about the process of drug development and notes that the community ran out of ideas for a time.

During this same period there was a move to more molecularly designed chemicals as well as the discovery of oncogenes, tumor suppressor genes, and a burst of enthusiasm for the human genome project. This fertile scenario led to the development of the major targeting agents such as Herceptin.

Segment 13
The Breast Cancer Research Group –Bringing Together Clinicians and Basic Scientists
A: The Administrator

Story Codes
A: The Researcher
B: Beyond the Institution
B: Institutional Mission and Values
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care
C: Professional Practice
C: The Professional at Work
C: Collaborations
B: Controversy
B: MD Anderson Culture

Dr. Hortobagyi explains that frustrations with research motivated him to accept a 1990 invitation from Dr. James Cox [Oral History Interview] to pull together a comprehensive group to study breast cancer. The Breast Cancer Research Group linked radiologists, surgeons and other specialists, as well as basic researchers interested in the disease. This request came at a time that the administration wanted to enhance the quality of research and to make it more collaborative and translational. Dr. Hortobagyi also notes the growing suspicion, at the time, that basic scientists would spend their time doing research for its own sake, without necessarily linking their research questions or discoveries to patient care. He explains that the process for awarding grants prevented scientists from taking bold steps or thinking outside the box. Dr. Hortobagyi describes the challenges of getting the specialties to work together. He describes setting up talks with luminary scientists and researchers –for only very low turnout. Laboratory scientists communicate differently than clinical specialists, he notes. Their days are also organized very differently, which made it difficult to find a time when everyone could gather. In

addition, the institution offered no incentives for communication across specialty lines –and he says this is still true. He offers observations on Dr. Ronald DePinho's support of basic scientists.

Segment 14
An Initial Translational Research Project: A Drug to Attack HER2-positive Breast Cancer
A: The Administrator

Story Codes
A: The Researcher
C: Professional Practice
C: The Professional at Work
C: Collaborations
D: On Research and Researchers
D: On Pharmaceutical Companies and Industry
B: Industry Partnerships
B: Devices, Drugs, Procedures
B: The Business of MD Anderson
C: Portraits

In this segment, Dr. Hortobagyi talks about his first experience with translational research. He explains that while leading the Breast Cancer Research Group, he identified individuals with a collaborative mindset (Robert Bast, Gordon Mills, Mien Chie Hung [Oral History Interview]) and undertook translational research for the first time. They had success addressing resistance to chemotherapy with gene therapy, but the field progressed and the results were not competitive. Combining forces with Mien Chie Hung, they then used the gene product E1-A to kill cells specific to HER2-positive breast cancer. The procedure worked, but they lacked resources to take the product to the drug phase.

Dr. Hortobagyi then explains that, at the time, individuals and institutions had little understanding about the legal issues attached to intellectual property and about raising money for development.

Dr. Hortobagyi explains that John Mendelsohn changed the Development Office and helped fund drug development. He also hired legal expertise so the intellectual property of individuals and the institution would be protected. Dr. Hortobagyi sketches the costs of drug development, noting that one can only develop a drug by partnering with industry and one "can't do that without going to bed with the devil."

Segment 15
The Next Phase of Gene Therapy Research and Funding from the Breast Cancer Research Foundation
A: The Researcher

Story Codes
A: The Researcher
C: Professional Practice
C: The Professional at Work
C: Collaborations
D: On Research and Researchers

B: Devices, Drugs, Procedures
D: Business of Research
B: Philanthropy, Fundraising, Donations, Volunteers
D: Understanding Cancer, the History of Science, Cancer Research

In this segment, Dr. Hortobagyi describes the next phase of his gene therapy research. He begins by explaining that the funding organization, the Breast Cancer Research Foundation, was started by Evelyn Lauder when she was diagnosed with breast cancer. Dr. Hortobagyi and others were asked to be scientific advisors. The Foundation brought together powerful women who raised a great deal of money, a lot of which came to MD Anderson. The gene therapy project was also funded by a SPORE grant. Dr. Hortobagyi sketches the state of the gene therapy projects. He explains why it was difficult to secure NCI funding for the E1-A project then discusses why it is so difficult to deliver a gene product. He tells the story of a University of Pennsylvania project in which some children died from gene therapy, an event that helped turn the NCI away from funding this kind of research. He then describes how the Breast Cancer Research Foundation uses different criteria than the NCI to award money to high-risk projects. The BCRF is now funding such areas of research as cancer vaccines, early genetic screening, the development of targeted agents, and diagnostic tests.

Interview Session Three: 23 January 2013

Segment 00C
Interview Identifier

Segment 16
Studies of Pro-Apoptotic Molecules: Translational Research and Thinking Outside the Box
A: The Researcher

Story Codes
A: The Researcher
C: Discovery, Creativity and Innovation
C: Professional Practice
C: The Professional at Work
D: On Research and Researchers
D: The History of Cancer Research and Care
A: The Administrator
B: Beyond the Institution
A: Career and Accomplishments
B: Institutional Mission and Values
C: Discovery, Creativity and Innovation
C: Patients, Treatment, Survivors
D: The History of Cancer Research and Care
D: The History of Health Care, Patient Care
D: Global Issues –Cancer, Health, Medicine

In this segment, Dr. Hortobagyi talks about two related studies of pro-apoptotic proteins (which instruct cancer cells to commit suicide) and reflects on the kind of creative thinking that leads to

great discoveries. He begins by explaining how he and Dr. Mien Chie Hung decided to submit a "truly different" proposal to the Breast Cancer Research Foundation (BCRF), one based on the observation that a gene product from Adenovirus-5 and E1A could cause HER2 positive cancer cells to commit suicide. This research proposal was partially funded by the BCRF and also by a SPORE grant. This gene therapy successfully transformed HER2 positive cancer from the most difficult to the easiest disease treated and has been applied to head and neck and other cancers. The next project was based on the observation that the Bik protein in the BCL-2 family was pro-apoptotic. Dr. Hung produced the genetic variant, BikDD, with an enhanced destructive effect.

Next Dr. Hortobagyi describes the new view of cancer that emerged in the 1990s as a result of discoveries in cell biology, and how this has influenced research. In the early 90s, he explains, physicians were working with ideas that had been known in the basic sciences at least ten years earlier. Dr. Hortobagyi explains that through his conversations with Dr. Mien Chie Hung, it began to dawn on both of them how to transport the basic science information into a new context. Dr. Hortobagyi notes that it's "an epiphany" to take a laboratory observation and then visualize its possible applications in clinical settings. He also connects his ability to think in these translational terms to his interest in setting up multi-disciplinary teams. He then explains an "inherent contradiction of translational research": despite the prevailing wisdom that scientific thinking is disciplined and logical, truly important discoveries require that you become undisciplined and think outside the box. Traditional thinking leads back to existing knowledge.

Segment 17
Thinking Outside the Box to Stage the World Summit Against Cancer for a New Millennium
A: Professional Service beyond MD Anderson

Story Codes
A: The Administrator
B: Beyond the Institution
A: Career and Accomplishments
B: Institutional Mission and Values
C: Discovery, Creativity and Innovation
C: Patients, Treatment, Survivors
D: The History of Cancer Research and Care
D: The History of Health Care, Patient Care
D: Global Issues –Cancer, Health, Medicine

To demonstrate thinking out of the box, Dr. Hortobagyi describes how he and Dr. Charles Jacquillat organized an important millennium event for the Congress of Anti-Cancer Therapy (formerly the International Congress of Neoadjuvant Therapy). He describes the "crazy" way of free-associating that led them to envision (and successfully plan) the World Summit Against Cancer for a New Millenium held in Paris. The event also introduced the *Charter of Paris*, a list of patients' human rights. Between fifty and sixty nations sent delegates to sign the Charter; MD Anderson president John Mendelsohn went to Paris to participate in the signing, and there is a photograph of the document in the Rose Building on MD Anderson's main campus. Dr. Hortobagyi also explains the purpose of the Charter –to draw attention to the fact that in most countries, cancer patients are undertreated, ill-treated, or ignored. He notes that the UACC adopted their Charter and that in 2012 the World Health Organization adopted the Charter as a basis for its continued efforts to encourage governments to improve patient care.

Segment 18
Therapy to Block Angiogenesis
A: The Researcher

Story Codes
A: The Researcher
C: Discovery, Creativity and Innovation
A: Overview
A: Definitions, Explanations, Translations
C: Professional Practice
C: The Professional at Work
D: On Research and Researchers
D: The History of Cancer Research and Care
D: On Pharmaceutical Companies and Industry

In this segment, Dr. Hortobagyi talks about research on anti-angiogenesis therapies funded by The Breast Cancer Research Foundation. He begins, however, by noting that once he had embraced the understanding that breast cancer is multiple diseases, rather than a single pathological phenomenon, he realized that other colleagues and basic scientists needed to undergo the same "epiphany." "We all needed to learn more and go beyond our slice of the world" in order for diagnosis and therapy to progress. Dr. Hortobagyi then describes his work on anti-angiogenesis therapy. He defines angiogenesis and lists MD Anderson faculty who have contributed to understanding the process. He then describes early work with Endostatin and Angiostatin, early anti-angiogenesis agents, which never provided adequate results because of their very short half-life. Work on the subject revived when Genentech developed Avastin (bevacizumab), a drug that caused tumor regression, but that also created serious side effects. Dr. Hortobagyi next explains that, with the revival of the field, he and Dr. Hung developed the Endo-CD project (Endostatin-cytosine deaminase fusion protein)[1] which was similar to gene therapy in that it involved molecular manipulations *in vivo*. He and Dr. Hung worked with molecular processes to make the earlier drug, Endostatin, more effective. He describes the chemical construct they created: a chemical compound with no activity was linked to Endostatin and used as a vehicle to deliver Endostatin directly to tumor vasculature. Another activating agent was then administered to activate Endostatin. With the drug so locally attached to the tumor, side effects were minimized.

Dr. Hortobagyi notes that during work on EndoCD, he was also conducting clinical trials on Avastin. He describes the disappointing results. He notes that the pharmaceutical industry had looked to the drug as a potential "cash cow," and he explains how the drug became a political issue in insurance reimbursement.

Segment 19
A New View of Breast Cancer and Research on HER2 Positive Breast Cancer
A: The Researcher

A: The Researcher
C: Discovery and Success
A: Overview
A: Definitions, Explanations, Translations

[1] See http://www.ncbi.nlm.nih.gov/pubmed/21610170, date of access, 24 January 2013.

C: Discovery, Creativity and Innovation
C: Professional Practice
D: The History of Cancer Research and Care

In this segment, Dr. Hortobagyi talks about the next stages for breast cancer research. He first provides a snapshot of how breast cancer was viewed ten to fifteen years ago. He then traces the many forces that came to together to revolutionize the understanding of the disease, which is now seen as many chemically and genetically unique diseases, rather than a single phenomenon. The factors Dr. Hortobagyi lists are: a new understanding of the significance o estrogen receptors in cancer cells, the completion of the Human Genome Project, the completion of gene expression profiles of various breast cancers, investments by the government in the 'war on cancer,' and the pharmaceutical industry's investment in cancer treatment drugs. By the mid -2000s, all of this work had led to an explosion of knowledge about the significance of breast cancer subtypes.

Dr. Hortobagyi then talks about his work on HER2 positive breast cancer. He notes that through his work on Herceptin, he was involved in advancing the understanding of this breast cancer subtype. He describes how he organized yearly by-invitation meetings of researchers: this event led to many collaborations that advanced the field. Dr. Hortobagyi then explains that his role in research changed. With more involvement in administration, he did more coordinating and facilitating of research for others. He notes his involvement in national organizations. He explains that in 2005 he joined the South West Oncology Group and became chair of the breast cancer committee, responsible for coordinating research. Dr. Hortobagyi comments on how important such organizations are for extending MD Anderson's reach and to generate enough participants in clinical trials.

Segment 20
Breast Cancer Service at MD Anderson in the Late Seventies
A: The Administrator

Story Codes
A: The Administrator
B: MD Anderson History
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
B: Growth and/or Change
C: Understanding the Institution
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care

In this segment, Dr. Hortobagyi talks about the state of breast cancer services at MD Anderson and in the country in the late seventies. He begins explaining the position of the Breast Cancer Service within the institution, lists his colleagues, then notes that the non-surgical treatment of breast cancer was evolving in the seventies (and eighties). Dr. Aman Buzdar shared Dr. Hortobagyi's commitment to research, and they both learned how to treat breast cancer via an "empirical" process that was common in institutions at that time, when medical oncology was not yet a specialty and institutions lacked formal training programs of the type common today. In general, health care institutions were less structured than they are today, and researchers had much more freedom.

Segment 21
The Breast Cancer Service: From Section to Department
B: Building the Institution

Story Codes
A: Professional Path
A: Contributions to MD Anderson
A: Career and Accomplishments
B: Growth and/or Change
B: MD Anderson History
C: Leadership
C: The Administrator at Work
D: On Leadership

In this segment, Dr. Hortobagyi first compares the formal processes by which Section Chiefs are recruited today with the informal process by which Dr. Hortobagyi first came to serve as Alternative Section Chief of the Breast Medical Oncology Service under Dr. George Blumenschein. Dr. Hortobagyi became Chief in 1984 when Dr. Charles LeMaistre removed Dr. Blumenschein. Dr. Hortobagyi then explains how, in 1992, institutional politics drove the re-classification of the Breast Medical Oncology as a Department.

Dr. Hortobagyi explains how his understanding of his administrative role evolved, beginning with his role as Alternative Section Chief, when he was “so junior that he didn’t know much.” Dr. Hortobagyi explains that as he matured, he came to understand that he had his own ideas of how work should be organized. He lists some of his first contributions to the Section/Department: he recruited the first three research nurses to the service; he and Dr. Benjamin worked with the Texas legislature to pass a bill in support of physicians’ assistants and nurse practitioners; he was the first to recruit nurse practitioners; he recognized the need to grow the department to grow the number of grants and research support and he visited other institutions to better understand what a breast center should look like. He describes his “gradual awakening” to the idea that the breast center should be re-thought from a patient-centered perspective. He then strengthened the Department to support clinical research, moved on to build up the educational mission of the Department, and finally integrated translational research into the Department and into the process of recruiting new faculty.

Interview Session Four: 28 January 2013

Note: The recorder is turned on during a conversation in progress. The notes appear below.

Before the recorder is turned on, Dr. Hortobagyi describes a leadership course [Innovations in Breast Cancer] developed around 1995 because, as he explains, medical education does not provide physicians with necessary leadership skills. Funds were secured from a pharmaceutical company to run the course twice per year (and then once per year) for ten years. For each session, eight to ten faculty with administrative responsibilities were selected to go through a three-day course; each class had international representation, including professionals from Europe and North America, Asia and other regions. The curriculum included discussions of team-building, debate, and effective and dispassionate argumentation. Dr. Hortobagyi lists some individuals who went through the course, including Francisco Esteva from MD Anderson and professionals from many other institutions.

Dr. Dr. Hortobagyi then explains how leadership vacuums become apparent and notes the ineffective ways in which leaders are often identified in institutions. Dr. Dr. Hortobagyi notes that MD Anderson hires “wonderful people” then stresses that the next step is to train them to put together a plan for professional growth. A professional needs to know how to move strategically from the goal “I’m going to cure breast cancer” to identify “all the hundreds of steps” required to achieve it.

Dr. Dr. Hortobagyi then speaks more about the Innovations in Breast Cancer program.

Dr. Hortobagyi finds the name of the leadership program he developed, “Innovations in Breast Cancer.” He then talks about how the program folded, noting funding and the fact that he had to leave when he became involved in ASCO. He says that “committees stand on the back of a few people, relying on a dynamic person or persons.”

Today, Dr. Hortobagyi says, he Chairs the Breast Cancer Committee in SWOG, and he describes how he tries to get people involved in activities. Many of the ideas for research studies that go to trials are his brainchildren, he says, observing that groups can be passive. For a program to succeed, there must be a passionate champion.

Dr. Hortobagyi reflects on his own leadership style and says that he is a consensus-builder. He notes that he loves to read history and lists some leaders from his readings. They all had a sense of history and a belief in their ability to move things forward, he explains, and he believes he has these qualities himself.

He says he has never been comfortable in the limelight and gives an alternative example of several past ASCO presidents who couldn’t give up the idea that they were president after their tenure was over. Dr. Hortobagyi himself is delighted when the group is acknowledged.

Dr. Hortobagyi then turns to the history of the Dept and Division of Breast Medical Oncology. Bringing the different components of breast cancer treatment together was a difficult management process that involved a paradigm shift to create a patient-centered model of care. At the time, services were separated. No shared clinic time with other

specialists (surgery, radiation therapy). The bi-weekly case assessment meetings underscored the need for a different approach: everyone was in the same room and perspectives were changed on how patient treatment should move forward.

From this came **the idea for a breast center, an entity that didn't exist at the time.** At this point, Breast Medical Oncology moved to the Rose Building (the Main Building) and the Lutheran Pavilion. They contributed to the design discussions during the planning and requested physical efficiencies, separate space for research, and to locate the breast surgical group adjacent to Breast Medical Oncology (that didn't happen).

The next opportunity to develop Breast Medical Oncology came when they outgrew that space just at the time the Mays Clinic was constructed. They had a group based on a SPORE and began to **bring the breast cancer community** together. Dr. Dr. Hortobagyi explains how this was all laid out in the new plan.

Segment 22
Creating a Patient-Centered Breast Service
B: MD Anderson Past

Story Codes
C: Patients
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
B: Growth and/or Change
A: The Clinician
C: Understanding the Institution
B: The Business of MD Anderson
B: The MD Anderson Brand, Reputation
C: Professional Practice
C: The Professional at Work
C: The Clinician at Work
D: On Care
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care

Dr. Hortobagyi notes that there was huge resistance, at first, to integrating all services associated with the treatment of breast cancer. He then talks about what convinced people this was the best move, beginning with the case of Eva Singletary, a patient who was literally followed throughout her treatment, beginning with the moment she set foot in MD Anderson for a diagnosis. This exercise revealed that the institution was organized in a bureaucracy centered, rather than a patient centered, scheme. Dr. Hortobagyi explains that there was also a rise in patient load and a concurrent rise in MD Anderson's reputation. MD Anderson faculty were also publishing important research, which drives growth and the institutions' reputation, Dr. Hortobagyi says. He then goes on to explain how MD Anderson discoveries have indirect effects on patient referrals.

Dr. Hortobagyi explains that, when the new Breast Center was constructed, there was a "retrenchment" as physicians were afraid that they would give up their own territory in a situation based on collaboration. A decade later, the Breast Service is based on a mentality of sharing and shifting traditional ideas of how a service should be run.

Dr. Hortobagyi gives the example of making room utilization more efficient, then explains that in the new “pod” layout of the Breast Center, it is easy to find a specialist for a consultation, sharing weeks of works ups.

Segment 23
Regulations on Clinical Trials and New Research Projects in Breast Medical Oncology
A: The Administrator

Story Codes
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
B: MD Anderson Culture
B: Growth and/or Change
A: The Clinician
C: Understanding the Institution
B: The Business of MD Anderson
B: The MD Anderson Brand, Reputation
C: Professional Practice
C: The Professional at Work
C: The Clinician at Work
D: On Care
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care

Dr. Hortobagyi begins this segment by talking about how clinical trials helped build a multi-disciplinary mentality in Breast Medical Oncology. He then observes that increasing costs and institutional/national regulations on clinical trials holds back research efforts. He then explains how he developed the research infrastructure in Breast Medical Oncology, beginning with his development of clinical trials with FAC and inflammatory breast cancer. Pharmaceutical companies provided drugs for these trials and other resources. Dr. Hortobagyi describes the different cost components of a budget for a drug trial (nurses, data managers, etc.). As the numbers of trials increased over time, he explains, research simultaneously became more complex, and he gives the example of his first research nurse, who could handle eight or nine clinical trials, while today many more individuals are involved.

Dr. Hortobagyi then gives an overview of regulatory practices governing trials, which also add to the complexity of research. He notes that a few people decided to be “slippery or dishonest,” and their actions resulted in a burden of regulation for everyone that slows research. He also describes how regulation has increased the cost of health care and absorbed the efforts of the best investigators, tapping their energy for tasks that add no value to their research.

Dr. Hortobagyi describes how difficult it was to set in place all the pieces required for an optimal research structure, underscoring how important it was to strategize for resources, efficiency, and to work within budget constraints. He returns to subject of physicians who lack leadership training, and who need these skills to manage complex initiatives. Dr. Hortobagyi gives an overview of the tasks he managed: providing the highest quality of care; insuring that all faculty and staff work at their highest level; influence the development of the Breast Center; increase research productivity, coordinate research activities, ensure that research breaks even; foster careers; educate the next generation.

Segment 24
Mentoring, Career Support, and Education in Breast Medical Oncology
A: The Administrator

Story Codes
A: The Administrator
C: Professional Practice
C: The Professional at Work
C: Leadership
C: Mentoring
D: On Research and Researchers
D: On Leadership
D: On Mentoring
B: Building/Transforming the Institution
B: Institutional Processes
C: Understanding the Institution
D: On the Nature of Institutions

In this segment, Dr. Hortobagyi discusses his efforts to support faculty careers via mentoring and administrative decisions. He begins by noting that the grant application process can be used strategically to encourage faculty to work together.

Dr. Hortobagyi notes that it is very challenging to lead bright people, and a leader must empower then and build on their strengths. He compares the "one size fits all" approach he took many years ago to his newer, nuanced approach of recognizing people's different strengths. He notes how he developed listening skills. He gives an example of how he continuously challenges people in positive ways so they can stretch, and underscores how important it is for a leader to be transparent about the purpose and goals of decisions to reduce conflict and increase faculty/staff buy in.

Dr. Hortobagyi gives the example setting expectations for faculty on clinical contracts versus those on 75% research contracts. Every month a report shows how much income a faculty member generates. Transparency is important to motivate faculty and to guide them through tenure and promotion hurdles.

Leadership principles are the same in all organizations, Dr. Hortobagyi says. However it is especially difficult to lead in academic institutions. Dr. Hortobagyi explains why medical academics are "fiercely independent."

Segment 25
Education in Breast Medical Oncology
A: The Administrator

Story Codes
A: The Administrator
A: Personal Background
A: The Educator
A: The Leader
A: The Mentor
B: Education

C: Education at MD Anderson
D: On Education
D: On Mentoring
C: Education at MD Anderson
C: Professional Practice
C: The Professional at Work
C: Collaborations
C: Leadership
C: Mentoring

Dr. Hortobagyi explains that medical education includes two parts: the technical information a physician needs to practice and learning that comes via mentoring. Dr. Hortobagyi describes good mentoring and the kinds of career questions a good mentor can help a fellow or young faculty member confront.

He then discusses principles of research mentoring and how it is connected to funding of medical education after the M.D. He notes that a fellow has six or more years of training after the M.D., but is "still green behind the ears," a situation in which mentoring is key for preserving quality of care and research.

Dr. Hortobagyi ends this session with the observation that he himself did not have strong mentors, but he observed how strong mentorship influenced the careers of many of his colleagues.

Interview Session Five: 15 March 2013

Segment 00E
Interview Identifier

Segment 26
A Brief History of Breast Medical Oncology
B: An Institutional Unit

Story Codes
B: MD Anderson History
B: MD Anderson Culture
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
B: Growth and/or Change
B: The MD Anderson Brand, Reputation
B: Institutional Mission and Values
C: Giving Recognition

In this segment, Dr. Hortobagyi begins an overview of the evolution of Breast Medical Oncology and the Breast Center. He recalls that in the early days, the Department needed to communicate better to develop patient care. As an example, he points out that scheduling sequential consults with specialists could take weeks, greatly slowing progress on a patient's

treatment plan. Bi-weekly meetings were established with all related specialties to aid communication and come up with a majority view of what needed to be come. Dr. Hortobagyi explains the specialties represented and how some individuals resisted collaboration on treatment plans. He notes that it took years for difficulties to smooth out, but that patients were happy and grateful. Dr. Hortobagyi says that the patients had figured out that it was good to get their doctors talking to one another. The multidisciplinary meetings were an educational tool and an instrument for cultural change in the department, he observes. Surgeons had been in charge of managing breast cancer, but slowly imagers and breast medical oncologists made inroads and with good results. He also says that conflict over treatment plans could give rise to clinical trials to prove a point (e.g. demonstrating the benefits of different types of surgery and of integrating chemotherapy at different stages of treatment and in combination with radiotherapy and immunotherapy).

Dr. Hortobagyi describes the successes that came from multidisciplinary discussions of treatment. “We were leaders in breast cancer management,” he says. “Everything we proposed and developed has survived the test of time.”

Segment 27
An Overview of Research Issues
A: The Researcher

Story Codes
B: Controversy
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
B: Growth and/or Change
B: Research, Care, and Education in Transition
A: The Clinician
A: The Researcher
C: Professional Practice
C: The Professional at Work
D: On Research and Researchers
D: The History of Cancer Research and Care
D: Ethics

Dr. Hortobagyi explains that recruitment of research nurses and research managers was a key to strengthening the research mission of Breast Medical Oncology. He then moves to a related discussion of conflict of interest, noting monetary dimensions of conflict of interest are only “the tip of the iceberg.” He explains that a Principle Investigator has a vested interest in the success of a clinical trial. The research nurse thus serves as unbiased party to collect and manage data. He explains the decision not to permit principle investigators to look at data before all the results of a trial are in.

Dr. Hortobagyi recalls the controversies at MD Anderson regarding the running of clinical trials, which some researchers believed were unethical. The discussions revealed, however, how difficult it is for a researcher to be unbiased and that the process of generating data needed management to insure that results were unimpeachable.

Dr. Hortobagyi notes the reasons why scientific misconduct was not discussed in the 70s and 80s.

Segment 28
Physician Extenders and a View of the Coming Physician Shortage
A: Overview

Story Codes
A: The Researcher
A: The Administrator
B: Beyond the Institution
B: MD Anderson and Government
D: Cultural/Social Influences
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care
A: Contributions
A: Activities Outside Institution
A: Career and Accomplishments

Dr. Hortobagyi explains that he worked with Dr. Robert Benjamin to encourage the Texas Legislature to pass laws enabling the use of physician extenders, then notes that this profession will play an increasingly important role as oncology moves forward. He then moves to a related subject: the shortage of physicians in chronic illnesses. Dr. Hortobagyi explains that he became a 'pseudo-expert' in the area when he was president of the American Society of Clinical Oncology and conducted a study which projected that, by 2020, there available physicians would only be able to cover 2/3 of the hours required by patients for treatment. He then lists the causes of this projected shortage and what is going to be result. He observes that Medicare patients are already seeing the effects, as they are having difficulty locating doctors. He also notes that, in the aftermath of the study, little has been done to ease the shortage. "How we deal with that will define us as a society," he says, and notes the other diseases that will experience the same shortfall as cancer.

Segment 29
The Evolution of Breast Medical Oncology and the Breast Center
B: An Institutional Unit

Story Codes
C: Understanding the Institution
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
B: Growth and/or Change
B: Critical Perspectives on MD Anderson
B: Institutional Processes
A: The Clinician
C: Professional Practice
C: The Professional at Work
C: Collaborations
B: Institutional Mission and Values
D: On Care
C: Leadership
C: Mentoring

In this segment, Dr. Hortobagyi continues to sketch the evolution of the Breast Service. He describes first, tiny Breast Clinic on the ground floor of the Bates Freeman Building, where about 800 patients per year were seen. From there, the Clinic moved (to where the Anderson Network offices are now located), then to the Rose building, then to the Faculty Tower. The faculty made a real effort to influence the design of the clinic when it moved to the 6th floor of the Rose Building. Dr. Blumenschein developed a list of what was needed, but he was unfortunately ignored, though they "got more real estate" and faculty offices were next to the Breast Clinic. Many more advances were made when the Clinic moved the new Cancer Prevention Building. Dr. John Mendelsohn requested input from administrators on design requirements, and Dr. Hortobagyi notes that his was a fairly public and transparent process. Dr. Hortobagyi wanted all functions located in the same area: offices, clinics, surgical suites, radiation therapy, and laboratory research related to breast cancer. (Not all of this was accomplished.)

Dr. Hortobagyi describes the "shift in your mind" that takes place when one adopts a logic of multi-disciplinary care for a service. He describes the importance of collegiality and "geography" for overcoming the "separate republics" that prevent physicians from working together. He reviews what is needed to get people working together, including the development of translational research projects and recognition of the importance of imagers and pathologists to what breast medical oncologists do. Dr. Hortobagyi notes that the Clinic was able to implement multidisciplinary care effectively for the first time when it moved to the Cancer Prevention Building.

Dr. Hortobagyi next notes that the practice of multi-disciplinary care would evolve if medical schools laid the foundation for inter-specialty interaction. He explains how MD Anderson's compensation system fostered interdisciplinary. He comments on the current administration (of Dr. Ronald DePinho), stating that decisions have been made that will change MD Anderson culture to the detriment of research and education.

Segment 30
Stepping Down as Chair of Breast Medical Oncology
A: The Administrator

Story Codes
C: Evolution of Career
A: Professional Values, Ethics, Purpose
B: Critical Perspectives on MD Anderson
D: The History of Health Care, Patient Care
A: Character, Values, Beliefs, Talents
A: Personal Background
A: Professional Path
A: Inspirations to Practice Science/Medicine

In this segment, Dr. Hortobagyi explains the issues surrounding his decision to step down as Chair of Breast Medical Oncology (effective on 31 August 2012). In part, he realized he no longer wanted the leadership position, he explains. In addition, cultural changes at MD Anderson have created a shift so that business people, instead of physicians and scientists, now lead the institution. He talks about how medicine in general is "in a profound state of disarray," and these factors dulled his enthusiasm, as MD Anderson is currently asking "how

can we function optimally within this (dysfunctional) system," not "how can we change the system." He also notes that leaders should not remain overlong in their positions. He lists some of the personal interests he would like more time to pursue (music, literature, poetry, history) and also notes his interest in medical policy issues. Finally, he observes that his professional life took precedence in the early part of his career, and now his private life is perhaps more important to him.

Segment 31
Contributions to International Policy Issues
A: Professional Service beyond MD Anderson;

Story Codes
A: Contributions
A: Activities Outside Institution
D: Global Issues –Cancer, Health, Medicine
C: Professional Practice
C: The Professional at Work
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care
C: Patients, Treatment, Survivors

Dr. Hortobagyi begins this segment on his work with international organizations by explaining why he has such firm professional connections in Hungary and Europe as well as in North and South America, and Latin America. He then talks about the Breast Health Global Initiative (which he co-founded) and a major project: developing guidelines for the treatment of breast cancer, taking into account the realistic availability of resources. Dr. Hortobagyi explains, for example, that in some areas of Africa, a physician may perform a mastectomy as a diagnostic procedure, and the samples must be sent to far-off labs for study, with results coming back after six months. Dr. Hortobagyi explains how the BHGI set about creating guidelines for minimal levels of care for breast cancer where possibility for care is extremely limited. Methods include using physician extenders as well as training women from the local community to give care. The Initiative has also developed research projects to study how to implement the guidelines. Guidelines were developed, discussed, published, and then republished in three different versions after more public discussion. Dr. Hortobagyi describes how fascinating it has been to participate in this project and he hopes it will force governments to rethink their obligations to their populations.

Segment 32
The MD Anderson Presidents
B: Key MD Anderson Figures

Story Codes
C: Portraits
C: Funny Stories
C: Personal Reflections on MD Anderson
C: Human Stories
C: Offering Care, Compassion, Help
C: This is MD Anderson
B: MD Anderson History

B: Building/Transforming the Institution
B: Growth and/or Change
B: Obstacles, Challenges
B: Controversy

Dr. Hortobagyi first gives an overview of R. Lee Clark and sketches a portrait of MD Anderson in 1974, when Dr. Clark recruited him. Dr. Hortobagyi tells a story to show how solicitous the Texas Legislature was of R. Lee Clark's requests for money. He goes on to talk about the many good recruitments Dr. Clark secured as well as his incredible vision. Dr. Hortobagyi then describes the situation in Texas in 1941, when Dr. Clark conceived of the new cancer center, then describes his administrative style. Dr. Hortobagyi recalls his fellowship period and notes that Dr. Clark always knew who he was and remembered the project he was working on. Dr. Hortobagyi also remembers that fellows would sleep on a couch in Dr. Clark's office, and he'd nudge them out in the morning when he came int.

Dr. Hortobagyi praises Dr. Clark's practice of developing international connections. As a result, he says, MD Anderson trained many international students who became leaders in the global cancer community. Dr. Hortobagyi then shifts to Charles LeMaistre, offering background on his research, then noting that he was a more reserved administrator, with primary skills in political interactions with the Legislature and with higher education. He talks about the difficult years of Dr. LeMaistre's tenure, when about two thousand employees were laid off, "dampening the spirit of the institution.

He then shifts to John Mendelsohn, who was able to "lift the institutions spirits in an hour" by going on record and saying that MD Anderson was doing fine. Dr. Hortobagyi give some background on Dr. Mendelohn's administration, noting his fundraising skills, his innocence, candor and ability to talk to anyone. He describes him as "a communicator."

Dr. Hortobagyi then talks about the growth of the Development Office under Dr. Mendelsohn and his ability to recruit good people. He also notes that Dr. Mendelsohn "didn't have a mean bone in his body," which was a disadvantage when it came to making painful decisions. Dr. Hortobagyi offers an example of decision making about laboratory space that was held back because of this limitation. He also observes that Dr. Mendelsohn's administration was tarnished in the last years of his tenure and that he became more enclosed with his inner circle and lost touch with the faculty. Dr. Hortobagyi then shifts to Dr. DePinho, saying that he was a surprise choice, never having led a patient-care institution. Dr. Hortobagyi hopes that he picks up those skills and that the four missions stay in balance.

Segment 33
Fostering Collaboration and Collegiality
A: View on Career and Accomplishments

Story Codes
A: Career and Accomplishments
A: The Leader
A: Character, Values, Beliefs, Talents
A: Professional Values, Ethics, Purpose

In this segment, Dr. Hortobagyi explains that he is most gratified that he was able together a diverse individuals interested in breast cancer into a collaborative and collegial group. He

reflects on his own leadership style: a reluctant leader, but one that is good at organization and gets pleasure from seeing others grow. Dr. Hortobagyi lists some of his leadership principles. In closing, he says that it is wise to remember that one looks good because of others. He makes some comments on awards and notes that he is currently enjoying his “senior statesman” status.

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Gabriel Hortobagyi, MD

Session 1—November 30, 2012

About transcription and the transcript

This interview had been transcribed according to oral history best practices to preserve the conversational quality of spoken language (rather than editing it to written standards).

The interview subject has been given the opportunity to review the transcript and make changes: any substantial departures from the audio file are indicated with brackets [ ].

In addition, the Archives may have redacted portions of the transcript and audio file in compliance with HIPAA and/or interview subject requests.

Chapter 00A
Interview Identifier

Tacey Ann Rosolowski, PhD
0:00:00.0
I am Tacey Ann Rosolowski, and I am interviewing Dr. Gabriel Hortobagyi at the University of Texas MD Anderson Cancer Center in Houston, Texas. This interview is being conducted for the Making Cancer History Voices Oral History Project run by the Historical Resources Center at MD Anderson. Dr. Hortobagyi came to MD Anderson as a fellow in 1974 and formally joined the faculty in 1976. For many years he served as the founding chair of the Department of Breast Medical Oncology. He recently stepped down from that role and is now a professor in that department and also holds the Nellie B. Connelly Chair in Breast Cancer. He also heads the Breast Cancer Research Program. Am I correct about those current titles? Thank you. This interview is taking place in Dr. Hortobagyi's office in the Breast Medical Oncology Department in the Cancer Prevention Building on the main campus of MD Anderson. This is the first of two planned interview sessions, and today is November 30, 2012. The time is 12:50. So thank you, Dr. Hortobagyi, for devoting your time to this project. I appreciate it.

Gabriel Hortobagyi, MD
0:01:13.5
My pleasure. Thank you for inviting me to join this.

Interview Session: 1
Interview Date: November 30, 2012

Chapter 1
A: Personal Background
A Family Escapes to Colombia

Story Codes
Story Codes
A: Personal Background
A: Character, Values, Beliefs, Talents

Tacey Ann Rosolowski, PhD
0:01:16.9
Well it is really a pleasure. I really enjoyed doing background research for this particular interview, and I feel like I already have learned a lot about breast cancer, which I didn't know very much about before. So I am going to be asking you a lot of questions about a lot of different areas of your research, of course, and your role of building up the important institutional program in breast medical oncology. But I wanted to start with some personal questions about your own background. So I wanted to ask you to please tell me where and when you were born and where you were raised.

Gabriel Hortobagyi, MD
0:01:53.9
Very well. So I was born shortly after the end of World War II in the summer of 1946 in a little town in Hungary called Szarvas, which is in the southeastern part of Hungary. Budapest, where my parents had lived, had been severely bombed by the Russians and the allies, so my parents took refuge with my paternal grandmother in this smaller community. I was born there but didn't stay there very long. And then I spent my first ten years in Hungary. Of those I spent about three years in an internal exile camp or a concentration camp because my family was on the wrong side of politics during the communist era. And then in 1956 my family—my entire family—took advantage of the Hungarian revolution, and we had escaped. We lived in Vienna for about six months until we arranged our destination, and a part of my family—including myself—we immigrated to Colombia in South America.

Tacey Ann Rosolowski, PhD
0:03:25.8
Can I ask you about that experience in the concentration camp? I was really moved to read that as part of your background. What do you recall about that? How did it affect you as a young person?

Gabriel Hortobagyi, MD
0:03:41.7
The human mind has incredible protective devices, so I have probably blocked many of my memories of my early years. I am always amazed that my wife, for instance, who has a somewhat similar background but not quite—she seems to remember stuff from when she was two and three years old. I don't. I have no memories from that very early stage of my life. In fact, probably my earliest memory is when I was about four years old. And as you know, some of this becomes a question of do I know what I think I know because I have heard so much of my family talk about it? Or do I really remember it myself? But one night—let's say three or four in the morning there is a knock on the door, and it is the secret police. And they tell us that we've got thirty minutes to pack one bag and that we are going. Where are we going? That is none of your business. We are going. Get ready. So they load us in a truck. The truck goes to the train station. Nobody tells you anything. Any attempt at conversation is either disregarded or punished, and then they load us in these cattle wagons. Three or four hours later, the train stops in the middle of nowhere in this tiny little town in the middle of the Hungarian plains, and they unload us. They distribute us into little groups, and then we are walked into this little town, which at that time must have had maybe 300 or 400 inhabitants or so. And then we were assigned to the home of one of the townspeople. In one room we slept—the five of us—my parents and my two sisters and I. And then I started to remember some things. Because my father was destined for hard work, he was picked up every morning around four by a truck and—with several other adult men—was taken to an area where a railroad track was being built. His task was to take a sledgehammer and break rocks and make the rocks into gravel or something like that.

Tacey Ann Rosolowski, PhD
0:06:41.5
What was your father's original profession?

Gabriel Hortobagyi, MD
0:06:44.3
My father was a military officer, and his college education—he was an economist. And so he did that for—the railroad building—for about three years until they let us go. My mother and my two older sisters were picked up a little bit later, and they were taken to a place where they would make—fifty years ago instead of this elaborate scaffolding that new buildings have they built—at least in Hungary—they built these curtain-type things out of cane or bamboo or reed to prevent debris from falling on passersby. So that was their job. They would split cane or a reed of some sort and tie it into these things. And I was assigned to a townsperson whose job was to collect cow and horse manure and distribute it to the fields. So he would pick me up on his ox-driven or ox-pulled cart, and I would ride shotgun with him and learn his exquisite vocabulary as

he enticed the animals to pull harder and harder. So in that little town I started my grade school about a year or two later. And then I don't remember too much. We were not beaten, we were not tortured, but it was pretty miserable living anyway. And then when Stalin died in March of 1953, there was a general amnesty and they let us out with some conditions about what we could and could not do. So that is about my recollection of this. Obviously there are no photographs of that era. I know that periodically the secret police would sort of barge in looking for shortwave radios or American dollars or other signs of espionage or where would we do that. So that's how it happened.

Tacey Ann Rosolowski, PhD
0:09:30.3
And so what year did you leave Hungary and go to Colombia?

Gabriel Hortobagyi, MD
0:09:36.0
The Hungarian Revolution started on October 23, 1956. We left Hungary on December 6, 1956, under the cover of night. And by then the Russians had invaded Russia—Hungary again. It was pretty dicey. So we walked across the border to Austria and eventually were settled in a refugee camp on the outskirts of Vienna.

Tacey Ann Rosolowski, PhD
0:10:08.9
Who helped you arrange that? I mean how did that happen?

Gabriel Hortobagyi, MD
0:10:13.6
Well, the last couple of years in Hungary, my mother worked for the state import/export agency, so she had a special permission to ride to the border area because during the Iron Curtain years an average citizen was not allowed to get within—I don't know—fifty or 100 kilometers of the border—of the external border of the country unless they had a document that stated they lived in that area or that they had special permission from the government. So my mother had that permission. So when it became clear that things were going to be really bad and there would be a blood bath, one evening we just picked up whatever fit in our pockets—a few critical documents and whatever valuables we had—and got on a train to as close to the border as we could. And then we got off and found someone who we bribed with some jewelry, and he walked us during the night through the border. It was—that's how it happened.

Tacey Ann Rosolowski, PhD
0:11:46.5
And going to Colombia—when did you make that trip?

Gabriel Hortobagyi, MD
0:11:53.2
We stayed in Vienna for about six months, and during that time my dad met the Colombian ambassador. He was offered a job in the military school in Colombia, so he accepted and we got granted refugee status and boarded a ship in Genoa in Italy. And then we arrived in Colombia on May 10, 1957. It was sort of ironic because by the time my dad was offered the job, Colombia was under a military dictatorship. And of course the military school and all the military had a big budget and whatnot. The day we arrived to Colombia the dictatorship fell, so my father was unemployed (laughs) before we even debarked.

Tacey Ann Rosolowski, PhD
0:12:58.4
(laughing) Your parents must have been so sick of history.

Gabriel Hortobagyi, MD
0:13:01.0
Yes. Yes. But we did well. Colombia at that time was a sleepy but very nice, very polite country. There was no drug problem. There was no insecurity. There was no major crime. So within a couple of years we were back on our feet. Both my parents were very hard workers, and they just rolled their sleeves up and started to work. Soon we had our own home, and my dad opened a business or two, and I finished my high school there and eventually medical school.

Tacey Ann Rosolowski, PhD
0:13:56.9
Uh-hunh (affirmative). And this is was in Bogota?

Gabriel Hortobagyi, MD
0:13:58.6
This was in Bogota—all in Bogota.

Tacey Ann Rosolowski, PhD
0:14:00.0
Uh-hunh (affirmative). .

Gabriel Hortobagyi, MD
0:14:00.1
Yeah.

Chapter 2
A: Educational Path
Becoming a Doctor

Story Codes
A: Character, Values, Beliefs, Talents
A: Personal Background
A: Professional Path
A: Inspirations to Practice Science/Medicine
A: Influences from People and Life Experiences
A: Professional Values, Ethics, Purpose
C: Professional Practice
C: The Professional at Work
C: Formative Experiences

Tacey Ann Rosolowski, PhD
0:14:01.6
And tell me how you became interested in the sciences and in medicine in particular. When did you know that you were going to focus in that area?

Gabriel Hortobagyi, MD
0:14:14.8
I never knew otherwise.

Tacey Ann Rosolowski, PhD
0:14:17.1
How did that happen?

Gabriel Hortobagyi, MD
0:14:20.8
In retrospect—and I think this is just my hypothesis. Whether it's true or not I don't know. My mother's father was a judge in Hungary, so it was sort of the equivalent of a federal judge in the eastern part of Hungary. And my mother grew up as an only child, and she wanted to be a doctor. But you know, in the 1920s that was not fashionable nor considered proper. So she was rapidly either dissuaded or forbidden to do that. But I think she never really gave up on it.

Tacey Ann Rosolowski, PhD
0:15:15.5
What made you think that?

Gabriel Hortobagyi, MD
0:15:17.4
Because from very early on I kept on being given books about science, about scientists, about medicine. While I was still in middle school, I was reading about scientific discoveries and medical stories and archeology and biology and physics and that stuff. And that's not the usual stuff that mothers give children unless they themselves, I think, have an interest in it. Now as it is, I was and am an avid reader, so I read a lot. And I sort of took it for granted that that was the only thing that would be of interest to me. So by the time we were in high school, everybody in my class knew that I was going to medical school.

Tacey Ann Rosolowski, PhD
0:16:27.4
What were the areas in which you felt you particularly excelled at that time?

Gabriel Hortobagyi, MD
0:16:32.8
I was a pretty good student. I was a pretty good student, and I was very fortunate because in my high school we had very good teachers in sciences. So biology, chemistry, physics were very strong. And so in Colombia the system is a little different. College and medical school are not separate. You sort of commit very early on, so by the time you are in your senior year in high school you have to commit. You either go to medical school or you become a lawyer or an architect or—I don't know—a mechanic or street sweeper or something. So I knew I was going to be a doctor. I applied to one single medical school. I got in at the top of my class, and I never thought of it as being—I saw my daughters many years later agonize about what they wanted to do, and they weren't sure. And even in the middle of college they were still not sure what they wanted to do. That never happened to me. I never understood that. In all fairness to them, I had far fewer options than they did. When I was finishing high school, if you wanted a professional career—well, what were your options? You became a physician or a dentist or an engineer or a lawyer or an architect. That was it. When I accompanied my oldest daughter for her college interviews about ten to twelve years ago, I remember going to UT in Austin and sitting down with the counselor—who was wonderful by the way—but she presented us with about 1000 different options that my daughter could focus on, and that was mind-boggling. Of course it was mind-boggling for my daughter because she was expecting some guidance, and what she got was the smorgasbord of you are in the candy store. You just pick what candy you like. So for me it

was much easier. It was much easier, and I never gave it a second thought. I was very happy, and I'm still very happy. I wouldn't do it any other way if I had the opportunity again.

Tacey Ann Rosolowski, PhD
0:19:29.5
So you received your BS—and I want to make sure I say this right—the Colegio Helvetia?

Gabriel Hortobagyi, MD
0:19:36.4
So that's a—that's the K through twelve school.

Tacey Ann Rosolowski, PhD
0:19:39.4
Oh, okay. So that's actually our equivalent of elementary, junior high, and high school.

Gabriel Hortobagyi, MD
0:19:45.2
Correct.

Tacey Ann Rosolowski, PhD
0:19:46.2
And that was 1963 you finished that program.

Gabriel Hortobagyi, MD
0:19:48.6
That's correct.

Tacey Ann Rosolowski, PhD
0:19:49.7
And then you went to the National University of Colombia in Bogota, receiving your MD in 1970.

Gabriel Hortobagyi, MD
0:19:56.9
That's correct.

Tacey Ann Rosolowski, PhD
0:19:57.8
And did you have a sense of your specialization during that time in medical school?

Gabriel Hortobagyi, MD
0:20:02.7
So that—that was less straightforward. That medical school at the time I attended it was the number one medical school in Colombia. And the University Hospital happened to be the only charity hospital in Bogota. It was a huge complex of about 3000 beds, and it was the place where if you were run over by a car or stabbed or shot or poisoned or whatever, you ended up in that emergency room because it was the only real emergency room in the city. At that time the city was small. It was about two million people. But as you can imagine—serving a city of two million people where the majority of the people were poor or lower middle class in terms of socioeconomic status—it was incredibly busy. So your medical education was accelerated simply because of the volume and because there were never enough hands to do everything. So what would be the equivalent of the clerkships—the clinical clerkships in the US—we actually started informally very early on. So when I was a first year medical student, which would be the equivalent of first year in college when most kids here take English and—

Tacey Ann Rosolowski, PhD
0:21:56.4
Basic bio.

Gabriel Hortobagyi, MD
0:21:57.0
—basic bio and stuff like that, I would go to class. And then in the evenings, some friends and I would head down to the emergency room to the University Hospital where the residents and interns were absolutely delighted to see us. And they would tell us, "Who do you want to suture?" And we would spend three or four hours stitching people up who had a broken scalp or whatever and doing the menial job that in the US you don't get to do until you are an intern.

Tacey Ann Rosolowski, PhD
0:22:32.4
Right.

Gabriel Hortobagyi, MD
0:22:34.4
When we got to our clinical clerkship in OB/GYN, the OB/GYN component of our hospital was a separate building where about 180 deliveries took place every day. You were only admitted if you reached a certain level of dilatation, so many of the little kids were born in the taxi at the entrance because there was no room. Many days there were two women per bed. So the medical student did many of the deliveries because the nurses—the nurse midwives and the interns and

residents only did the more complicated stuff, so we got to do a lot of the deliveries. So by the time I finished medical school and before my internship I had probably delivered—I don't know—eighty, 100 kids—all uncomplicated deliveries and whatnot.

Tacey Ann Rosolowski, PhD
0:23:46.3
Is that when your interest in treating women began to take shape?

Gabriel Hortobagyi, MD
0:23:52.5
No, not really. Not really. And in fact with the exception of those who dedicate their lives to OB/GYN, most other physicians will tell you that that is not one of the most attractive specialties. But what did attract my attention during my training was surgery. I had outstanding surgical teachers, and they were not only extremely good technically but they were very bright physicians. They knew their science. They knew their biology. So they approached it not from the point of view of, "Gee, let's do one more surgery," but "How can we take care of this problem and what is the best way? And if it comes to surgery, yes, we will do that." But that was not the major focus for them. So I loved that. I loved the rapid pace of that. At any one point in time we had five surgical—ten surgical teams. And at any one point in time two surgical teams were on call, and they were busy. They were busy. Surgery went on twenty-four/seven. And as a medical student and as an intern and as a resident, you got to do a lot.

Tacey Ann Rosolowski, PhD
0:25:24.8
And it is interesting because it sounds like you were developing the hand skills for surgery pretty early.

Gabriel Hortobagyi, MD
0:25:31.5
Yes.

Tacey Ann Rosolowski, PhD
0:25:32.2
And then were also working in this really vibrant intellectual environment where people were kind of taking a more global perspective on it. Was that also an interdisciplinarity where there are different treatments that were being applied by the individuals involved?

Gabriel Hortobagyi, MD
0:25:46.8
No. We are talking about the 1960s. It was a pretty classical—pretty old-fashioned medical education in that sense. But I did get a lot of steering towards surgery both because of my own interests—I've always had sort of a Type A personality. I take charge of stuff, and that is sort of ideal for a surgeon. So I did that, and then I did my internship and my one year of rotating internship in that same hospital.

Tacey Ann Rosolowski, PhD
0:26:34.0
So that's the hospital San Juan de Dios.

Gabriel Hortobagyi, MD
0:26:35.8
San Juan de Dios.

Tacey Ann Rosolowski, PhD
0:26:36.7
Yeah.

Gabriel Hortobagyi, MD
0:26:37.0
Exactly. That was—during that year I did not go home. Someone from my home would stop by once a week to pick up my laundry and bring me some goodies, but the rest of the time I spent there.

Tacey Ann Rosolowski, PhD
0:26:54.9
Would you like me to pause the recorder while you take—

Gabriel Hortobagyi, MD
0:26:56.8
No. Thank you. And it was because we were so busy and our—

Tacey Ann Rosolowski, PhD
0:27:09.0
So you basically—from 1969 to 1970 you never went home.

Gabriel Hortobagyi, MD
0:27:12.3
Right. Now my family lived in the same city, but it was a number of blocks away. And so for instance—so we had five rotations each for about ten weeks. The emergency room rotation sticks out in my mind because we were on call—meaning in the emergency room—twenty-four hours, and then we were given twelve hours off, and then the next twenty-four hours on, then the next twelve hours off. If you think through that, it means that your sleep cycle is totally screwed up for ten weeks because one day you get to sleep during the day, and one day you get to sleep at night. One day you get to sleep during the day—if you get to sleep, because very often after finishing your call you still had other things to do. So it was very intense hands-on training. Now in the internal medicine rotation, we were assigned probably twenty, twenty-five patients in an open ward. And you were it. You had to take care of those people. Now the residents who were above you supervised and helped, but they also had other obligations like that, so it was very busy. So you didn't go dating or you didn't go to the movies or you didn't go out dancing or drinking or—you know, none of the stuff that twenty-some-year-olds do normally. But it gave a very good foundation to be a physician.

Chapter **3**

A: Educational Path

A Small Town Offers Good Training

Story Codes
A: Character, Values, Beliefs, Talents
A: Personal Background
A: Professional Path
A: Inspirations to Practice Science/Medicine
A: Influences from People and Life Experiences
C: Evolution of Career
A: Professional Values, Ethics, Purpose
C: Professional Practice
C: The Professional at Work
C: Formative Experiences

Gabriel Hortobagyi, MD
0:27:12.3+
And then at the completion of that [rotations] in Colombia—as in many other third world countries—in order to get—you don't get your license until you pay the government with about a year of service. So the Ministry of Health designates a place where you are being sent, and you will be a government employee and you will practice as a physician in that area, which is usually an underserved area.

Tacey Ann Rosolowski, PhD
0:29:29.4
Can I just ask a quick question? Is that because the medical education—the higher education—was very low cost or free? I mean—how did that work?

Gabriel Hortobagyi, MD
0:29:39.7
Okay—so this was a government—this was a public school. All right, let's say UT except that it was a national. So tuition was based on two things. One was your ability to pay, so in my case it was based on my father's previous or last year's income tax return. And secondly, it was based on performance. So when I went to medical school my father was fine—he was certainly not wealthy—so it was not very expensive. But by the second year—since the top five in the class got full tuition support—so I essentially paid for tuition the first year, and the rest of my medical education, my parents; and later on we just bought the books and—so yes, in a way it is to give

back what the state gave you or the government gave you, which was in my case an almost free medical education. So I was sent to this little town of about 30,000 people about four hours from Bogota in the mountains. And there was a 100-bed hospital there, and I was the only doctor. Actually that is not true; there was a retired pediatrician who lived in town, and he worked part time to take care of the kiddos, which was great because I didn't have the stomach for pediatrics. It is terribly painful to watch those little tots as sick as they get. So I lived in this place for about a year.

Tacey Ann Rosolowski, PhD
0:31:53.6
What was the name of the town?

Gabriel Hortobagyi, MD
0:31:55.2
Pacho.

Tacey Ann Rosolowski, PhD
0:31:57.2
Pacho.

Gabriel Hortobagyi, MD
0:31:57.9
Pacho. It is in the same department or province as Bogota. And it is in the central—Colombia has the Andes divided into three ranges, and Bogota is in a plateau in the central range. Pacho is sort of on the other side of that same range, and on the Bogota side of the range are the richest emerald mines in the country. And the only reason I mention that is that there is a lot of smuggling, and all of the smugglers came our way because, of course, going towards Bogota they would risk being caught by army and police and whatnot. But they were gangs of smugglers so they attacked each other, and I had plenty of work to do with people who had been cut up or shot up or hurt in some way or another. So I would make rounds in the hospital in the morning. I would make rounds over a hundred beds, which were usually full. Now it wasn't like it is today here because fifty years ago—and especially in a place where many people lived a long distance away—they couldn't afford to go back and forth. So sometimes they stayed for simple treatments, but that required daily administration. They would stay in the hospital for two or three months. So it wasn't exactly that they were deathly ill, but it was full at all times. And so I would do that in the morning, then I would do a little surgery depending on what was needed. And in the afternoons, three times a week I would go out on a bus or on a helicopter or a Jeep with the captain of the police to a smaller town two or three hours away and would do outpatient consultation there and then come back either the same day or early the next morning. And then I

would do—in between I would do emergency room calls and whatnot. So that was—that went on for a year, and it really makes you a good doctor.

Tacey Ann Rosolowski, PhD
0:34:32.3
How so?

Gabriel Hortobagyi, MD
0:34:35.0
Because you are it. When you are in a medical school in a university hospital, you are protected. If you don't know what to do you just asked the guy next door or the passerby saying, "Hey, how do you do this? What's the answer to this?" There, there's nobody. In the 1960s in a third-world country in a small town, there were not even phones. So it wasn't like, gee, I'll call the world's expert in appendicitis or whatever it was. You had to figure it out. You were on your own, and the life and health of that individual sitting across from you depended entirely on you. So it forces you to grow up.

Tacey Ann Rosolowski, PhD
0:35:26.1
Can—is there an event of treating a patient or some patients that you really recall from that time that really made you grow as a physician?

Gabriel Hortobagyi, MD
0:35:37.0
Well, sure. First of all you start off—you get there and you're shell shocked during your first week because, "Oh, my God. I'm alone. What do I do?" You know? And then there are things like—I remember they brought in a man they had found in a cornfield, and he was chopped up to pieces. Because his sons wanted to inherit and the guy wouldn't die, they caught him in his cornfield and—with machetes—they hacked him and left him for dead. It turns out that he didn't die, but several days later he was picked up and brought in. And he had—I don't know—eighty or 100 cuts. So I worked on him for probably the best part of an entire day just cleaning him and sewing him up and rehydrating him. Of course we didn't have a blood bank. So you did the best you could with what you had. And I had to do things for which I was totally unprepared. So one of the cuts lifted the top of his skull—not just the scalp but his skull—so his brain was hanging out. And surprisingly he was awake and fine and thinking, and I had no idea what to do with it because the brain was swollen because of the injury, and I couldn't just stick it back. And of course I had no training in neurosurgery, so I had to figure out what to do. And eventually the guy recovered and survived and did fine but you have to think quick on your feet, and you have to be prepared to do your best realizing that you are going to make mistakes. So that reminds me.

There was another one that was fascinating. There was this woman who came in and she was extremely pregnant, but she didn't remember when she had had her last period because she had been continuously pregnant for about eighteen years. She had had sixteen previous children, so she never recovered between pregnancies. She came in and she looked huge, and I examined her and she seemed to be in labor, so I admitted her to the hospital. I go back in the evening to check on her change—next day no change—the following week no change. And she is happily there resting and eating in the hospital because, of course, she left her sixteen kids at home to fend for themselves. So a month later she is still there. Nothing is happening—she is getting bigger, so I sent her home. She comes back a week later—same thing. I readmit her—again the same story. So at that time we didn't have ultrasound or any of these things, so I ended up taking an x-ray of her abdomen. Well, it turns out that she had triplets. So she is there—we don't know how long her pregnancy has been going on, and after a while—just judging by the size and the one x-ray—I said, "Well, it must be time." But she had no intention of delivering. She was just perfectly happy eating and sleeping there.

Tacey Ann Rosolowski, PhD
0:39:37.0
Well, it was a retreat for her.

Gabriel Hortobagyi, MD
0:39:39.0
It was a retreat for her. So I finally induced her with Pitocin, and then that didn't work very well. So I ended up doing a C-section and three healthy boys were born. And in fact, the middle name for all three of them was Gabriel because she was very happy. And so I will always remember that because it made me look like a fool—or at least feel like a fool—because I had no idea what I was doing. The C-section—I had done plenty of C-sections by then, but this thing—and then you realize how people until really the 1940s or '50s—they just did it like that. I mean it was an art and certainly not a science. So that was an interesting one. And then there were a couple of—well, not a couple—a number of cases where people would come in with symptoms that didn't match anything, and you wouldn't find anything. Then you would work on them with very limited resources and—because I was also the head of the laboratory, and I was the radiologist and everything. So it was it—I was it. There was nobody else to help me, nobody else to consult with. And the hospital—the hospital director—well, I was the hospital director. But the administrative director was a nun who was an RN, and she was the only RN in the hospital. There were two that were an LDN equivalent—so no graduate nurses. And then there were a bunch of girls from town who were trying to do the cleaning and changing the beds and bathing the patients and doing the gofer stuff. So I couldn't even consult with experienced nurses saying, "Gee, what do you do here?" because there weren't any. I had taken some books with me—some medical books—so I would in the evenings go in and read a while. But you couldn't do much of

that because the hospital generator was turned off at eight p.m. So you could light a candle or have a flashlight and do some reading, but other than that you got up at sunrise, and you went to bed after the lights were turned out because otherwise there was not much to do. So then as you become familiar with your surroundings and you become more comfortable in your skin then yeah, I can do this. Then comes the social problem. So you are in this town and, of course, I was single at that time, and you become the most eligible bachelor in town, right? So you are invited to every wedding, every funeral, every baptism, and every birthday celebration. And the four personalities in town were the priest, the captain of the police, the judge—who was a young woman who was doing the same thing I was so she had been assigned by the government to work in this town for a year—and I. I mean the four of us by force became not only acquainted but friends because we were the only—we were the high—most highly educated people in town. So there were not many places to meet, so you would meet in the main square in front of the church, and there were two bars. You know, there was the church, and then on the other side of the square there were two bars. So you would sit at a table chatting, and people from town would pass by saying, "Doctor, here goes a drink for you." And then they would bring attention of the passerby for drinks; and then while that is very pleasant and sort of interesting, after a while you realize if I stay here I am going to become an alcoholic. And then it also dawns on you that there are no intellectual challenges because there is nobody who knows more than you—certainly about medicine in my case—and that if you stay there it is very hard to stay on the top of your game because it is very comfortable. You've got—well, you are in very modest surroundings. You have no needs really. You have no material needs. They feed you; they did my laundry; and they mended my clothes and my shoes. So I had—I only had to concentrate on my profession. But then you sort of start sinking into this very comfortable surrounding that demands very little from you. And I became aware of that probably about halfway through that year saying, "Oh, my God. I've got to get out of here."

Tacey Ann Rosolowski, PhD
0:45:34.6
Right. Sure. Well, I suppose for some people it would be hugely attractive because you have such a huge position in the community.

Gabriel Hortobagyi, MD
0:45:40.8
Right. Right. Right.

Tacey Ann Rosolowski, PhD
0:45:41.3
Yeah.

Chapter 4
A: Joining MD Anderson/Coming to Texas; *Choosing to Focus on Cancer*

Story Codes
A: Character, Values, Beliefs, Talents
A: Personal Background
A: Professional Path
A: Inspirations to Practice Science/Medicine
A: Influences from People and Life Experiences
C: Discovery and Success
C: Human Stories
C: Offering Care, Compassion, Help
C: Patients
C: Cancer and Disease
C: Professional Practice
C: The Professional at Work
C: Evolution of Career
C: Formative Experiences
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care

Gabriel Hortobagyi, MD
0:45:43.7
So at that time I took my tests to come to the US. I applied to a number of hospitals and centers, and I was accepted in several, and then I had to make a decision. And then I came to Cleveland. I came to Cleveland—the two finalists were Toronto and Cleveland, and Toronto—I applied in Toronto because one of my sisters lives there. I said, "Well, at least I would have someone." And then I applied to Cleveland because Cleveland is probably the second largest Hungarian city in the world outside of Budapest.

Tacey Ann Rosolowski, PhD
0:46:31.7
And this is—so and this was when you went to the clinical residency in internal medicine at St. Luke's Hospital at Case Western Reserve.

Gabriel Hortobagyi, MD
0:46:38.7
Right. Right.
Tacey Ann Rosolowski, PhD
0:46:39.6
And that was 1971 to ’74—I’m just saying for the record.

Gabriel Hortobagyi, MD
00:46:42
Yeah.

Tacey Ann Rosolowski, PhD
00:46:42
So I didn’t realize it had such a huge Hungarian community.

Gabriel Hortobagyi, MD
0:46:47.4
Oh, yes. It’s a huge community. You know like the Italians and the Ukrainians and the Pols around the turn of the century and the early part of the twentieth century, many came to the rust belt—

Tacey Ann Rosolowski, PhD
0:46:59.8
Yeah.

Gabriel Hortobagyi, MD
0:47:01.3
—because that is where the jobs were.

Tacey Ann Rosolowski, PhD
0:47:02.2
Cleveland—or Chicago was a huge Polish community.

Gabriel Hortobagyi, MD
0:47:05.6
Chicago, Toledo, Detroit, Cleveland, Buffalo—all of these areas are full of European immigrants, and the Hungarian community in Cleveland happens to be huge. So there were—between the first, second, and third generation—probably close to a third of a million. So in the area where St. Luke’s was, there were a number of stores that—like in Miami today—they had

signs that said, “English is spoken here,” because otherwise you could conduct your entire life in Hungarian. There were multiple Hungarian churches, multiple Hungarian newspapers, schools, community halls, et cetera, et cetera, et cetera. In fact, in retrospect it was funny that you would walk into a McDonald’s and people would greet you in Hungarian, and you would have to ask for your stuff in Hungarian in order to be served. And it turns out that I didn’t really do much with the Hungarian community because I was too busy training and whatnot but that’s when—so when I took the decision that I didn’t want to stay in this little town very long, then it also dawned on me that I had been doing surgery feverishly for a number of months or years and that the excitement was sort of vanishing because I needed something that was more intellectually stimulating. So then I went to Cleveland, and in Cleveland I had a wonderful team of mentors and teachers. And that’s when I started to think of oncology.

Tacey Ann Rosolowski, PhD
0:49:04.7
Really?

Gabriel Hortobagyi, MD
0:49:05.8
Not from the very beginning but towards the beginning of my second year. I spent three years there.

Tacey Ann Rosolowski, PhD
0:49:12.4
What got you started thinking about oncology?

Gabriel Hortobagyi, MD
0:49:16.7
Well, when I came to Cleveland I came with the intention of staying maybe a couple of years and then going back to Colombia because by then I had spent the most important formative years of my life there and had friends and acquaintances. My family was there. We were in a comfortable situation. And in fact, I had several offers for positions—both at the university and in practice—so I went with that idea. And then as you start your training in the US, you realize how huge the difference is in terms of the way medicine is practiced, the resources that are involved, the opportunities that are involved in further training and doing research, and a number of things that you couldn’t do in South America at that time. So then I started to change. It was sort of an internal crisis of I can’t go back; and yet how can I not go back? How can I abandon everything I have and start anew? But then you sort of solve your internal struggle. And what got me started on oncology was the fact that as you settle the issue of do I stay or do I go, you start thinking, “Well, if I stay what am I going to do?” And then you start thinking, well, general

internal medicine is interesting but maybe not that interesting. Now what are the specialties that would be interesting? And then at that time I perhaps mistakenly had thought cardiology being a very old specialty—a lot had been discovered. There were fewer opportunities perhaps. Perhaps it was less interesting because there was more known—the same for pulmonary diseases, same for a number of other specialties. And I started to get interested in hematology and the infectious diseases and endocrinology, and I said, "Gee, what could bring all of these things together?" And then oncology came increasingly to the surface.

Tacey Ann Rosolowski, PhD
0:51:50.1
So you were really looking for kind of the uncharted territory in a sense.

Gabriel Hortobagyi, MD
0:51:54.4
Yeah. Yeah. The Wild West of medicine. And then it dawned on me that as we were making rounds in the mornings—and this was a much nicer hospital than San Juan de Dios, so these were either individual or semi-private rooms, and you would walk in with the professor and the residents and whatnot—and I would notice that increasingly we would bypass the rooms of patients with cancer. Patients with leukemia and lymphoma were treated, but there was virtually nothing to be done for patients with advanced solid tumors like breast cancer, lung cancer, colon cancer, et cetera. So the teacher sort of shortcut the process in saying, "Oh, that's—they are getting their pain medication." And I remember that sort of irritated me, and I said, "You know, there must be something we can do about these folks." And then a couple of things happened. One was that there happened to be two young women in their mid-thirties or so who were admitted—not at the same time but over a relatively short period of time—with advanced breast cancer—widespread advanced breast cancer. They were bedridden and in really terrible shape and suffering and whatnot. And the initial approach was, well, let's give them enough morphine so that they die in peace and whatnot. And I said, "No, that can't be the end." Then I started to do reading, and there was not much to be read at that time. There were no textbooks in oncology. There were one or two journals—cancer was one of them. Most of our leading journals from today didn't exist at that time. So I did a little reading and found this abstract that had been presented at the American Society of Medical Oncology a couple of years earlier about chemotherapy. So I harassed my professor until he authorized me to give chemotherapy to these women—much against his best judgment—and both of them walked out of the hospital. I said, "You know, there is a new world here, so we need to do something about this."

Interview Session: 1
Interview Date: November 30, 2012

Chapter 5
A: Joining MD Anderson/Coming to Texas; *Inspired by Dr. Emil J Freireich*

Story Codes
C: Portraits
A: Joining MD Anderson
A: Personal Background
A: Professional Path
A: Inspirations to Practice Science/Medicine
A: Influences from People and Life Experiences
C: Funny Stories
A: Character, Values, Beliefs, Talents

Gabriel Hortobagyi, MD
0:51:54.4+
So that was one [inspiration to specialize in oncology]. And then the other one was—and then early in my second year I got a notice that there would be an American Cancer Society-sponsored conference in Columbus, Ohio, where Ohio State is. So I drove down and registered for that, and one of the speakers was [Emil] J Freireich. And he gave a super talk—one of those go get them and—

Tacey Ann Rosolowski, PhD
0:55:15.2
What did he say? What do you remember?

Gabriel Hortobagyi, MD
0:55:17.4
Oh, it was—it was so inspiring because he didn't give the usual pathology talk of this is the way cancer looks under the microscope and there is not a damn thing we can do about it anyway. So—but it is an interesting thing. He essentially started talking about how to cure cancer, and it was such a different view of the world. So I went back to Cleveland and I wrote to J and applied for a fellowship, and then it was pretty much decided in my mind that I wanted to do oncology. So then—not wanting to put all my eggs in one basket—I applied to a few other places, went and did some interviews, and then eventually got accepted here.

Tacey Ann Rosolowski, PhD
0:56:27.1
Now did I read that J Freireich wrote you back and said you were hired.

Gabriel Hortobagyi, MD
0:56:32.1
Yeah.

Tacey Ann Rosolowski, PhD
0:56:32.9
And he didn't even interview you.

Gabriel Hortobagyi, MD
0:56:33.9
Correct.

Tacey Ann Rosolowski, PhD
0:56:34.5
And now I want to know what you wrote in that letter.

Gabriel Hortobagyi, MD
0:56:40.2
Nothing special, actually. I just wrote to him that I had gone to his—that I am a second-year resident in such and such place, that I had listened to him at the ACS conference and it knocked the socks off my feet, and I am going to train in oncology and I wanted to train in his department. I think that is all I wrote. I have never been good at sucking up to anyone, and I've never been very good at embellishing things either. So I just wrote that. And it is true—they never interviewed me here.

Tacey Ann Rosolowski, PhD
0:57:31.2
I was just curious—I mean—I didn't think you had sucked up or anything, but I was thinking—wow, I was wondering how maybe you communicated that interest that you have in the Wild West of medicine because that is certainly what they were doing here.

Gabriel Hortobagyi, MD
0:57:42.9
Yeah.

Tacey Ann Rosolowski, PhD
0:57:43.6
Exactly what they were doing here.

Gabriel Hortobagyi, MD
0:57:44.9
That is exactly what it was.

Tacey Ann Rosolowski, PhD
0:57:45.7
I know. So how did it work out? How did you end up? What were the practicalities of moving from Cleveland down here to MD Anderson?

Gabriel Hortobagyi, MD
0:57:59.4
What were the practicalities? By that time I had, of course, established a little group of friends in Cleveland. And in fact, I found some childhood friends of my mother who happened to be living in Cleveland. I had a couple of girlfriends in Cleveland, and so it became a little bit harder to separate, but eventually that happened. So I loaded all of my earthly belongings in my car. I have to tell you a funny story. During my first year in Cleveland, public transportation in Cleveland was not exactly tops—a little bit better than in Houston but not tops—so I needed a car. I needed a car, but what most Americans don't realize is that as a newcomer immigrant you don't have credit. And of course you don't have credit because you don't have credit. And to get that first credit card is—it is like pulling teeth. So I had to pay cash for everything, and then I wanted to buy a car but didn't have enough money to buy a car. So I went up to a dealership and negotiated a price for a car that I just fell in love with. It was a Dodge Challenger. It was a beautiful navy blue Dodge Challenger with a huge engine. So I went up to my boss—the head of medicine—in saying I want to buy this car but I need someone to cosign for me. But of course, I didn't know what possessed me—and more importantly what possessed him to sign for me—because I would not for someone totally unknown. I mean it is crazy. So he said, "What do you want to buy?" So I said, "I want to buy this Dodge Challenger." "How much is it going to cost you?" "It's $4500." "You're crazy. You can buy a car for $500. You can buy a used Chevy or a Ford. You don't need such a car." "No, I need to have this car." And he cosigned for me. He cosigned for me, so I got my brand new, gorgeous car. And from then on I was a free man. And I of course paid off the car in a couple of years and got him off the hook for it, but I still remember him—Dr. Wieland. So I loaded all of my earthly belongings into this Dodge Challenger—which was a two-door—and drove down to Houston. So you can imagine how many earthly belongings I had—very few. In the process of driving down—oh, and so I drove into town. I had no idea what Houston was like. In fact, folks in Cleveland were asking me, "Are you crazy? What are you going to do in

Texas? Nobody goes to Texas. They shoot people there." And in retrospect, to realize the image that Texas had—and to some extent still has outside of this beautiful state—

Tacey Ann Rosolowski, PhD
1:01:50.7
Yeah, I moved down just a little over a year ago, and people said the same—virtually the same thing to me—

Gabriel Hortobagyi, MD
1:01:55.4
Yeah.

Tacey Ann Rosolowski, PhD
1:01:56.1
—when I was making my plans.

Gabriel Hortobagyi, MD
1:01:58.8
So I drove in and found the medical center. Then of course, there was no GPS at that time, so I found it. And I found a little motel down on South Main. I didn't know that was hooker's alley, but it was the—what was it called—the Roadrunner. And I remember I paid $14.99 a night. And at that time I didn't have great ambitions, so it didn't matter. So I unloaded stuff, came up to the hospital, and introduced myself to everybody and actually started a few days earlier than July 1.

Tacey Ann Rosolowski, PhD
1:02:42.1
And that was in 1974?

Gabriel Hortobagyi, MD
1:02:43.7
That was in late June 1974. And of course there were no cell phones. I didn't have an apartment so there was no home phone, and nobody in my family knew where I was. And my dad died during that time. He died in a car accident, and they were trying to get hold of me and they couldn't. And finally several days later they got a hold of Freireich, and Freireich called me and gave me the news. And then—by then my dad had been buried, so there was not much I could do about it. So I just stayed and continued my stuff. And July1, I remember I went up to the chief of the breast service, and it was Dr. Blumenschein—George Blumenschein. I told him who I was, and I told him that I wanted to do breast cancer research and to make some room for me because as soon as I finished my mandatory rotations I would come to the breast service. And it turned

out that I never finished the mandatory rotations because after the first two rotations I just crossed over to breast. And I stayed there ever since.

Chapter 6
B: An Institutional Unit
Developmental Therapeutics in 1974

Story Codes
B: MD Anderson History
B: Institutional Politics
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
C: Understanding the Institution
A: Personal background
A: Character, Values, Beliefs, Talents
A: Personal Background
A: The Researcher
C: Understanding the Institution
B: MD Anderson Culture
C: Evolution of Career
C: This is MD Anderson
C: Education at MD Anderson
D: On Research and Researchers
D: On Education

Tacey Ann Rosolowski, PhD
1:04:11.7
So how did that work? Because I am little confused from the details that are on your CV because it said from ’74 to ’75 you were in Developmental Therapeutics.

Gabriel Hortobagyi, MD
1:04:22.6
That’s right.

Tacey Ann Rosolowski, PhD
1:04:22.9
And then from ’75 to ’76 you were in medical oncology. So that was when you crossed over to—

Gabriel Hortobagyi, MD
1:04:31.1
So that—so when I arrived in 1974, this institution had a serious political split. The Department of Medicine was a traditional department of medicine that was started when MD Anderson was founded in maybe the 1940s. And they did excellent patient care, but there was relatively little research being done. So Dr. [R. Lee] Clark—in the mid-1960s—called the NCI and said, "I need a couple of go-getters to start the—jump start the real research department of oncology." So they sent down J Freireich, [Emil] Tom Frei—who then later went to the Dana-Farber—Ti Li Loo, and I think [Gerald] Gerry Bodey—and the four of them were not welcomed by the Department of Medicine. So they established for them a different department that was called Developmental Therapeutics. So when I arrived here there were two separate and intensely competitive programs—competitive with each other. I didn't know that the other program existed in the Department of Medicine, so for me it was irrelevant. So I was in Developmental Therapeutics, which was headed by J Freireich, and all of the really well known investigators were in that department. But soon after I arrived I realized that not only was this political split—but that like the Pope did in the 1400s where he gave the east to the Portuguese and the west to the Spaniards—somehow the way it ended up is that developmental therapeutics had access to only some types of cancer like melanoma and leukemia and sarcoma and whatnot, and all of the others were in the Department of Medicine, including breast cancer. So because I wanted to do breast cancer, I couldn't stay in Developmental Therapeutics because there was no—I mean there was an occasional patient with breast cancer who just happened to be referred to a member of DT, but the bulk went to medicine.

Tacey Ann Rosolowski, PhD
1:07:21.6
Can you tell me because—I mean that puts you in a very odd position, obviously.

Gabriel Hortobagyi, MD
1:07:25.5
Oh, yes. Oh, yes.

Tacey Ann Rosolowski, PhD
1:07:28.4
I'm kind of getting that. So—well, I'm very interested to know, first of all, like how Developmental Therapeutics was when you got there and what you got from that. But then, of course, how you dealt with the whole political problem once you crossed over. So how do you want to tell that story? (laughing) I am leaving that one to you.

Gabriel Hortobagyi, MD
1:07:48.6
Now you are talking about sensitivities. So when I arrived I had no clue about any of this, so I reported to Dr. Freireich's office, and Dr. Freireich passed me on to—I think it was Ken McCredie. He was an Australian who was the head of leukemia, and he was also in charge of the fellowship program. He was a big burly man like most Australians—pretty loud and not terribly discrete or polite. But he was a wonderful guy and a great physician and a wonderful oncologist. So he immediately assigned me to the leukemia service, and I knew close to minus two—as opposed to zero—about leukemia. So I was assigned to leukemia with Michael Keating. I don't know if he is on your list, but he should be. So Michael was another Aussie, and he was, I think, a year older than me, and he had had a little bit more experience in oncology and leukemia before coming over. So he and I were on the leukemia service, and they worked us to the bone. I was still single at that time, and Mike was married. So we would start rounds around six in the morning. We would work throughout the day. We would have thirty, forty inpatients, and those patients are as sick as dogs. And then in between we had to do conferences, and at that time we had to run the patients down to x-ray ourselves and draw blood, and we did a lot more stuff than our trainees do today. And then we had to catch up on paperwork. And then we had to do some of the research projects of some of the attendings. And then we had special assignments at midnight, so we would crawl home between one and two in the morning only to get back at six. (laughs) So this went on for a couple of months, and it really tries your mettle. But it was fun, and I learned an incredible amount about—from these folks.

Tacey Ann Rosolowski, PhD
1:10:17.7
Well, I suppose that also just—it's almost like being at war, you know. You're in the trenches with people.

Gabriel Hortobagyi, MD
1:10:22.9
Absolutely.

Tacey Ann Rosolowski, PhD
1:10:23.0
You create these bonds.

Gabriel Hortobagyi, MD
1:10:23.4
It's boot camp. It's boot camp but with real bullets. So then I was assigned to the outpatient clinic of DT, and that was under the control of another Aussie—actually [M. Andrew] Andy

Burgess. And Andy was sort of the quiet—imagine the Clint Eastwood type—sort of quiet but extremely smart and a very, very nice fellow. And so he took me under his wings, and he taught me a lot about oncology and about common sense. He had a lot of common sense, and he was not as outspoken and as aggressive as McCredie, but he was a wonderful person.

Tacey Ann Rosolowski, PhD
1:11:19.2
Could you explain that common sense piece to me? What is that about?

Gabriel Hortobagyi, MD
1:11:24.0
Common sense is a misnomer because there's the least common sense in a human being. There are a lot of very smart people in this world, either by book or because they are just quick at grasping concepts and whatnot. But despite that, it is surprising how many people make absolutely wrong decisions because they don't have the ability to place certain decisions in the context of real life. And I think common sense is just that ability—which is mostly innate—to figure out among the various options one has at every step what would make sense really—what would really make sense not because you read it in a book, not because someone necessarily told you but because it is just the only logical thing to do that fits into your context. It fits in your surroundings. It fits in your—what you are doing at that time. And the number of individuals—very bright individuals including many of my colleagues—don't have that—don't have that. And yet they have to make decisions every day.

Tacey Ann Rosolowski, PhD
1:13:06.8
What were some instances in which you learned that from Dr. Burgess?

Gabriel Hortobagyi, MD
1:13:12.2
Well, you know, there are many small things. So suppose that we are talking about treating someone with testicular cancer with the best treatment, which at that time had just become a platinum-based regimen, and then he listens to you and says, "Yeah, that is a wonderful idea, but you do realize that this person has renal failure, and platinum is just going to kill that kidney." So platinum is out of the picture, and it doesn't take great science. It's just—it makes no sense to do otherwise. It's a small thing. Or you are talking about someone who is very obese and who needs to lose weight, and you go into this thing of well, we need to put him on a diet and an intensive exercise program, and then Mike turns around and says, "That is fine, but you realize that this guy is in a wheelchair and has not walked in two years." That's common sense. It doesn't take a genius, but a lot of people don't figure it out. And then it goes all the way up to much more

important and perhaps more weighty decisions. So Mike was very famous for that. He talked to me about taking care of patients in the ambulatory setting, and we also became very good friends. During that time there was also another fellow here whose name was Jeffrey Gottlieb. I don't know if you've heard of him.

Tacey Ann Rosolowski, PhD
1:15:21.1
I don't think so.

Gabriel Hortobagyi, MD
1:15:23.8
So Jeff Gottlieb was a young man. He was—he might have been thirty-three or thirty-four at that time, and J Freireich had appointed him as the chief or the head of solid tumors within Developmental Therapeutics. That was a big title with a very small property, and Jeff—Jeff was very, very bright and very outspoken and very [redacted].

But from the first day we met and we talked, he says, "You know, you seem to have a good voice, do you sing?" And I said, "Yeah, sure I sing. In fact I used to sing with the Cleveland Symphony." He says, "Well, what are you doing tonight?" I said, "Working, I assume." He said, "No, no. You are coming with me." So we went downtown to Jones Hall. That was the major center, and I auditioned and he was already a member of the Houston Symphony Chorale, and I became a member of the Houston Symphony Chorale. [redacted]

Tacey Ann Rosolowski, PhD
1:17:06.2
What part do you sing?

Gabriel Hortobagyi, MD
1:17:08.4
Bass baritone, too.

Tacey Ann Rosolowski, PhD
1:17:13.5
Did you sing with the Chorale after that as well?

Gabriel Hortobagyi, MD
1:17:16.6
I did. I continued to sing until late—oh, maybe early 1979. And at that time our oldest daughter

was born, and then it became apparent that the chorale work was—took me away from home for too much.

Tacey Ann Rosolowski, PhD
1:17:41.3
When did you get married amid all of this amazing workload?

Gabriel Hortobagyi, MD
1:17:45.5
I got married in November of 1976.

Tacey Ann Rosolowski, PhD
1:17:49.0
And what is your wife's name? And how did you meet her?

Gabriel Hortobagyi, MD
1:17:53.4
My wife's name is Agnes, and I met her in Toronto in May of 1976. The ASCO (American Society of Clinical Oncology) meeting was held in Toronto in May of 1976. But I arrived to Toronto, I called my sister, and I asked whether she knew—she had any nice friends that I could take out for dinner perhaps. So she gave me my wife's phone number, and I called her, and eventually we connected and went out for dinner, and we got married on our third date.

Tacey Ann Rosolowski, PhD
1:18:35.5
I get the sense that people in DT make quick decisions.

Gabriel Hortobagyi, MD
1:18:39.9
Yeah.

Tacey Ann Rosolowski, PhD
1:18:42.6
So I guess good ones since it has lasted forty years.

Gabriel Hortobagyi, MD
1:18:44.9
That's right.

Tacey Ann Rosolowski, PhD
1:18:45.9
Yeah?

Gabriel Hortobagyi, MD
1:18:46.2
That's right. It was a wonderful, wonderful thing. Her parents were absolutely frantic, because how can you marry someone you don't know?

Tacey Ann Rosolowski, PhD
1:18:58.5
Well, congratulations.

Gabriel Hortobagyi, MD
1:19:00.3
Well, thank you. Thank you. She is a wonderful human being and a great partner. So at that time I stopped singing, and anyway I was too busy preparing for my boards—for my board exam in 1976. And so that was it. So I—

Tacey Ann Rosolowski, PhD
1:19:32.5
Excuse me, but what were you working on in Developmental Therapeutics? You didn't tell me what your focus was.

Gabriel Hortobagyi, MD
1:19:37.7
Okay. In Developmental Therapeutics I was quickly recruited by one of the faculty members, who was Jordan Gutterman, and he gave me a project of immunotherapy with BCG (Bacillus Calmette–Guérin) in breast cancer.

Tacey Ann Rosolowski, PhD
1:20:01.5
Oh, okay.

Gabriel Hortobagyi, MD
1:20:03.1
And my role was to run a clinical trial and to recruit patients and make sure that they got all their treatment and that I interacted with the immunotherapy nurses and the research nurses and eventually to write papers about this and whatnot. And then from that came several other projects

with other types of immunotherapy, and I worked on that for the first probably four or five years of my career.

Tacey Ann Rosolowski, PhD
1:20:32.6
And as you were getting into immunotherapy did you find that that was satisfying this need that you had to be looking at the broader picture? And how is that working with your need for the intellectual stimulation piece of oncology?

Gabriel Hortobagyi, MD
1:20:49.7
So at that time it was very, very satisfying because I felt in the middle of this tornado of intellectual activity. In retrospect I was so busy with so many tasks and so many things that there was relatively little time for innovative and creative thinking. And that came actually a little bit later—certainly way, way beyond my fellowship years, but my fellowship years prepared me for the basic concepts of doing clinical research and understanding what was known and what was thought to be known and to continuously question and to continuously search and to become systematic in what you do. And it is a process. Nobody is born with that. And as opposed to now when we have a much more structured training program for our fellows, in those years it was a little bit of sink or swim. You were thrown in the water and said, "Take this project and run with it." But there was not really an attempt to educate you. These are the processes of research, and this is what you need to do, and this is how you go about it and whatnot.

Tacey Ann Rosolowski, PhD
1:22:30.8
Do you—

Gabriel Hortobagyi, MD
1:22:30.9
Not because there was no willingness but because these were the early days of (both speaking at once).

Tacey Ann Rosolowski, PhD
1:22:37.5
Yeah—people were learning on the job.

Gabriel Hortobagyi, MD
1:22:39.2
Absolutely.

Tacey Ann Rosolowski, PhD
1:22:39.3
I mean making it up. Now did you—if you think about if you had entered a training program now, would you have flourished as quickly or do you—with your learning style did you—was that tornado situation more nourishing to you do you think?

Gabriel Hortobagyi, MD
1:23:04.4
So I've always been fiercely independent, and I have been to a large extent a loner. So I think that environment was perfect for me. With what I know today, I probably could have trained in a number of other areas. I probably could have or should have spent some time in the lab to acquire additional skills, but I don't know how I would have done there. I did some lab research back in Cleveland, but there too I was pretty much left to my own devices. After giving me some very basic instructions I was essentially told, "Run with it."

Tacey Ann Rosolowski, PhD
1:23:56.9
And hope you figure it out.

Gabriel Hortobagyi, MD
1:23:58.1
Yeah. And I work well in those circumstances. I do less well when there are—when I am one of five people who are in charge of the same thing. I am uncomfortable there because I am not fully in charge.

Tacey Ann Rosolowski, PhD
1:24:18.3
Uh-hunh (affirmative). I kind of get the sense actually when I—because I have spoken to a few people who worked in Developmental Therapeutics, and it is almost as if that particular program is selected for people who all worked well.

Gabriel Hortobagyi, MD
1:24:28.1
Yeah.

Tacey Ann Rosolowski, PhD
1:24:28.6
I mean they are all kind of loners, all take charge.

Gabriel Hortobagyi, MD
1:24:30.9
Right. Right, right, right.

Tacey Ann Rosolowski, PhD
1:24:31.7
All very independent people.

Gabriel Hortobagyi, MD
1:24:33.3
Right.

Tacey Ann Rosolowski, PhD
1:24:34.5
So it doesn't surprise me that you say that.

Gabriel Hortobagyi, MD
1:24:36.5
And that was sort of the Wild West spirit because there was so much to discover, and there was so much room for exploration. But there were no real rivalries in the sense that there was plenty for everyone to do.

Tacey Ann Rosolowski, PhD
1:24:54.3
So it really was a good—I mean a good place for big egos at the time.

Gabriel Hortobagyi, MD
1:24:57.5
Right. Absolutely. And there were plenty of them. Oh, believe you me. At the same time in the reverse of that is that if you got into this program—and for instance, several people on the other side in the Department of Medicine who got into that training program who did not have this incredible personal drive and this ambition to get ahead on their own—they got lost because there was not a real effort to say, "Now let me pick you up little birdy, and I will spoon feed you through the next two or three years." All right. And that may be a deficiency, but that was the—those were the times, and I don't think things were very different in any of the other major cancer centers at that time of which there were few.

Interview Session: 1
Interview Date: November 30, 2012

Chapter 7
B: An Institutional Unit
Building Knowledge of Breast Cancer in the Division of Medicine

Story Codes
A: The Researcher
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care
B: MD Anderson History
C: Mentoring
C: Leadership
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
C: Discovery, Creativity and Innovation
C: Professional Practice
C: The Professional at Work
C: Personal Reflections, Memories of MD Anderson
C: MD Anderson Past
A: The Researcher
B: Understanding the Institution
B: Multi-disciplinary Approaches
B: Institutional Mission and Values
C: MD Anderson Past
C: This is MD Anderson

Gabriel Hortobagyi, MD
1:24:57.5+
So I did the two months in leukemia, and then I did the two months in the clinic—in the Developmental Therapeutic clinic. And then—so that was July, August, September, October. And either November first or December first, I went up to Dr. Blumenschein, and I said, "Okay, now I am ready to start with breast cancer. Do you have room for me?" He said yes. So then still being—the good fortune was that Dr. Blumenschein being in the Department of Medicine and Dr. Freireich being in Developmental Therapeutics got along very well. And I think the background of that—well, I will come back to that. So he said, "Fine." And nobody in DT got offended for my crossing over. In fact, they sort of—I think they looked at me as the Trojan Horse who went over to the Department of Medicine and was going to divide and conquer. So I did that, and the same day I started one of the fellows from the Department of Medicine, Aman Buzdar, who is my colleague in my department here, also started. And the two of us have worked

together ever since. So then I finished that first year in Developmental Therapeutics but working essentially full time in the breast section and doing all of my research in breast with immunotherapy, which was all based in DT and sort of walking that fence trying to stay out of trouble and minding my own business.

Tacey Ann Rosolowski, PhD
1:27:51.4
So this—so you are no longer working on Jordan Gutterman's project?

Gabriel Hortobagyi, MD
1:27:54.8
No, I am still working with Jordan Gutterman's project.

Tacey Ann Rosolowski, PhD
1:27:56.2
Oh, okay.

Gabriel Hortobagyi, MD
1:27:57.0
But it is immunotherapy but now fully applied to breast cancer.

Tacey Ann Rosolowski, PhD
1:28:02.1
Oh, okay.

Gabriel Hortobagyi, MD
1:28:03.7
And from that time on I just stayed with breast cancer. So—

Tacey Ann Rosolowski, PhD
1:28:09.5
What was the project that you initiated within the Department of Medicine when you began then?

Gabriel Hortobagyi, MD
1:28:16.5
Okay. Well, there were several projects. So the first one was—and in fact I am going to talk about that next week in San Antonio—was the development of preoperative chemotherapy for locally advanced breast cancer. And that has been one of my major projects over the years. Then

with Buzdar we also developed the same thing for inflammatory breast cancer. Then we developed the first clinical trial for adjuvant chemotherapy in primary, operable breast cancer. Then we did—then I started a database of patients with breast cancer to look at the natural history of patients with breast cancer and understanding a little bit more the subtypes and what happened. And then I became increasingly a bit busy, so—

Tacey Ann Rosolowski, PhD
1:29:14.6
Not that you weren't already.

Gabriel Hortobagyi, MD
1:29:17.0
Not that I wasn't already, but that—and then I found out within just a few weeks or months of my being in the breast section that my boss, Dr. Blumenschein, had only arrived a year earlier, and before that he was a hematologist at the National Cancer Institute at the National Institute of Health. So he didn't know much more about breast cancer than I did or that Dr. Buzdar did, which was a revelation, but also a little surprising saying, "Now what? Who am I going to learn from?" And he was a delightful guy, a wonderful human being, and a very good doctor, but he was also very busy. So George Blumenschein married the daughter of the dean of the medical school at the University of Chicago before going off to the NIH. So when he was finishing his fellowship in hematology I think his father—his father-in-law who knew Lee Clark, who was the first president of MD Anderson, saying, "You know, my son-in-law is finishing his hematology. He is looking for a job. Would you have something for him?" So he was hired as Director of Education at MD Anderson because the previous chief of the breast service was retiring. They also threw him the chief of the breast service. Now at that time, being the chief of the breast service meant that he was there, the retiring past chief was there—Nylene Eckles—and there was a Hawaiian-Japanese guy—a Charlie Tashima—that was it. That was the breast service. So did he know much about medical education? Probably not, but that was the job he got. And did he know much about breast cancer? No, but that was the job he got. And he was one of those who could never say no, so he said, "All right, we will just grab the bull by the horns, and we will get it done." And he was a very bright guy, and he did a good job. But all of the sudden we were now Blumenschein, Tashima, Buzdar, and I, and we were the four who were leading breast medical oncology forward. And of course we knew relatively little about breast cancer, and then we had to learn very quickly on the job. The previous chief of the breast service, Nylene Eckles, was a petite—well, I wouldn't call her petite but a short woman. She must have been four foot eleven or maybe five feet tall [redacted]. She had an MD PhD. And she always wore these horrible-colored sneakers, and makeup and dress was not ever a priority. She was a wonderful physician. She really knew about breast cancer, but she had two serious shortcomings—one that despite being the head of the breast service for twenty-some years she never wrote anything. So

if you ask around the breast cancer community about Nylene Eckles, nobody knows who she is or who she was, and yet she took painstaking care of her patients. And she kept her private medical record of each patient, carefully taking notes; and in fact later when she retired, she gave them to me. So I have them in a deposit box somewhere. And the second she had was that she was a very poor teacher. So you would be in the clinic with Nylene, and they would walk into a room where a patient was and Nylene would say, "Oh, this is Ms. Johnson. We need to give her some estrogen." So you would finish the thing, and you would step out to the hallway and say, "Nylene, why should we give her estrogens?" "Oh, because that's what she needs." You'd say, "No, no, no. Can you go through the thought process of what made you think that she would benefit from estrogens better than from A, B, C, D, E, F, G?" "I don't know. That just popped in my mind."

Tacey Ann Rosolowski, PhD
1:34:48.3
She just didn't have the gift.

Gabriel Hortobagyi, MD
1:34:50.1
No.

Tacey Ann Rosolowski, PhD
1:34:50.8
Didn't have it.

Gabriel Hortobagyi, MD
1:34:52.7
So here's this treasure—this incredible brain that went to—well, not to waste but to waste for us as a junior faculty.

Tacey Ann Rosolowski, PhD
1:35:04.5
Did she have that information in her notes at all?

Gabriel Hortobagyi, MD
1:35:06.7
No. No. She was a very decisive person. In fact, she was very curt and even with the patients who loved her. But she was not a warm and fuzzy person. She would just go in and rake the patient over the hot coals if they hadn't done what she told them exactly to do. And then she was usually right, and she was very respected within the institution because she held her ground with

all of the other specialties. None of the surgeons would talk down to her because she would get back to them with the same coin.

Tacey Ann Rosolowski, PhD
1:35:49.1
And that is tough, too, for women at that time.

Gabriel Hortobagyi, MD
1:35:51.2
Exactly. She was a very tough woman. She was a very tough woman—very gifted—but those who—those of us who surrounded her did not benefit much from that wisdom except by watching and trying to learn by extrapolations or something like that.

Tacey Ann Rosolowski, PhD
1:36:13.8
Let me—I'm sorry to interrupt you, but I just wanted to let you know it is twenty-five after two.

Gabriel Hortobagyi, MD
1:36:18.4
Right.

Tacey Ann Rosolowski, PhD
1:36:18.6
And we are scheduled to stop at 2:30.

Gabriel Hortobagyi, MD
1:36:20.1
Right.

Tacey Ann Rosolowski, PhD
1:36:20.2
So I didn't want to take more of your time today. I mean I can go a little later if you would like or we can stop.

Gabriel Hortobagyi, MD
1:36:25.8
I can't.

Tacey Ann Rosolowski, PhD
1:36:26.2
Okay.

Gabriel Hortobagyi, MD
1:36:27.4
I can't, so within the next few minutes we probably need to stop.

Tacey Ann Rosolowski, PhD
1:36:31.4
Okay.

Gabriel Hortobagyi, MD
1:36:33.0
Because I have some other things that I need to do.

Tacey Ann Rosolowski, PhD
1:36:34.3
Absolutely. Absolutely. We have another session scheduled next week.

Gabriel Hortobagyi, MD
1:36:36.8
All right.

Tacey Ann Rosolowski, PhD
1:36:37.4
So that's fine. So did you want to continue with some more observations about Dr. Eckles or tell me more about how you kind of managed this sort of vacuum of experience with breast cancer that happened in the Department of Medicine?

Gabriel Hortobagyi, MD
1:36:56.5
So I got as much out of Nylene's experience as I could under the circumstances, and then there were some very talented people from other disciplines. There were a couple of wonderful breast surgeons like Charlie McBride and Ed White and Marvin Romsdahl, and there was a fantastic radiation oncologist, Eleanor Montague, and a fantastic breast pathologist, Steve Gallagher. And so I learned a lot from them. They were much better at teaching, and they were much better at sharing their experiences. And they had worked together for a long time, so I learned a lot from them. I had my shortcuts, too, because while I didn't necessarily have the immediate mentorship

that my junior faculty that I would have today, I did have mentorship from other sources. And then realizing that one of the things that I worked on and insisted was to actually bring together even closer those various disciplines, realizing that we were so interdependent, and our patients depended so much on the decisions we made that it would be best to make those decisions jointly than as opposed to in sequence and independently.

Tacey Ann Rosolowski, PhD
1:38:42.4
How did you make that happen?

Gabriel Hortobagyi, MD
1:38:44.6
We organized a weekly or twice-weekly meetings in which specific patient cases were presented, and they would be discussed by the group—sometimes acrimoniously, sometimes harmoniously. But it really took probably a decade and a half until that was—that came to the point where everybody felt that there was benefit in doing that.

Tacey Ann Rosolowski, PhD
1:39:17.1
Really?

Gabriel Hortobagyi, MD
1:39:17.8
And that people were not just challenged unnecessarily, but that this was a patient-focused thing.

Tacey Ann Rosolowski, PhD
1:39:30.2
Why do you think it took so long for people to be convinced about the collaboration?

Gabriel Hortobagyi, MD
1:39:34.5
Because physicians are fiercely independent—and especially physicians in certain specialties—and I point first at the surgeons. Even within that surgical group of very accomplished and highly skilled surgeons, there were no two who did the same thing. And each of them felt that they knew better than the other two or three how to treat breast cancer. And therefore to question why was—to question their integrity—to question their skills. And in retrospect, perhaps some of that is because they couldn't tell me why they did it differently than the next person, why they cut here as opposed to here. But that is just my theory. But it takes a process until you are comfortable enough in your skin to say, "Okay, so this person from a different

specialty is asking me something that goes to the fundament of my—what I think is my knowledge about my specialty. How dare he?" And as opposed to reacting like that say, "Well, he is asking me either because he doesn't understand, and I haven't explained it well enough or because there might be another option that I should consider." But that takes taking a step back and looking at the bigger picture. And I think that ability to step back is what helped me tremendously over the next several decades to bring our group together and make it a more productive and more interactive group. But it means sometimes—and I am not exactly a humble person—but it sometimes means swallowing your pride and swallowing your tongue and just becoming a better listener and sometimes just serving as the lightning rod for other people to vent and do their thing until they realize that I am not trying to threaten them or take anything away from them.

Tacey Ann Rosolowski, PhD
1:42:02.3
Dr. Hortobagyi, it is 2:30 now, so why don't we finish for today, and we will resume next week.

Gabriel Hortobagyi, MD
1:42:08.4
All right. Well, thank you very much—very enjoyable. I hope I didn't ramble too much.

Tacey Ann Rosolowski, PhD
1:42:14.3
No. Not at all. It has been a pleasure speaking to you. And I am turning off the recorder at 2:30.

1:42:19.0 (end of audio)

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Gabriel Hortobagyi, MD

Session 2—January 7, 2013

Chapter 00B
Interview Identifier

Tacey Ann Rosolowski, PhD
0:00:01.1
We'll start up again. This is Tacey Ann Rosolowski, and today is January 7, 2013. The time is 1:14, and I am in the office of Dr. Gabriel Hortobagyi in Pickens—no, in the Cancer Prevention Building on the main campus of MD Anderson, and we are having our second interview session today. So thank you for giving me this time.

Gabriel Hortobagyi, MD
0:00:27.1
Thank you for having me.

Interview Session: 02
Interview Date: January 7, 2013

Chapter 8
A: The Researcher
Discovering the FAC Regimen for Metastatic Breast Cancer

Story Codes
A: The Researcher
B: MD Anderson History
A: The Researcher
C: Discovery and Success
C: Patients
C: Cancer and Disease
C: This is MD Anderson
B: Understanding the Institution
B: Institutional Mission and Values
C: Healing, Hope, and the Promise of Research
A: Overview
A: Definitions, Explanations, Translations
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care

Tacey Ann Rosolowski, PhD
0:00:28.1
It's wonderful, and we were just talking about how today we were going to begin with a focus on the history of—the evolution of your own research, and you were going to talk about kind of the big phases into which that was broken up.

Gabriel Hortobagyi, MD
0:00:46.0
Right. Let me start by saying that in my view, very few individuals discover or invent anything. Most of us who have made some progress have taken information from various sources that were available at the right time, and we just saw the relationships and the interactions of these various sources of information, synthesized, and put them together. In other words, we stood on the shoulders of giants, as the old saying says, and we put together a package from various sources and moved the field forward that way. When I arrived at MD Anderson as a trainee, there were a number of very exciting things happening, and these exciting things provided incredible

opportunities to make progress—progress for the field, progress for our patients, of course, and secondarily, progress for individuals who were willing to work hard and think imaginatively about the field. At the time I arrived, there was a generational change taking place within MD Anderson, and some of the original pioneers were either reaching the peak of their career or were already on their way to retirement. That opened opportunities in terms of employment and initiating new research without having necessarily to step over toes of other people who might have similar interests.

Tacey Ann Rosolowski, PhD
0:02:51.9
Was there an intellectual and philosophical shift that that enabled as well, with the old guard moving out of the institution?

Gabriel Hortobagyi, MD
0:03:02.1
Clearly there was. At the time I arrived—as we might have covered in an earlier conversation—there were two departments of medicine, for instance, and one department was a very well structured, very traditional Department of Medicine where I believe the major emphasis was on providing excellence in patient care, and there was much less effort and passion dedicated to innovation. The other department, which was called Developmental Therapeutics, was much more focused on innovation and moving the field forward with much less emphasis on just providing traditional care. That meant that that department was not interested in excellence in patient care. It's just that was not the primary driver of the department, and the second department was much more recent. It had just been established a few years earlier. It was populated by a lot of young people who were bright-eyed and bushy-tailed and wanted to move things forward and had a fairly visionary leadership, too—Dr. Freireich and Dr. Bodey and Dr. McCready and others—and I happened to join that department as a trainee.

0:04:35.1
That provided me not only the opportunity but also the environment to focus on innovation and focus on how to make things better. And as I may have mentioned earlier, it was the first time we were really thinking of cancer in terms of we can take care of this. We can control it. We can perhaps cure it in a number of circumstances, and we don't need to look at cancer as a uniformly fatal disease where there is no hope, which was the prevailing attitude in many areas.

Gabriel Hortobagyi MD
0:05:16.7
The second part is that around that time, a number of very important new drugs were being discovered: the anthracyclines, adriamycin, epirubicin, and daunorubicin were just coming

online. They were in phase II studies. Cisplatin was just in phase I finals at that time. Vinorelbine was a new drug. Tamoxifen was a new drug. All of these were still looking for someone, some champion to move them forward. The third part is that we had a group of very bright individuals who were my immediate mentors—Jordan Gutterman; J Freireich, of course; Jeff Gottlieb; and others—who were so totally focused on moving the field forward that you couldn't possibly think of anything else. When you put all of this together, then I had the opportunity of putting together a combination. I can't claim total credit for that because it was really a group effort—the fluorouracil-doxorubicin-cyclophosphamide combination, also known as FAC—which was first put together in this institution. I was one of the lead investigators in making sure we found the place for that in breast cancer.

Tacey Ann Rosolowski, PhD
0:07:07.10
Can you describe to me what were the characteristics of these drugs that made them so effective and that made them so effective together?

Gabriel Hortobagyi, MD
0:07:19.9
The anthracyclines—especially adriamycin, which is more relevant to our discussion—the anthracyclines are a group of antibiotics that are produced by a group of fungi, and they have a very specific target today we know, which is the inhibition of topoisomerase II, which is critically important for processes of cell division and DNA repair. By interfering with that process, they produce lethality in cancer cells and in other cells. These drugs were found to be some of the most effective drugs not only in breast cancer but in lymphomas, in Hodgkin's disease, in gastric cancer, in a variety of other tumor types. Fluorouracil is one of the most commonly used drugs—or was at that time—and it was a broad-spectrum cytotoxic agent with a significant efficacy in breast cancer, in colorectal cancer, in lung cancer, and so on. Cyclophosphamide is a classical alkylating agent which is much better tolerated than the original alkylating agents like nitrogen mustard and busulfan and others. And again, it is a broad-spectrum antibiotic that is quite effective in breast cancer, in lymphomas, in lung cancer, et cetera. And what makes these three drugs such a natural combination is that they have different mechanisms of action. They have largely non-overlapping toxicity, and they have different mechanisms of resistance; and therefore, there is every reason to believe that by combining them, not only would one get a higher response rate by perhaps targeting different cell populations within the same tumor but that there would be a built-in mechanism to prevent the evolution of drug resistance against any of them because evolving drug-resistant populations would be attacked—one drug would be attacked by the other two—and that one could do this with almost full doses because the toxicities were not overlapping. One was not just adding toxicities by adding one drug to the other.

0:10:25.0
Those were important characteristics of this particular combination, and when put in practice, well, it turned out to be a very, very effective regimen. And arguably, it is even today one of the most effective combinations—certainly in the area of breast cancer. We developed this in metastatic breast cancer, and the initial analysis that I did suggested that two out of three patients with metastatic breast cancer had an objective response to it—meaning a greater than fifty percent reduction in tumor area—and that some of them had what we call the complete clinical remission with the disappearance of all physical and radiographic evidence of metastatic disease. So that was very encouraging.

Tacey Ann Rosolowski, PhD
0:11:20.1
Can I ask you how long—what was the response time required to see those results?

Gabriel Hortobagyi MD
0:11:28.2
In metastatic disease, on average it takes about nine weeks to start to see an objective response. Now that means reaching the criteria by which we define partial remission or greater. But you start seeing responses much earlier, sometimes within the first three weeks. Sometimes in patients who were symptomatic, we would see—we would experience pain relief within just a couple of days. The rapidity of the response was quite notable. Now there is a delay between a biological response and until one can document that by radiography or nuclear medicine or some other imaging methods, so that's why it takes about three cycles or about nine weeks, to document an objective response. But this is a very effective regimen. Once we started to see how effective this regimen was in metastatic disease, then we started to think along several lines of research.

Tacey Ann Rosolowski, PhD
0:12:47.8
Before you do that, can I ask you how did you come upon this particular group of drugs from those three categories?

Gabriel Hortobagyi MD
0:12:59.3
Prior to the early 1970s, essentially all of chemotherapy for breast cancer, which was very modest, was based on single agents. You used one drug at a time. There were a few exceptions. There was a pioneer from New York, Ezra Greenspan, who put together two and three drugs and obtained some improved responses. But brilliant as he was, he only published in the private

journal of the Mount Sinai Hospital in New York, so it never reached a broader circulation or readership. Another very bright individual from that time in Roswell Park, Richard Cooper—who is in one of those photos up there and is a good friend—he put together a five-drug combination with cyclophosphamide, methotrexate, fluorouracil, vincristine, and prednisone, which later became known as the Cooper Regimen, and he presented his very exciting results at an ASCO meeting, but he never went beyond an abstract. He never published a full paper. So essentially combination chemotherapy was nonexistent, for all practical purposes, in the early 1970s.

0:14:32.4
But we already knew that there were a number of drugs—not many, mind you—but we knew that alkylating agents were effective against breast cancer—somewhat modest efficacy, but they were effective, and 5-fluorouracil was effective against breast cancer. The most exciting new development when I arrived was adriamycin. That was arguably—and even today—one of the two most effective drugs against breast cancer. At that time it was clearly the most effective drug against breast cancer, and there were some others which were of marginal efficacy: vincristine, the corticosteroids, the nitrosoureas, perhaps mitomycin C. But those were either much more toxic or much less effective. These three drugs were clearly the ones to pick on. A fourth drug that would have been perhaps an important contribution was methotrexate, but methotrexate has overlapping toxicities with both 5-fluorouracil and with adriamycin, so it would not have been a good choice. By deduction and elimination, these three drugs became the winners, and there was some previous experience combining 5-fluorouracil with cyclophosphamide, and then there was some pilot experience combining adriamycin with cyclophosphamide, so then it was a natural step to go to the three-drug combination.

Tacey Ann Rosolowski, PhD
0:16:13.4
Well, I'm curious. How did that happen? I mean, did you sit down with your group of collaborators and say, “Let’s put all the pros and cons on the table” for each of these? What was that process like?

Gabriel Hortobagyi, MD
0:16:27.7
There was a continued process of communication and looking at the drugs that existed at the time and the common solid tumors that we had in front of us to deal with, and there were some limitations in terms of what we could address—one, because a very common solid tumor, prostate cancer, was entirely in the hands of the urologists. The medical oncologists did not see prostate cancer in the early 1970s. The colorectal cancer seemed largely resistant to many drugs, or at least that was the reigning belief. There was not much enthusiasm for getting into colorectal

cancer. Melanoma seemed highly resistant. Sarcoma seemed highly resistant. Breast cancer was sort of the poster child of let's develop combination therapy, because after the lymphomas, it seemed to be the most responsive type of cancer, and we had in front of us the example of lymphomas. The group of Dr. Freireich when they were at the NCI and then later with credit claimed by Vincent DeVita, they put together MOPP and other combinations that ended up being curative. At that time, we were thinking we can do the same thing in breast cancer. We have now three or four drugs that are substantially effective that we can combine, and we think that we can combine them, so let's put them together. The initial idea was to administer each of these drugs once per week. That didn't work out quite well, so it turned out we could give adriamycin best once every three weeks and cyclophosphamide best by giving it once every three weeks. With 5-FU we wanted to give it every week, because at that time it was thought that that was the best regimen.

Tacey Ann Rosolowski, PhD
0:18:43.9
So you didn't mix all the drugs together in one cocktail.

Gabriel Hortobagyi, MD
0:18:46.6
No, no, no. But it turned out that because of myelosuppression—a drop in blood count—it was not possible to give 5-FU every week. We could do it the first week and the second week, and then we had to skip the third week, and this was arrived at largely by empirical testing. Now it would have taken us much longer today because of the regulations and because of all the restrictions about how you go about research. At that time you could take drugs—those that were commercially available—and you could administer them in any way that you considered was safe and appropriate. You could experiment with schedules and doses, and adding adriamycin to that was relatively easy. We worked this out in a relatively short period of time—just a few months—by treating some with a one-dose schedule and the next few with another dose schedule, and there was no encumbrance to that type of research. And then once we came up with the combination, then we wrote a protocol, a clinical trial. Then we tested it formally.

Tacey Ann Rosolowski, PhD
0:20:12.7
Who was involved in this first push of the research with you?

Gabriel Hortobagyi MD
0:20:16.8
Jeff Gottlieb, Bob Livingston, who was an assistant professor at that time, and George Blumenschein. That then went forward. In the meantime, my immediate mentor was—or one of

my immediate mentors—was Jordan Gutterman, and Jordan Gutterman and Evan Hirsch were heavily focused on harnessing the immune system, immunotherapy of cancer. That was the Holy Grail of oncology at that time, and there was much, much excitement about that. Our initial emphasis was on the administration of BCG, or Bacillus Calmette-Guerin, as a way to enhance the immune reaction of the host. One of my priorities at that time was to add BCG to this new redeveloped combination of FAC, and some of my early papers were based on that. The initial results seemed very promising. Later we put it through more formal tests, and the results were much less conclusive. And eventually we abandoned that line of research, but that kept me busy for several years.

Tacey Ann Rosolowski, PhD
0:21:58.0
Were there important lessons learned from that period of experimentation?

Gabriel Hortobagyi MD
0:22:03.7
Very. Secondarily we figured out that the more a patient reacted to the administration of BCG—the stronger the local reaction—the better the patient would do. Initially we thought that was the effect of BCG. Later we figured out that it was more a question of the patient's immune status baseline. And in fact, I did a series of studies in which I looked at baseline immune response by skin tests and other immunological tests to look at the patient's immunocompetence. And it turned out that those who had the greatest immunocompetence at baseline lived longer and had a higher probability of response to chemotherapy and longer duration of response to chemotherapy. One starts with one hypothesis and sometimes ends up with another. But that observation certainly ended up twenty years later guiding many of the current examples of the immunotherapy in breast and other cancers.

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Chapter 9
A: The Researcher
Treatment for Locally Advanced Breast Cancer
Story Codes
A: The Researcher
C: Discovery and Success
C: Patients
C: Cancer and Disease
C: This is MD Anderson
B: Understanding the Institution
B: Institutional Mission and Values
C: Healing, Hope, and the Promise of Research
A: Overview
A: Definitions, Explanations, Translations
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care

Gabriel Hortobagyi MD
0:23:28.8
We also looked at a variety of other immunological agents like corynebacterium parvum, levamisole, the Coley's vaccine, et cetera, and all of them were very nonspecific. And in retrospect, I think we were observing the same effect—that if you were more competent at baseline you would do better—but that the nonspecific stimulation of the immune system had limited success, certainly when applied to a large group of patients. But in the meantime, and based on the success in metastatic disease, then another door opened, and that was the situation with locally advanced breast cancer. In the early '70s in this institution, we were seeing a lot of women with newly diagnosed locally advanced breast cancer.

Tacey Ann Rosolowski, PhD
0:24:38.8
Can you explain to me what that means, "locally advanced?"

Gabriel Hortobagyi MD
0:24:41.3
Locally advanced breast cancer means that the tumor in the breast reaches very large size, sometimes spreading to several of the regional lymph nodes without necessarily spreading to other organs or metastasizing. To a large extent, that is the effect of late diagnosis, either because of neglect or denial or lack of access to medical care. Sometimes it is because some very

aggressive breast cancers actually do not form a detectable mass. They just grow sort of sheet thin, and the patient or the woman doesn't notice that there is a mass in her breasts. She just notices perhaps that her bra doesn't fit well on one side, whereas previously it did. But most of the time, these used to be neglected tumors that had ulcerated. They were foul smelling and bleeding and whatnot, and you had to wonder what was going through the mind of that person or the minds of those who surround her because some of these—you could smell them from down the hallway. If you were to be the spouse of that person, it was impossible to imagine that you didn't know that there was something wrong.

0:26:20.6
Be that as it may—and of course, this was before the establishment of mammographic screening and early detection of breast cancer, which changed the situation dramatically. But at that time, we were seeing probably 300-400 locally advanced breast cancers per year. And of course, it helped that we were a public hospital, that we were a state hospital, and women without other resources were able to find care here. But it also was a consequence of the southern part of Texas being less prosperous and having a greater degree of poverty.

Tacey Ann Rosolowski, PhD
0:27:13.1
Was that 300-400 statistic higher than in other areas of the country?

Gabriel Hortobagyi MD
0:27:18:0
Oh, yes. Oh, yes, although locally advanced breast cancer has mostly been a phenomenon of the South. Our counterparts at Memorial Sloan-Kettering in New York—they haven't seen one in decades, so when we talk about locally advanced breast cancer, it's like what is that?

Tacey Ann Rosolowski, PhD
0:27:41.7
And is that a lack of access? I mean, what's the cause?

Gabriel Hortobagyi, MD
0:27:44.6
It's a combination of all those things. It's lack of education, lack of access, lack of resources—all of those things. Those large tumors, as you might imagine, would require very extensive surgical procedures and very extensive radiation therapy procedures in order to try to get control of them. But despite heroic surgical interventions and very high doses of radiation therapy by some of the pioneers of both fields in this institution—and they were truly extraordinary, skilled people—it was an exercise in futility. Because despite these huge operations, the majority of these patients

would die of their breast cancer within just a couple of years and it was because—women don't die of breast cancer from having a lump in the breast. Women die of breast cancer because some of the cancer cells develop the ability to spread to other organs and gain access to the general circulation—to the blood circulation—and they travel wherever that takes them. And once breast cancer reaches those dramatic dimensions, then there is a great preponderance of cells that have the ability to metastasize.

0:29:15.1
So after dealing with this for a decade or two, our surgeons and radiation oncologists—who at the time I arrived still looked at medical oncology as what are these upstarts trying to accomplish here? They don't have anything to contribute. We are the ones who cure cancer. And they were not really referring patients to us, so finally they sort of relented with this group of patients, because they noticed themselves that they were not making any progress, and they were banging their heads against the wall. We started to see these patients, and it was very dramatic because we said, "Well, we've got this FAC regimen. Let's use it in these patients. The majority of them are going to die, so there is no real safety issue here; and at the same time, they are dying of metastatic disease. This is like having metastatic disease except that now we have something that is very easily measurable." We started to treat a number of these patients, including a subset of them that had what we call inflammatory breast cancer, which is a very specific subtype of locally advanced breast cancer where the skin of the breast becomes red and acquires, because of swelling, the appearance of orange skin, which at that time we called peau d'orange—probably because some French investigator described it some years earlier. Inflammatory breast cancer is the most lethal form of breast cancer. If you treat the inflammatory breast cancer with surgery alone or radiotherapy alone or the combination of those two, about ninety percent of those patients have metastases within two years, and ninety-five percent of them are dead by five years. It's a horrible, horrible disease.

0:31:34.6
We started to treat all locally advanced breast cancers with chemotherapy first. We gave them three cycles of our new cocktail; and lo and behold, the great majority of them had a magnificent response. About ninety percent achieved an objective response with a greater than fifty percent reduction, and about ten percent of them had a complete response, and the majority actually became operable with much less extensive surgical resection. Then we came up with this multidisciplinary regimen in which we started with chemotherapy for three cycles. Then we did either surgery or radiation therapy, depending on what was feasible at that time, and then we continued chemotherapy afterwards until we figured out we had to stop. Then all of a sudden, these patients were not only less disfigured but they started to live. And while it wasn't a total cure rate, we went from a five-year survival of about ten percent to a five-year survival of about

fifty percent, and that was a very substantial jump. And all of a sudden, the reigning pessimism about locally advanced breast cancer started to change.

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Chapter 10
B: Building the Institution
A Great Step for MD Anderson: Building Multidisciplinary Teams

Story Codes
B: Critical Perspectives on MD Anderson
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
B: Institutional Mission and Values
C: MD Anderson Past
B: Controversy
D: On Research and Researchers
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care
C: Professional Practice
C: The Professional at Work
C: Collaborations
A: The Administrator
D: On Research and Researchers
D: The Healthcare Industry
D: Fiscal Realities in Healthcare
B: Beyond the Institution
D: Global Issues –Cancer, Health, Medicine

Gabriel Hortobagyi, MD
0:33:08.3
In the meantime, I became quite uncomfortable about the less than collegial interaction between the various specialties in the breast cancer field here. And especially there was a not very collegial interaction between medical oncology and surgery with a little bit more neutral interaction with Radiation Oncology. I started to organize a biweekly conference in which we invited everybody interested in breast cancer to come and discuss specific cases.

Tacey Ann Rosolowski, PhD
0:33:55.8
I'm sorry to interrupt you. I missed the second division or department that you were interacting with. Medical oncology and surgery and then medical oncology and—?

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Gabriel Hortobagyi, MD
0:34:05.6
Radiation.

Tacey Ann Rosolowski, PhD
0:34:09.3
So you began to invite people to discuss cases.

Gabriel Hortobagyi, MD
0:34:11.8
Right.

Tacey Ann Rosolowski, PhD
0:34:14.1
And about what year was this?

Gabriel Hortobagyi MD
0:34:16.6
This is 1975 probably. And then at the beginning a few would come, but then increasingly more and more would show up, and then we would discuss specific cases. We would look at their x-rays. We would look at their pathology. We would talk about them, and we would try to reach a consensus about what was the combination of treatments and the order of treatments that would best suit those patients. And then eventually when you start to talk to people and to listen to people, more importantly, all of the mistrust goes away. And then slowly we built a mutually respectful team that persists to this day. I think probably arguably that is one of the greatest steps forward we took in this institution, because we did that probably twenty years before the concept of breast centers started to come around, and we were doing this well before the ’90s. Today there is a lot written about comprehensive breast centers and multidisciplinary care and whatnot, but that was really developed in this institution, and it was developed thanks to the willingness of all of my colleagues to come together and put their anger and mistrust and ill feelings aside.

Tacey Ann Rosolowski, PhD
0:35:53.5
With that process, was it a bumpy ride at first?

Gabriel Hortobagyi MD
0:35:58.0
Oh, it was a bumpy ride for about ten years. It didn’t happen overnight.

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Tacey Ann Rosolowski, PhD
0:36:04.2
How did it work? Did you and others come in and sort of smooth feathers? Or was there an agenda? How did you manage it? That's a big cultural change.

Gabriel Hortobagyi MD
0:36:16.2
There was always an agenda, and we had a number of patients that were listed. We specifically invited those who were responsible for the care of those patients in the various departments, and then we started to talk not only about those patients but in discussions it was obvious that there was a difference in opinion about something. We would start talking about, okay, that's wonderful. Here there are two experts with great experience in this who disagree completely about a matter of great importance. Why don't we put that to a test? And then we would develop protocols, clinical trials that would then test whether it is better to do this first or the other things first.

Tacey Ann Rosolowski, PhD
0:37:13.9
What were some of the clinical trials that came from this process?

Gabriel Hortobagyi MD
0:37:17.4
Well, the first clinical trial was, for instance, the sequence of chemotherapy first followed by either surgery or radiation therapy and then followed by more chemotherapy. Then based on that we were able to determine that neither surgery alone nor radiation therapy alone was sufficient for this and that we actually needed both of them. Then the next protocol included both of them, and then we tested the sequence, and then gradually we developed that. Viewed with today's eyes with what we consider to be level one evidence and the gold standard of clinical trials, which is the randomized trial, those were modest steps because randomized trials were not acceptable in this institution in the early '70s. In fact, there were several intellectual leaders who were vociferous against randomized trials and considered them immoral, because if you thought you could do better with something, how could you even test the other aspect? Those were philosophical discussions about whether real equipoise exists when you really have an idea that you think you can do better.

Tacey Ann Rosolowski, PhD
0:38:46.3
What was your view of that at the time?

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Gabriel Hortobagyi MD
0:38:49.5
Well, I thought all along that science moves because one comes up with a hypothesis and that sometimes that hypothesis is right. Sometimes it is wrong, but the only way to figure out what is right and what is wrong is by testing it. And by testing it, you have to put aside your own prejudices and your biases; and therefore, the randomized trial is an important tool. Not the only tool, but it is a very important tool. And in that, I found myself in disagreement with some of my colleagues, especially some of my mentors. But gradually one is able to implement things, and eventually, several years after my arrival, we were able to initiate some randomized trials, and we then initiated and completed a number of randomized trials over the years that have had a substantial impact on the management of breast cancer.

Tacey Ann Rosolowski, PhD
0:39:58.2
Can I ask another kind of historical question about this? Because it sounds like—I mean, this being in the early ’70s, this is one of those basic ethical dilemmas. And was this something that all research institutions were wrestling with with cancer questions? Or was that more—it happened more at MD Anderson because of the leadership here? How would you evaluate that?

Gabriel Hortobagyi, MD
0:40:27.8
Well, randomized clinical trials were first developed in the 1940s, probably with antibiotics. But they were few and far between until the 1960s. There were a couple done in the 1950s, but they were not considered the standard. Clinical research essentially was I will do this, and then I check back later to see how I did. That was, of course, valuable in some ways because you could test whether your idea was feasible or not. You can test whether you caused some benefit or whether you caused some harm. But in the absence of comparing it in an unbiased manner to something that a large proportion of your colleagues considered the standard, it was not a very useful technique because it was always intended to fulfill your biases and prove that you were right, and that’s not the point of science. That’s not the point of investigation. In this institution, everybody struggled with that controversy, and it required a cultural change on the part of everyone. And even today some specialties do better than others in that respect.

0:42:19.7
And I'm not just talking about the oncology world but in general. I can tell you, for instance, oncology—and in that I include all oncology, surgical, radiation, medical, et cetera—we are light years ahead of the rest of medicine in terms of randomized trials. Just as an aside, for instance, when I was president of ASCO, I asked my outcomes research committee to put together a review paper or position paper or consensus paper about PET scanning and breast cancer—

Positron Emission Tomography and breast cancer—because in the radiology field it was being seen—and I'm talking six or seven years ago—as the greatest thing since sliced bread, and there was very little evidence for that. There were a number of small papers of fifteen, twenty, thirty patients—each no controls—and that was their conclusion. I asked the members of this committee to identify a number of leaders in the radiology community, bring them together, and try to either design clinical trials that would give us the answers or try to come to a consensus. And after a year of deliberations, there was absolute impossibility to even come close to a consensus because the oncologists wanted this particular imaging modality to be put to a test in a randomized trial, and the radiologists absolutely saw no reason to do it.

0:44:20.7
You see other examples in our day. For instance, our institution has invested a huge amount of money and places a lot of emphasis on proton therapy. We have a huge thing down the road about proton therapy, and those of us who are not radiation oncologists—we are still waiting for some evidence from a control trial that using the very expensive technology of proton therapy is any better than using standard external beam photon therapy or electron beam therapy. And it is not because the radiation oncology field is so polarized that some radiation oncologists think they already know that it is better, and therefore, they see no reason to test it. And others don't think that it is ever going to be better, and they don't see any reason to test it for that reason. The same in the prostate cancer field. As you know, there has never been a consensus reached about when you have early prostate cancer, are you better treated by a prostatectomy—therefore surgical excision—or by radiation therapy to the prostate? And that has never been put to a test because those two specialties cannot come together to design a trial. And I think it's tragic for medicine to find ourselves in a situation where you reach an impasse where no evidence-based answer comes forth because we believe that we are scientists but we don't act like scientists.

Tacey Ann Rosolowski, PhD
0:46:14.6
I was just going to say that I've had a number of conversations with people who have mentioned that clinical research seems to be a poor handmaiden when it comes to a comparison with laboratory research. But this cultural issue might be a very strong factor in that.

Gabriel Hortobagyi MD
0:46:36.6
It's a huge factor in that. Clinical research is hard enough because when you're in the lab and you deal with test tubes, you have absolute control over the circumstances. You can define the temperature. You can define the number of cells. You can define the nutrients. You can define the time. You can define the amount of drug you put in there or whatever your experiment is. Or if you're dealing with animals, you can pick the exact type of mice or rats or monkeys or dogs.

You can define when you transplant the cancer, when you give them the carcinogen. You can define how long you watch them. You can define how large you let the tumor grow before you do A, B, C, or D. Everything is under your control. When you deal with human beings, you can't. We are a highly inbred species. We have subtle differences, but we are all somewhat different. We all have a life, so I can tell my patient, "I want you to receive drug X every three weeks." Well, she may be able to do that the first two times, and then the third time she runs into a car accident, or her child is sick, or some other thing happens. She develops the flu, and she misses that appointment. Well, what can I do about it? It's a fact of life. Or I give the same dose to Mrs. Jones as to Mrs. Smith, and Mrs. Jones tolerates it perfectly well, and Mrs. Smith gets deathly ill with that same dose. Well, the two of them have different metabolisms, so on and so forth. You have to deal with that, and you have to do the best you can, and you have to realize that you cannot control everything. We know from large clinical trials that we get compliance. Depending on what we are trying to accomplish, compliance is anywhere from fifty to seventy percent with what we are trying to establish. So then you have to make statistical adjustments to that to make sure that you don't lose the power of the observation. It's very complicated, even when everybody is committed to it. Now if nobody is committed to that, then it's impossible to do, but you're correct. Clinical research is much harder because of that than laboratory research and in some ways much more frustrating because of that. Because sometimes you do a clinical trial. You run a clinical trial for five, ten years, and at the end of that, you have nothing to show for it because of all of these intricacies and these complexities. Well, but I digress.

Tacey Ann Rosolowski, PhD
0:49:41.4
Actually, if you don't mind, I'd like to ask one more question, because as your own persona as a researcher evolved, how did you come to your own intellectual peace with that process and learn how to be flexible in the face of all those frustrations?

Gabriel Hortobagyi MD
0:50:06.8
Well, first of all, it's because I'm a natural skeptic. So while I have a lot of respect for my elders and those who preceded me, the more I learned about science and the more reading I did, the more I realized that the way to make progress was to continuously question pretty much everything and to really look for the evidence behind every sweeping statement. And there are many sweeping statements in medicine. And yet, when you look at what we do as physicians, much of what we do—the majority of what we do—and now I'm talking about medicine in general—has never been proven by what we call level one evidence. Much of it is anecdotal, and there are millions of examples in medicine where we do things for years or decades or centuries that have absolutely no basis in fact. And even in modern times, we continue to do things because we lose the mental discipline or the scientific discipline that should be an absolute necessity in the practice of medicine. Now I don't want you to go away with the idea that I'm a

purist and that I want the randomized trial to support absolutely everything we do because that day will never come. There are far too many questions, too many details, too many complexities for us to be able to test them in a randomized trial. And randomized trials are very expensive, very labor and time consuming, so that is not possible. But certainly some of the basic issues, some of the basic principles, need to be established.

Tacey Ann Rosolowski, PhD
0:52:31.9
What are some of those principles that you feel have not been demonstrated but right now need to be very desperately?

Gabriel Hortobagyi MD
0:52:39.7
Well, I mentioned to you, for instance, the situation in prostate cancer where depending on what door you walk into in this institution or to your physician when you are first diagnosed with prostate cancer, you are told to do this or that. Entirely different treatments with different complications, and we don't know whether they have similar or very different efficacy because we have never compared them. We have done that in the breast cancer area, and we have done that in colorectal cancer and in lung cancer and whatnot. Why not in the area of prostate cancer? And unfortunately, by doing certain comparisons in one cancer it does not guarantee you that the answer will be the same in others. Those types of things need to be established. I think technical progress is one thing.

0:53:43.8
Clinical utility is something else. For me to accept that proton therapy is better than electron beam therapy or even something as basic as cobalt-60—which still is the equipment used in many third-world countries and does a perfectly good job—I think there is a need to demonstrate that, to demonstrate that both in terms of what is good and what is bad about that because we always imagine that everything that is new is better, but most things have two sides. Most technical improvements are a double-edged sword, and we need to understand that. And the only way we can understand that is by comparing the new one with the old one. I think those are critical issues, and some of the things we do that are new in addition to the importance of understanding in what way are they better or in what way are they worse are incredibly more expensive. I can give, for instance, someone adjuvant chemotherapy for breast cancer for about $1000 for the entire course; or I can spend $200,000 with our newest and greatest adjuvant chemotherapy and biological therapy program with all the bells and whistles. Now it just happens that we have non-randomized trials all throughout the process between the most basic and the most expensive one, and we know that there are some incremental benefits along the way.

0:55:59.9
But by having done that, then I can go back and do what I did, for instance, with others in a group called Breast Health Global Initiative where we developed guidelines for countries of limited resources. You can think that we live in a very rich and very prosperous country, and therefore, we can afford everything for everybody. I don't think that's true, but we are certainly privileged to live in a country with lots of resources. But when you live in Ghana or Mali or Bolivia or hundreds of countries like that, you can't because people's average daily income is under a dollar, and the entire healthcare budget for the country is less than one-tenth of the annual budget of MD Anderson. You can't say we're going to give the $200,000 adjuvant regimen to everyone with a certain type of breast cancer in Mali. It just doesn't work. We were able to backtrack and say the incremental benefit from going from $1000 to $200,000 is this much. Is that worth it for the public health of that country, recognizing that it was not optimal? But you can't do that if you have never done any of the comparisons. You don't know what you're missing. You don't know what is worth that incremental cost. So I think identifying some basic questions in each of our specialties and identifying some options and comparing them is very important. Now today one of the emerging specialties in medicine—specialty in oncology—is comparative effectiveness research, and I think that's critically important.

Tacey Ann Rosolowski, PhD
0:58:20.7
I'm sorry. I missed the first word.

Gabriel Hortobagyi, MD
0:58:22.4
Comparative.

Tacey Ann Rosolowski, PhD
0:58:23.7
Oh, comparative—comparative effectiveness.

Gabriel Hortobagyi, MD
0:58:25.3
Comparative effectiveness research or CER, and in fact, part of the ACA, the Affordable Care Act, is to dedicate a certain amount of resources to doing that—to compare treatments that are seemingly focused on the same condition and trying to figure out which is better. Which is better in terms of effectiveness, and which is better in terms of cost, and which should be the standard of care for our community? And while some people think of that as, oh, that will lead to

rationing, when we scream about we don't want to pay more in taxes, then we need to figure out who is going to pay for our healthcare.

Tacey Ann Rosolowski, PhD
0:59:24.7
And what exactly we're paying for.

Gabriel Hortobagyi MD
0:59:26.4
And what exactly are we paying for, and is it worth paying for that?

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Chapter 11
A: The Researcher
Adapting LABC Treatment for Stages 2 and 3 Breast Cancers

Story Codes
A: The Researcher
C: Discovery and Success
C: Professional Practice
C: The Professional at Work
C: Cancer and Disease
B: Understanding the Institution
B: Controversy
A: Overview
A: Definitions, Explanations, Translations
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care

Gabriel Hortobagyi MD
0:59:26.4+
So we developed then this process, and the process became sort of the classical approach to locally advanced breast cancer. It was chemotherapy. Eventually we increased it to six months then a surgical resection, which initially was a mastectomy. It later became a mastectomy for some, breast-conserving surgery for some others, and then radiation therapy. And then for patients with certain subtypes of breast cancer, hormonal therapy, and for certain other subtypes of breast cancer, Herceptin, and that is today the standard of care for all locally advanced breast cancers. And in the process of doing that, we became so encouraged by the results that we said, "We don't have to limit this to these horrendously large tumors. But we could probably do this in patients with earlier—still large—but earlier tumors." And so then we moved to the large, operable stage III tumors and eventually to stage II tumors. And then secondarily, I was invited to help design a national clinical trial that compared my strategy with the traditional strategy of surgery first followed by adjuvant chemotherapy for clearly operable, earlier breast cancer. And that demonstrated that the two approaches were clearly interchangeable in terms of survival and that there were some advantages for doing chemotherapy first.

Tacey Ann Rosolowski, PhD
1:01:17.0
And those advantages were?

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Gabriel Hortobagyi MD
1:01:19.1
That in many cases patients who were only candidates for mastectomy after chemotherapy could be offered breast reconstructive surgery, that by not removing the tumor upfront you were actually able to watch what your chemotherapy was doing. Was it working or was it not? Because once you remove the tumor, you are sailing blindly. You have no idea whether your treatment works or not, and when you're talking about six months of chemotherapy, doing that condemns that patient to receiving that treatment whether she's benefiting from it or not. And I think that is not acceptable because you can tell within a month or two if things are not working, and at the very least you can stop something that is not working from producing toxicities and side effects. And in the best of cases, you can also change to a different chemotherapy regimen that might work better, so that's another aspect of it. By doing that and by taking some intermediate outcomes—like how much residual disease is there after chemotherapy at the time of surgery—you can make up your mind about the value of that initial treatment much faster than if you remove the tumor and you have to watch for years, sometimes decades, to figure out who benefited and who didn't. And fourth because you can—from the point of view of pure science—you can sample the tumor as you go along with treatment and figure out what are the biological consequences of administering chemotherapy or Herceptin or a vaccine or whatever you're administering before surgery. All of those are advantages are very, very important; and as a result of that, forty years later most of the national trials that are looking at new drugs or new procedures are using the new adjuvant chemotherapy or adjuvant systemic therapy model. And I think that's very gratifying, because for many years, people didn't believe that that was a good idea or that that was possible or that that was wise.

Tacey Ann Rosolowski, PhD
1:03:43.3
What was the reason for the lag time in accepting that?

Gabriel Hortobagyi MD
1:03:48.0
Well, physicians are fairly conservative, and to some extent it was because in the early years we didn't do what in retrospect would have helped very much, which was to do a randomized trial in the early '70s. We would have shortcut the process certainly by a decade, perhaps two. It was the NSABP's national trial that was started in 1988 and was reported about seven years later that actually helped make the transition, and then people looked back and said, "Ah, yes. MD Anderson has been saying that since the mid '70s. Maybe they were right."

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Tacey Ann Rosolowski, PhD
1:04:39.4
So why wasn't this particular process taken through randomized trials?

Gabriel Hortobagyi MD
1:04:44.5
It was not possible to run a randomized trial at MD Anderson at that time.

Tacey Ann Rosolowski, PhD
1:04:49.5
Okay, so that's where that cultural—

Gabriel Hortobagyi, MD
1:04:51.9
Yes, that's where that cultural thing was a problem. In fact, if I look back at the 1970s, we had I believe four breast surgeons, each of them very accomplished, very well known. Each of them knew that he treated breast cancer better than the other three, and each of them did something different, which in retrospect didn't make any difference. But it was their surgical procedure, and anyone who tried to talk to them about the other guy's surgical procedure had to be totally wrong. Radiation Oncology was much more disciplined, and they had sort of a team. Surgery was the last to come on board in terms of trying to do the same thing. And even today, if you look around the surgical community around the country, it is a cottage industry, and it is a highly operator-dependent—no pun intended—discipline where, depending on where you train, you learn a different technique. And it is very hard to get surgeons to do a clinical trial where all of them are asked to do the same procedure the same way. And in fact, one of the greatest accomplishments of Bernie Fisher—who was a surgeon who was the leader or the chairman of the National Surgical Adjuvant Breast Project—was not necessarily the outcome of protocols, although he contributed much to that, but to convince about 2000 surgeons about the country or around North America to do the same things, to comply with the protocol requirements and therefore test certain procedures—the radical mastectomy, the modified radical mastectomy, lumpectomy and radiation, axillary dissection and then later sentinel lymph node biopsy. That was inconceivable even in the small microcosm of our institution to ask those four surgeons to do that. All of them are gone or dead so I don't want to name names, but that was the situation at that time. Under those circumstances, to do a trial which requires everyone to do the same thing would not have been possible. But two of my most senior mentors would have opposed it with everything they had because that was just the wrong thing to do in their minds.

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Tacey Ann Rosolowski, PhD
1:08:00.6
When at MD Anderson did that particular mentality open up, loosen?

Gabriel Hortobagyi MD
1:08:10.1
In 1988-1990.

Tacey Ann Rosolowski, PhD
1:08:18.1
Very slow in coming then.

Gabriel Hortobagyi, MD
1:08:19.2
Yeah. Yes, it was very slow. It was very slow, and of course in the interval, I myself and my colleagues at my level—Dr. Buzdar and our peers in Radiation Oncology and Ssurgery—we were all evolving, too, because we had been taught this thing of thou shalt not do a randomized trial, or it is fine to do an empiric observation. I remember in the late 1970s and early 1980s there was a very important annual meeting in Tucson, Arizona, and it was organized every year by an oncologist by the name of Sydney Salmon, who was the head of the cancer center in Tucson, and it was called the Adjuvant Therapy of Cancer. It started with breast cancer because that's where the initial clinical trials were done to demonstrate that adjuvant therapy—meaning postoperative chemotherapy—improved disease-free and overall survival. But eventually it included other tumor types. It included some hematological malignancies and colon cancer, et cetera. About the fourth or fifth meeting—so I think I'm talking about the early 1980s—they organized a debate in which Chuck Moertel, who was I believe the head of oncology at the Mayo Clinic and a passionate proponent of randomized trials, and J Freireich, who was of course the VP here and a passionate opponent of randomized trials—they put them up to debate the issue. It was a pretty dramatic discussion, and it brought to a point the difference. And by that time, most of the country was on the side of randomized trials, and we were still opposing it tooth and nail. And I think after that we pretty much had to evolve because the NCI got into the game, too, and I think behind the scenes indicated to MD Anderson leadership that we have to change. Because the field was evolving we evolved, and eventually many of the national trials were led by MD Anderson faculty members, so we have come a long way in that sense.

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Chapter 12
A: The Researcher
From Adriamycin to Molecularly-Designed Drugs

Story Codes
A: The Researcher
C: Discovery and Success
B: Devices, Drugs, Procedures
C: Discovery, Creativity and Innovation
C: Professional Practice
C: The Professional at Work
D: On Research and Researchers
D: The History of Cancer Research and Care

Gabriel Hortobagyi MD
1:11:47.0
Okay, so that was locally advanced breast cancer. That was multidisciplinary planning and implementation of therapy. Now I already mentioned that Adriamycin was introduced by us into the management of metastatic breast cancer and then neoadjuvant chemotherapy. But we also were the first to introduce Adriamycin into the adjuvant treatment of breast cancer. In the early ’70s—again, I'm talking about 1974 or so—we got a number of patients referred to us from the outside by surgeons who had already operated on them. They didn’t go to our surgical department. They came directly to us because our own surgeons were not referring patients to us for adjuvant chemotherapy. They didn’t believe that that would work. We said, “Well, this regimen FAC works so well on metastatic disease and locally advanced breast cancer it should work in these high-risk patients with many positive lymph nodes.” So we put together a protocol for that, and we were the first to report on the results of adjuvant chemotherapy with FAC or with an adriamycin-containing regimen. That continued to be our standard, and eventually it was accepted by the world, probably in the mid 1990s, as being better than all other regimens.

1:13:28.2
By the 1990s, we were the first institution to report that Taxol was every bit as effective as Adriamycin and therefore a force to contend with. And then soon thereafter, we introduced it into adjuvant chemotherapy in sequence with our FAC regimen, at first compared directly to FAC and secondly in sequence with FAC. That turned out to be the next standard. There are multiple ways of doing that, and some centers and some groups give Adriamycin and Cytoxan before followed by Taxol. We have always done it the other way around. There is actually some scientific evidence that suggests that if you do Taxol before and Adriamycin second you get a

better result than if you do the reverse sequence. The reason is not completely understood, but clinical trials have shown that. Then shortly thereafter we started to work with Taxotere, which is a first cousin of Taxol, and again demonstrated Taxotere was a substantially effective drug, that it was not the exact same drug as Taxol, and some tumors that were resistant to Taxol responded to Taxotere and vice versa.

1:15:01.9
Then we also showed that the weekly administration of Taxol was better than giving the drug every three weeks, so small incremental steps there. But all of that was going on, and during much of the 1980s I focused—along with my colleagues—with the early development of new drugs. And over the decade of the 1980s, for instance, we must have tested no less than forty different new drugs in phase I and phase II studies, and at the end of that we had very little to show for it. It was a very frustrating decade of very hard work and very little in terms of returns. By then we had done the Adriamycin part. We had done the development of FAC, the development of multidisciplinary therapies for locally advanced and early breast cancer, so we were sort of at the top of the world in that. But then we came to a screeching halt.

Tacey Ann Rosolowski, PhD
1:16:17.8
What do you think the reason was for that lull?

Gabriel Hortobagyi MD
1:16:22.3
Well, it was to a large extent the fact that new drug development in oncology in the early years was a process of finding natural substances that seemed to kill cells and then trying to develop them into drugs. When you start with that, then you find the low-hanging fruit, the alkylating agent, the antifolates, the fluoropyridines, the anthracyclines, and the vinca alkaloids in the platinums. And then I think the community sort of ran out of ideas at that time, and everything else was sort of slightly better but not a whole lot. And then we started to look at analogs—just minor chemical permutations on the same molecule—and it takes years and years to figure out whether something is better or not than a previous one, especially if the difference is minor. Most of the drugs that we tested were just not terribly good. During that time, there was already an evolution towards a more molecularly designed group of chemicals, because technology and science had advanced to this stage to understand that these drugs were not just killing cells at random but that they had a specific effect.

1:18:16.6
Then people started to work on that and work backwards. So if this group of drugs does this to a cell's mechanism, how can we enhance that effect by developing a better molecule? That was an

entirely conceptual approach, very different. Then the discovery of oncogenes came and the discovery of tumor suppressor genes and then the enthusiasm for developing the Human Genome Project to understand how our cells were structured. Then gradually as we started to understand that process, then first the newer drugs like the taxanes and gemcitabine and vinorelbine and other drugs came about, and then came the major targeted agents—Herceptin, Rituxan, Tykerb, Avastin, and a number of others. But those were already based on very firm scientific hypothesis in structure, function, interactions, and that was a watershed event. What we are doing today to develop new drugs, while not a whole lot more efficient in terms of numbers, it is I think a much more scientifically valid approach to do it. And actually, over the past year, more oncology drugs were approved than for any other discipline by the FDA. I think we are doing better. We still need some technological improvements to improve the efficiency of the process. We still start out with 100 drugs or candidate drugs and come up with one or two out of that. It's a very inefficient process. But at least some of the drugs we are developing are clearly superb drugs. The Gleevecs and the Herceptins are a clear example of that.

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Chapter 13
A: The Administrator
The Breast Cancer Research Group –Bringing Together Clinicians and Basic Scientists

Story Codes
A: The Researcher
B: Beyond the Institution
B: Institutional Mission and Values
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care
C: Professional Practice
C: The Professional at Work
C: Collaborations
B: Controversy
B: MD Anderson Culture

Gabriel Hortobagyi MD
1:20:45.4
Then in part because of frustration with traditional new drug development, in part because we were learning so much about science and science was becoming so much more exciting, and in part because I was asked in the early 1990s to actually pull together a more cohesive group—everybody who was interested in breast cancer—then I organized what is now called the Breast Cancer Research Group. Then with the Breast Cancer Research Group, we faced the challenge of not only bringing together the surgeons and the radiotherapists and the medical oncologists and the radiologists and the pathologists but all of those plus all of the basic scientists who had any interest in anything resembling breast cancer. The Breast Cancer Research Group has about 200 members, maybe more, from about thirty-seven departments throughout the institution. And if you think there are cultural differences between surgeons and radiotherapists and medical oncologists, that's nothing compared to the chasm between laboratory scientists and clinical investigators. It's different planets. That kept me occupied for the next couple of decades.

Tacey Ann Rosolowski, PhD
1:22:31.2
What year were you asked to put together this group?

Gabriel Hortobagyi MD
1:22:33.8
I believe 1990-1991.

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Tacey Ann Rosolowski, PhD
1:22:36.7
And who suggested this to you?

Gabriel Hortobagyi MD
1:22:40.9
I think it was Jim Cox [Oral History Interview], who was at that time the executive vice president and physician-in-chief for a short period of time. I think it was between the time about Hickey retired and Charlie Balch or David Hohn took over. I don't remember exactly, but it was Jim Cox who was the head of Radiation Oncology for a long time.

Tacey Ann Rosolowski, PhD
1:23:18.5
What was going on in 1990 that made it then that you were asked, do you think?

Gabriel Hortobagyi MD
1:23:25.6
I think there was an effort on the part of institutional leadership to enhance the quality of our science and to make our science more collaborative and more translational because there was an increasing perception—and I think it was real—that basic scientists, laboratory scientists could spend their entire lifespan doing research for the sake of research. And our entire research enterprise in this country is based on sort of a circular methodology. In order for you to do research, you have to get research funding. But in order to do research funding, you have to have completed your research because otherwise you are told it's not possible to do what you're proposing to do. Laboratory researchers became quite comfortable with getting their first grant somehow and then sort of tweaking in a minor way their early application for the renewal so that by the time they went for the renewal, they had already completed what they were proposing to do, and then they perpetuated their funding by doing that. And while that was sort of good for the individual investigator—and in some ways good for the institution in a very cynical manner—because research funding kept coming, it was bad for the field because you didn't make progress because you couldn't take bold steps. You couldn't take risks because the review system was so conservative that if you took risks and if you thought outside the box, you were almost certain to be rejected and disapproved.

1:26:00.8
And over the years, when I started to look at what people were doing in different parts of the institution, I realized that they were individuals who were pretty bright individuals who had worked in the same thing for twenty, thirty years. We had no idea what to do with their

discoveries, and they were just planning to continue doing the same for the next twenty to thirty years. And of course we are a cancer center, so we are supposed to convert knowledge into something that is useful for people, and that wasn't happening. The other part that became very evident is that laboratory scientists and physician scientists are trained differently. They speak different languages, and they don't like to listen to each other because they don't see the benefit—or at least that was the case twenty years ago. They didn't see the benefit of getting involved with these people who worked with rats all their lives, and nothing ever came out of that. And by the same token, the basic scientists said, "Well, these guys don't understand science. When I talk to them about the cell cycle and I talk to them about growth factors and when I talk to them about A, B, C, or D, they look at me with glazed-over eyes, and they don't understand me. So why waste my time?" To some extent that is true even today. It is very hard. They are such different cultures. So for instance, I started to organize conferences. I called one Translational Breast Cancer Research Conference. And to try to get everybody in the same conference room at the same time, it was like trying to get Martians and folks from Mercury on the moon.

1:28:10.1
The surgeons get up at five-o'clock in the morning. They're at work by 6:45 or 7:00. By three-o'clock they are dead, and they go home. The basic scientists waltz in at 10:30 or 11:00 in the morning. They have a leisurely lunch, but they are still here at seven-, eight-, nine-o'clock. Try to find an hour of the day or day of the week when those two shall meet. So over the years, we've got a lot of very famous and exciting speakers from outside because nobody is a prophet in his own lab. To put one of us to speak, it would not be good enough. I got Nobel Prize winners and Lasker winners and people who were plenary speakers at the ACR or ASCO or whatnot and tried to alternate between basic scientists and physician scientists. And if I organized the meeting early in the morning—like seven- or eight-o'clock in the morning—I lost all of my basic scientists, regardless of who the speaker was. They wouldn't come. If I organized it at noon, nobody would come because everybody is in clinic or at lunch. If I organized it in the afternoon, then I lost the surgeons and many of the clinicians, and the basic scientists would come if I had free food for them. It was really, really a challenge to do this, and it continues to be a challenge. If you walk through the hallways and you ask random people with white coats whether they believe in translational research, they will all nod, and they will agree with the concept, even though each of them will define translational research differently. But when you ask them, okay, "How are you cooperating with people who are not in your narrow area of interest?" you will still get a lot of answers of, "I'm not." And I think that's part of what is holding us back. But I'm not trying to point fingers, because there are many other systemic issues within this institution and other institutions that perpetuate that.

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Gabriel Hortobagyi MD
1:30:47.4
There is no incentive for the basic scientists to "waste their time" talking to dumb clinicians, and there is no incentive for the clinicians—who are increasingly being asked to see more and more patients and generate more income—to spend time trying to understand stuff that is not going to be of immediate application to what their major responsibilities are. It's a difficult problem, but we need to get over that, and certainly President [Ronald A.] DePinho has been making the right noises, although not necessarily the right moves, to make this happen. I think he does believe that this is important, but since he has never been on the clinical side, he doesn't quite understand what it takes to do that from this side. I think he understands it better from the laboratory research side.

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Chapter 14
A: The Administrator
An Initial Translational Research Project: A Drug to Attack HER2-positive Breast Cancer

Story Codes
A: The Researcher
C: Professional Practice
C: The Professional at Work
C: Collaborations
D: On Research and Researchers
D: On Pharmaceutical Companies and Industry
B: Industry Partnerships
B: Devices, Drugs, Procedures
B: The Business of MD Anderson
C: Portraits

Gabriel Hortobagyi MD
1:30:47.4+
With that, then with those initial meetings I identified out of the 200-some people three or four individuals from the basic sciences who were really highly collaborative—so Mien-Chie Hung [Oral History Interview], Bob Bast, Gordon Mills, and later others—and with those, then we started to put together joint grant applications and joint papers and projects, and that became very, very exciting. And that's when I started to get involved in true translational research, and that was the beginning of my interest in gene therapy. The first gene therapy program we got into was in the days of high-dose chemotherapy and bone marrow transplantation. Our first project—and this was before perfecting hematopoietic stem cell reinfusion, and therefore the abrogation of severe myelosuppression and potentially lethal myelosuppression—the idea was to take a mechanism of resistance to chemotherapy, and using gene therapy approaches, infect with that normal blood cell precursors so that while the cancer cells would be sensitive to chemotherapy, the blood cell precursors would be resistant. This was sort of the world upside down, we did that, and it was very exciting. And we transfected the P-glycoprotein into what today would be called probably hematopoietic stem cell, and then we infused that into patients before giving them high-dose chemotherapy. It worked beautifully in the lab. It worked beautifully in preclinical things, and we had some signal from our phase I trial that it might work some. But in the meantime, the field improved so much without that gene therapy that it became sort of an, okay. So what?

1:34:58.4

So we said, "Well, we learned some things," and of course, we did learn some things. Through the process we learned the difficulty of taking something that works very well in vitro or in a test tube and actually trying to deliver that product in vivo to a human being and making sure that it gets to the target cell and only to the target cell. Then we tried a number of delivery systems, and we did a lot of fairly sophisticated experiments that were very exciting. We got a number of publications out of that, so from the traditional academic point of view it was good. But it was five years of research that didn't really move the field forward in the sense that we intended to move the field forward. Then we took what we learned from that experience, and then with Dr. Mien-Chie Hung, we developed a different gene therapy proposal, and that one was trying to use a gene product from adenovirus 5, which is called E1-A, to try to kill cells which we initially thought was specific to HER2-positive breast cancer, but it turned out it was not specific to that. That particular proposal we took all the way from the first concept in the lab to completing phase I and phase II studies, and it actually worked. But once we got there, we realized that neither we nor the institution had the resources to take this to a drug for FDA approval, so we looked for a partner in industry. We licensed it to a company. The company took the license, started to develop it, went bankrupt, and refused to give us back our license. So the thing is sitting in limbo somewhere, and it's never going to make it beyond that.

Tacey Ann Rosolowski, PhD
1:37:22.6
How frustrating!

Gabriel Hortobagyi MD
1:37:25.0
It is. Frustration is frequent in this field. In the meantime—

Tacey Ann Rosolowski, PhD
1:37:33.0
Can I ask with the licensing issue, is that a place where contracts come in, if writing a contract differently would have protected you?

Gabriel Hortobagyi MD
1:37:48.9
Sure. If you go back even thirty years, I as an individual investigator and Mien-Chie Hung as another individual investigator and the institution as a whole had very primitive or no idea about the legal issues, the intellectual property issues, and the issues of how to obtain money for these things. Before Dr. [John] Mendelsohn was recruited, under Mickey [Charles A.] LeMaistre, we had a development office that essentially sat in the office and waited for checks to arrive. That was our fundraising effort. When Dr. Mendelsohn arrived, he essentially changed that on the

model of Memorial Sloan-Kettering, which was already raising something like $100 million a year, and we developed what is today one of the most successful development offices in the world. And initially much of that went to support research. Today much of that goes to support bricks and mortar. At the same time, Dr. Mendelsohn recruited some legal expertise and developed the Technology Transfer Department, and we gradually learned how to deal with this. But when we started working on this, we had no idea about those complexities. We had no idea how malignant the environment is in the pharma world and how difficult it is for an inexperienced and rather naive investigator to try to survive.

1:39:57.2
We also had very little idea of how complicated and how costly it is to develop a drug and take it from concept to, "I'm going to sell it to the pharmacy." Today it is considered that to do that pharma in general dedicates—it's hard to tell exactly how much, because there is a lot of smoke and mirrors, and pharma adds a lot of other costs, including the cost of drugs that are never developed or that were unsuccessful. But they consider that to develop a new drug—take it from concept to a drug—takes anywhere from $2 billion to $4 billion. Between friends, that's getting to be real money, and when you deal with the average size of an R01 being, I don't know, $250,000, it takes a lot to get even close to that. You cannot develop a drug by yourself. You can do it by partnering with the industry, but partnering with the industry is going to bed with the devil. You need to learn how to do that and not get burned.

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Chapter 15
A: The Researcher
The Next Phase of Gene Therapy Research and Funding from the Breast Cancer Research Foundation

Story Codes
A: The Researcher
C: Professional Practice
C: The Professional at Work
C: Collaborations
D: On Research and Researchers
B: Devices, Drugs, Procedures
D: Business of Research
B: Philanthropy, Fundraising, Donations, Volunteers
D: Understanding Cancer, the History of Science, Cancer Research

Gabriel Hortobagyi MD
1:41:29.0
In the meantime while we were involved in that first and second gene therapy project, Evelyn Lauder, the daughter-in-law of Estee Lauder, developed breast cancer. And being a wealthy woman, she said, "How come you cannot guarantee me that I get cured of breast cancer? I need to do something about this." So she started the Breast Cancer Research Foundation, and she recruited Larry Norton, who was my counterpart at Memorial, to be the chair of the Scientific Advisory Board, and Larry's first act was to call me saying, "Could you help me with this?" Larry and Nancy Davidson and a fellow from the NIH called Peter Greenwald and I became the Scientific Advisory Board for the Breast Cancer Research Foundation, and these incredibly powerful women started to raise a heap of money, and we were charged with distributing that. Part of distributing that ended up being a lot of money coming to MD Anderson, and part of that supported the research of several of my colleagues, including Mien-Chie Hung and our gene therapy project.

1:43:11.0
We developed the next couple of gene therapy concepts entirely on the basis of BCRF funding, and while Mien-Chie got some NIH funds for that, it was very hard because, again, it was thinking outside the box. But it was also with the first gene therapy project that we got our first SPORE—breast cancer SPORE—and one of the projects was our first gene therapy—actually our second gene therapy project. That was very gratifying because despite gene therapy not being terribly popular in the NIH circle, we got funds for that. Between the NIH and BCRF, we

were able to take several of these things to the clinic. We are about to get our fourth gene therapy proposal into phase I trial. And in fact, sometime within this month we are going to submit to the FDA.

Tacey Ann Rosolowski, PhD
1:44:23.3
What were the projects that were initially funded, and why were they innovative in a way that would not have made them appealing to the NCI?

Gabriel Hortobagyi MD
1:44:37.3
Well, the second one, which was the E1-A project—by the time we got to the stage of requiring extra funding from the NCI, there were some events nationwide in which there were some—you could call them accidents with gene therapy where people got hurt because people were sloppy. Investigators were sloppy and mostly because by then the field had become aware of how difficult it was to deliver the gene therapy product to the right target.

Tacey Ann Rosolowski, PhD
1:45:31.4
What happened to these individuals? I have no idea what the effects might be of a mistake in that way.

Gabriel Hortobagyi MD
1:45:37.3
One of the approaches to delivering a gene product to your cell is to load a virus with the DNA sequence that you want to deliver and then inject the virus into people. Well, it is somewhat unpredictable where that ends up. For instance, you can use a retrovirus—for instance, the HIV virus. We don't use that, but that's a retrovirus, and it has certain properties that are favorable. There are other retroviruses that have been used, and there was a project in Philadelphia for a genetic deficiency disease. The scientist developed a protocol and started to administer this virally delivered DNA sequence to children and young people, and he killed a couple of them. Of course, that is a huge problem in and of itself, but then it also became apparent that both him and members of his lab and the IRB from UPenn were negligent and had done a lot of inappropriate things without following procedure. That gave a pretty bad name to UPenn and this investigator but also in general terms to the field.

1:47:23.0
Also, by the mid-1990s, late 1990s, there were a number of publications from other investigators working on gene therapy that suggested that in their hands and with what they were doing it

wasn't working very well, and the problem is largely the delivery system. For instance, with our E1-A project, we were able to infect about one or two percent of the target cells with what we were doing. Out of let's say your ideal target of 100 cells, we were able to transfer the gene in question to one or two cells. Even with that, we had a biological effect, but it was very hard to improve on that. We went away from viruses, and we started to use other vehicles which improved a little bit the efficiency of the project, but it was still in the single digits. NCI reviewers considered that there were more exciting projects to look at, and when a review committee decides that an area is exciting, then a lot of investigators looking for funds go in the same direction. That was a problem. To a large extent, we are not doing viral delivery of gene sequences, but we use other methods. But it still continues to be a problem, and until we figure out a truly revolutionary way to increase the efficiency of the delivery aspect, gene therapy is going to be restricted to institutions like this because it's complicated. It's very labor intensive, very effort and resource intensive.

Tacey Ann Rosolowski, PhD
1:49:39.4
What did the Breast Cancer Research Foundation see in the proposals that you put to them?

Gabriel Hortobagyi, MD
1:49:45.7
The Breast Cancer Research Foundation is structured differently from the NCI, the DoD, Komen, Avon, et cetera. These other agencies have a pot of money. They identify a number of prominent scientists, which turn out to be in many cases not to be very prominent because the most prominent ones always write back saying, "I'm sorry, but I'm too busy. I cannot review for you." And then they review a series of projects. They score them according to the ideas of each of the reviewers, and then they distribute the money. In the BCRF what we decided to do was to say, "We are not interested in reinventing the wheel. That funding system is out there. If anyone wants to follow that, that's fine. We don't think that's the best way to enhance the quality of research." What we decided to do was the reverse. We said, "Let's build on accomplishment. Let's identify—depending on how much money we have—five or ten or twenty or thirty or forty of the most accomplished cancer researchers in the country, and let's solicit from them proposals, and let's fund them, and let's emphasize that we want proposals that are high risk." And we got some of the most outstanding investigators in the country, and we continue to fund a number of them, and the response has been incredible. The utilization of funds has been incredible, and the accomplishments of these people have been wonderful.

Tacey Ann Rosolowski, PhD
1:51:48.3
What are some of the areas that these researchers have been working in? Just a sampling.

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Gabriel Hortobagyi MD
1:51:54.7
Cancer vaccines, some of the early genetic screening methods, development of specific targeted agents for very specific types of genetic abnormalities. For instance, one of our grantees—who was one of the three original describers of the HER2 gene, which was done in 1983—just a couple of months ago came up with a new chemical compound which is going to be based on his preclinical data—a better anti-HER2 drug than anything else we have out in the market or in development—and it is based on painstaking work over a number of years based on a different concept from developing an antibody or a tyrosine kinase inhibitor. There are individuals working on biomarkers. One of the problems of targeted therapy, for instance, is that most of what we consider targeted therapy is not targeted because we don't have biomarkers to identify the target population. Biomarkers are not big business, because while you can charge $10,000 a shot for a drug, you cannot charge more than a couple hundred dollars for a test. So drug companies don't get involved in developing tests, and because of that, that has held the field back by decades. These folks are developing biomarkers. They have developed new diagnostic methods that are much more precise than immunohistochemistry or FISH or a number of other things. We try to get not only different disciplines and different orientations so as not to get ten people doing the same thing but try to identify people where the need is or the needs are. We have grantees in France, in the UK, in Israel, in Singapore, but they're handpicked and selected based on their area of expertise and their track record.

Tacey Ann Rosolowski, PhD
1:54:48.3
We're at about ten minutes after 3:00, and we were scheduled to stop at 3:00. I just don't want to abuse your time. Would you like to stop for today and make another appointment?

Gabriel Hortobagyi MD
1:55:00.7
How are we doing in terms of your overall plan?

Tacey Ann Rosolowski, PhD
1:55:06.7
Well, we're doing great. This kind of material is exactly what I'm delighted to have recorded. I would suspect that we would need probably another two sessions.

Gabriel Hortobagyi MD
1:55:19.5
Okay.

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Tacey Ann Rosolowski, PhD
1:55:20.5
Is that okay?

Gabriel Hortobagyi MD
1:55:21.5
Yeah. Then let's reschedule, because I do need to do some other things this afternoon.

Tacey Ann Rosolowski, PhD
1:55:27.5
I'm turning off the recorder at ten minutes after 3:00.

1:55:30.4 (end of audio)

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Gabriel Hortobagyi, MD

Interview Session 3—January 23, 2013

Chapter 00C
Interview Identifier

Tacey Ann Rosolowski, PhD
0:00:01.5
All right. We are recording. I am Tacey Ann Rosolowski. Today is January 23, 2013. It is about twelve minutes after 1:00. I am sitting in the office of Dr. Gabriel Hortobagyi, and we are about to begin our third session. So thanks very much for allowing me to come and speak to you again.

Gabriel Hortobagyi, MD
0:00:26.2
Thank you for having me.

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Chapter 16
A: The Researcher
Studies of Pro-Apoptotic Molecules: Translational Research and Thinking Outside the Box

Story Codes
A: The Researcher
C: Discovery, Creativity and Innovation
C: Professional Practice
C: The Professional at Work
D: On Research and Researchers
D: The History of Cancer Research and Care
A: The Administrator
B: Beyond the Institution
A: Career and Accomplishments
B: Institutional Mission and Values
C: Discovery, Creativity and Innovation
C: Patients, Treatment, Survivors
D: The History of Cancer Research and Care
D: The History of Health Care, Patient Care
D: Global Issues –Cancer, Health, Medicine

Tacey Ann Rosolowski, PhD
0:00:28.3
We were just plotting and planning our attack here for the first part of the interview. We ended up the last session talking about the Breast Cancer Research Foundation. You spoke a lot about the organization of that and how the foundation started, but I wanted to have an opportunity to ask you more about the research that you are doing with grant funding from that organization. So however you want to organize that story or I can ask you questions, whichever you would prefer.

Gabriel Hortobagyi, MD
0:01:02.6
After I was asked to join the Scientific Advisory Board to the BCRF, our first task was to select the first few awardees. We wanted to make sure that the leading scientists in the major cancer centers were included among those, especially if they had a proven track record of productivity and novel ideas. So when I came home from that meeting, I immediately contacted my co-conspirator, Mien-Chie Hung, with whom I have had the great pleasure of working for well over twenty years. We put our heads together to come up with a truly different proposal, and we had a

number of research projects ongoing and planned at that time. But we said, "Well, let's do something totally different," and that's what we came up with. The first project, which was based on the—actually no. It was the E1A proposal. That was based on an observation that Mien-Chie had made in the lab on a gene product from Adenovirus-5, which is one strain of adenovirus. This gene, E1A, had the property of convincing HER2 positive cancer cells to commit suicide. So we then worked on this concept. Later it became apparent that it was not restricted to HER2 positive breast cancer. In fact, it wasn't restricted to breast cancer, and eventually it became a broader gene therapy program that was applied to head and neck cancers, ovarian cancers, et cetera. It was—strictly speaking—gene therapy in the sense that we would take this DNA segment, encapsulate in liposomes, and then administer it to patients. We got some partial support for that project from the BCRF. We also got some support for that from our first SPORE application—the Specialized Program of Research Excellence in breast cancer. Then the BCRF funding works one year at a time because, of course, it depends entirely on the success of that year's fund raising. So we never got enough in one particular—any one particular year to support the cost of the entire project. But for all the time ever since—I guess 1992 or so—we've gotten a very sizeable chunk of funds from the BCRF—of course, upon presenting results and annual reports and then accounting for how we spent the money and whatnot. In retrospect, it was an incredibly wonderful source or resource because it—the BCRF—was willing to take risks with these projects, which were really out of the mainstream and that were considered high risk. I know that Mien-Chie had applied to other more traditional sources of funding not very successfully. So the two places where we actually found a solid source of support were the BCRF and eventually the SPORE mechanism. So that was good. That was our first project. From there, we went onto the second project, which was based on the observation that one of the proteins that is in the BCL-2 family—this group of proteins essentially modulates the process of cell suicide. Some of them are pro-apoptotic. Some of them are anti-apoptotic. It is the balance of this entire family at any one point in time that determines whether the cell lives or dies.

Tacey Ann Rosolowski, PhD
0:06:38.4
I am not sure I understood you correctly. Is that VCL-2 or—

Gabriel Hortobagyi, MD
0:06:44.2
BCL-2.

Tacey Ann Rosolowski, PhD
0:06:44.5
BCL-2.

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Gabriel Hortobagyi, MD
0:06:45.2
That is correct.

Tacey Ann Rosolowski, PhD
0:06:45.3
Okay.

Gabriel Hortobagyi, MD
0:06:50.4
So the cell—the BCL-2 family is a large family of proteins, and its members, of course, determine the direction in which the cell will go. One of the pro-apoptotic molecules was Bik. Dr. Hung in the lab produced a number of mutant versions of Bik. One of them, BikDD, which had two mutations in the molecule, turned out to have a much more enhanced pro-apoptotic activity than the parent molecule. So we ended up using the mutated version—BikDD—for our subsequent experiments and eventually our translational project.

Tacey Ann Rosolowski, PhD
0:07:54.4
When did you first discover or—to me it is such an amazing paradigm shift to suddenly realize that you can use these tiny mechanisms within the body itself and harness that to work against disease. That's just a totally different way of thinking. When did that really enter your consciousness and approach and become a powerful source of inspiration for your work?

Gabriel Hortobagyi, MD
0:08:26.2
It's hard to put an exact time and place because these things happen gradually.

Tacey Ann Rosolowski, PhD
0:08:34.4
Uh-hunh (affirmative).

Gabriel Hortobagyi, MD
0:08:35.2
As a physician, I had a predominantly clinical and empiric training. I went to medical school in the 1960s. So at that time our knowledge and our understanding of biology—viewed with today's eyes—was so limited and so primitive. Yet by then there had been a very substantial investment in the basic sciences and in biology in general. But there was a lot of time between the discovery of many of these mechanisms of cell biology and until those discoveries gradually

infiltrated our consciousness in medicine. So probably much of what we started to work with in the early 1990s was already known in basic science circles five to ten years earlier. But with many early discoveries, the importance of the discovery is not known until later. Even the discoverer himself—we might have touched in another discussion—sometimes they didn't know what to do with that. It takes a while of throwing around the idea and digesting it and sleeping on it until you figure out—the light bulb comes on and says, "Gee, why didn't I think of this?" Probably somewhere in the early 1990s in conversations with my colleague, Dr. Hung, it started to dawn on both of us that there might be possibilities here. Once you then discover that here is an observation that earlier you thought of as—this is just interesting but not a terribly useful piece of information—and now I think of it differently. I think of it as, "Gee, I can take this piece of information and actually take it to the clinic eventually. I see the pathway." Whether that pathway will turn out to be the right one or not is a different matter. It is really, in a way, an epiphany. Once you take that step—from my point of view as a clinician—I think it is sort of the reverse process for basic scientists like Mien-Chie Hung where he can—instead of just being in his cocoon in the lab looking at, "Gee, let's learn more about the cell. I don't quite know nor do I care about where this goes later." Then in our interactions as we started to jointly think in translational terms—in terms of I am starting to understand the basic biology, and he is starting to understand the clinical needs—putting this together. You sort of pave a translational pathway.

Tacey Ann Rosolowski, PhD
0:12:02.6
Well it seemed like that symbiosis between two collaborative thinkers who want to work translationally as well. That seems really key. You're kind of jump-starting each other—

Gabriel Hortobagyi, MD
0:12:13.8
Absolutely.

Tacey Ann Rosolowski, PhD
0:12:14.7
—and helping each other out with kind of complementary knowledge fields, if you will.

Gabriel Hortobagyi, MD
0:12:18.2
Right.

Tacey Ann Rosolowski, PhD
0:12:18.8
Yeah.

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Gabriel Hortobagyi, MD
0:12:21.2
In a way that was an indirect consequence of my earlier work in trying to bring together physicians of different disciplines because while qualitatively it's different, it is the same basic concept of first learning to—stepping back and learning to understand why you think of the same problem differently than the surgeon across the table from you or the radiation oncologist across the table from you. Then you try to figure out the why of the differences. Then you try to figure out how these two perspectives can actually merge and become symbiotic and complementary as opposed to being confrontational and—

Tacey Ann Rosolowski, PhD
0:13:20.6
Adversarial.

Gabriel Hortobagyi, MD
0:13:21.7
—adversarial. The same thing in a way was this coming together of a fundamental laboratory scientist and an empiric clinician, if you wish—realizing and recognizing gradually that there were incredible possibilities in the future for that.

Tacey Ann Rosolowski, PhD
0:13:44.4
Is there something different about the—I'll use the word creative—you would use a different word—but the creative process of visualizing that possible use and then figuring out the pathway to see if it is possible to put that to use in a clinic? You're taking risks. You're creating alternative scenarios that you have to work with. Is that process different in translational research and particularly with studies that work with the mechanisms of cell biology? Is that different from other kinds of investigative proceedings?

Gabriel Hortobagyi, MD
0:14:27.2
I don't know that it is really different. But I think there is an inherent contraction in it. So we think of science—true and the best science—as a highly disciplined activity in which you follow some very strict rules in order to develop an appropriate and reasonable hypothesis.

Tacey Ann Rosolowski, PhD
0:15:06.3
Uh-hunh (affirmative).

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Gabriel Hortobagyi, MD
0:15:07.5
Then you build a logic-based pathway towards either proving or disproving that hypothesis. You sort of think through the process of how you are going to get there. That is supposed to be at the heart of creativity. In reality, the process of creativity that leads to truly important discoveries has to break that mold because you have to become sometimes undisciplined in order to—what we call today—think outside the box. You have to let a little bit of that rowdy, crazy side of you to say, "I know what the rules are, but I am going to think a little bit outside the rules for a moment." Then you have to imagine why that might be a better way to think.

Tacey Ann Rosolowski, PhD
0:16:16.8
Uh-hunh (affirmative).

Gabriel Hortobagyi, MD
0:16:20.5
The reason that is important is because the traditional thinking and the traditional and disciplined thinking almost always limits to you existing knowledge. By definition, existing knowledge is limited. All right. So in order to go beyond that limit, you have to think differently. Otherwise, you always come up with the existing limitation—the wall within which your knowledge exists.

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Chapter **17**
A: Professional Service beyond MD Anderson
Thinking Outside the Box to Stage the World Summit Against Cancer for a New Millennium

Story Codes
A: The Administrator
B: Beyond the Institution
A: Career and Accomplishments
B: Institutional Mission and Values
C: Discovery, Creativity and Innovation
C: Patients, Treatment, Survivors
D: The History of Cancer Research and Care
D: The History of Health Care, Patient Care
D: Global Issues –Cancer, Health, Medicine

Gabriel Hortobagyi, MD
0:16:20.5+
In a different part of my life, I have had another very exciting association with another colleague. It has less to do with science, but I think it illustrates a little bit the same process of how you get beyond what you think your limitations are. Since about 1983, I have been organizing or co-organizing a meeting—a scientific meeting—in Paris. The first time this very well-known French clinical investigator, Professor [Claude] Jacquillat, invited me to present the paper because he became interested years after we had started here in neoadjuvant chemotherapy. Since my group had done the bulk of the work with neoadjuvant chemotherapy up until then, he invited me to do that. He assigned to me one of his trainees as my bodyguard during my stay in Paris to sort of cater to my needs and make sure that I was well cared for—I showed up on time for the conferences and all of that. This young man later became one of my best friends, and when his boss died—died of cancer, in fact, of kidney cancer—he took over as not only the head of the department in Pitié-Salpêtrière but he also took over as the co-organizer of this meeting, and then he asked me to join him as the co-president of the meeting, and we have been doing that ever since every year.

Tacey Ann Rosolowski, PhD
0:19:05.2
Let me just pick up the detail—this was Professor Jac—and I think I missed—

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Gabriel Hortobagyi, MD
0:19:10.5
Jacquillat. That's J-A-C-Q-U-I-L-L-A-T.

Tacey Ann Rosolowski, PhD
0:19:18.8
—L-L-A-T. Oh, Jacquillat. Okay. Thank you.

Gabriel Hortobagyi, MD
0:19:23.3
The young man is Professor [David] Khayat. That's K-H-A-Y-A-T. And David Khayat and I have been organizing this meeting now for a while. I remember first as we organized every yearly meeting, we would sit down and think of what would be the interesting topics to include here, but who would be the best speakers and then try to put together a well-rounded program. Then we realized that as we became more experienced that we also needed to organize a social program so that those who came from out of the country and out of the city would have a better exposure to Paris and to French culture and French art and all of those things. And then as we got closer to the year 2000—remember the big millennium when everything was going to happen? So one day we are sitting in at an ASCO meeting at a coffee shop or a bar or something like that. We were thinking of what can we do to sort of make an impact for the millennium with our meeting. Of course, we had limited resources. We couldn't go too crazy. So we are enjoying our while there, and we just started to free associate. So we said, "Well, you know, why don't we ask whether we can rent the Cathedral of Notre Dame for a concert." So the other guy laughs, saying, "That's a crazy idea. There's no way we can pull that off." So the other one says or I did—I don't know who—this is just the two of us throwing crazy ideas. "Maybe we could ask the mayor of Paris to throw a cocktail party for all of our speakers." "Yeah." "Well, maybe we could then ask the president of France to give a reception in the presidential palace." "Yeah. That sounds great." "Well, maybe we could organize a reception dinner at the Versailles Palace—the palace of Louis XIV." And this went on and on. It was like a soufflé that grows and overflows its thing. If someone more reasonable than us had been listening to us, they would probably have called the men with the white coats—with the shirts. But we sort of got all excited about this. Then we had all of these things written down on a napkin, and we said, "Oh, my goodness. How are we going to do this? But it's a great idea." So we thought about it for a couple of days. Again we met, and I said, "You know this not such a crazy idea. I think we can pull this off." So then we said, "Well, this is all fluff. So why don't we put some really high-powered science behind it to justify the fluff?" I said, "Okay. So why don't we organize a world summit on cancer research? And let's invite a number of very high-profile investigators."

00:23:15

So eventually we put together a list of about forty, forty-five Nobel Prize winners. You have to realize that we were relatively unknown in the context when you are contacting people of the Nobel Prize sphere and heads of state and what not. To make a long story short, we contacted a number of them. About half of them accepted to come and speak. So we put together this incredible program with the top biomedical investigators of the latter part of the twentieth century. Then we said, "Well, we have our meeting—our traditional meeting—which is already done with the program. So what are we going to do with these people?" So then we asked for City Hall in Paris to be lent to us. We were able to infect with enthusiasm the mayor, who later became President Chirac. He said, "Let's do that. We have a wonderful large conference area. You can take that for a one-day conference for the world summit, and I put the City Hall's resources to your disposal. And that evening I'll organize a reception." The City Hall in Paris is this gorgeous nineteenth century classical building with these great staircases and incredible frescos on the ceiling. So we had ourselves a summit. We had ourselves a reception. So then we said, "Okay, well, check one off. Now let's go to the president's palace and see if we can play the two against each other." So we went to—we managed to get an appointment with one of the secretaries of the president and explained our plan. And I said, "You know, it would be a shame if all of these personalities came and the leadership of the country is nowhere. So we would also propose that we write a charter." And by then we had written like a ten-point rights of cancer patients, which we wanted to call initially the Charter of Versailles. Actually we wanted to call it the Treaty of Versailles, but you might remember that World War I ended up in rather tragic circumstances for some countries in Versailles. So we said, no, that's not a good idea.

Tacey Ann Rosolowski, PhD
0:26:16.6
(laughing) Bad precedent. Bad connection.

Gabriel Hortobagyi, MD
0:26:18.7
Bad connection. So we changed it to the Charter of Paris. Then we said—to sort of entice the president and his entourage, we said, "We can bring all of these personalities, plus we can invite a bunch of heads of state or their delegates to come and sign this in the French president's palace." So then he got all excited about it. He said, "Okay. So I'll offer a signing ceremony here followed by a reception at the *Palais de l'Élysée*." So check number two, and then we did something similar with the Versailles Palace. Eventually, not only did we get the Museum of History—not the Museum of History—the Minister of History or whatever that it's called—to give us for free for one night the Versailles Palace but we convinced two of the top chefs in Paris to provide food for free.

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Tacey Ann Rosolowski, PhD
0:27:27.6
Wow!

Gabriel Hortobagyi, MD
0:27:28.2
For 700 of our closest friends. So you can't do this unless you let that crazy side of yourself think big and think way beyond where our traditional thinking would restrict us because had we been rational about this we would have said from day one, "This is not possible. Let's not even try it. We are just going to waste a lot of time being frustrated, and at the end of it won't have anything." Instead we kept feeding each other's craziness in this. I say craziness for lack of a better word, but it's just—

Tacey Ann Rosolowski, PhD
0:28:16.0
It could be enthusiasm, creativity—

Gabriel Hortobagyi, MD
0:28:18.1
Right. Right.

Tacey Ann Rosolowski, PhD
0:28:19.4
—energy—all of those good things. Yeah. I don't want to miss out on some of the details. I'm not sure if I was able to get the name of this organization that you were participating with Dr. Jacquillat.

Gabriel Hortobagyi, MD
0:28:36.1
Okay. Originally it was called the—oh, what was it called? The International Congress of Neoadjuvant Therapy—yes. Then eventually in the late '90s after Claude Jacquillat died, we renamed it the International Congress of Anti-Cancer Therapy. The acronym for that is ICACT—I-C-A-C-T. In fact, I'm just going for that next Wednesday because it's our annual meeting.

Tacey Ann Rosolowski, PhD
0:29:24.1
You'll enjoy Paris in the almost spring.

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Gabriel Hortobagyi, MD
0:29:29.1
Since I've digressed, I might as well tell you that for the signing of the Charter of Paris, we got something like fifty or sixty nations to send us either president, prime minister, or head of health to sign this charter. I invited Dr. Mendelsohn, who is also one of the signers of this document. He was there at the Élysée Palace and City Hall and at Versailles. He got a copy—which is exhibited somewhere in the Rose Building—of this beautiful charter which has the rights of the cancer patient and the signatures of several hundred people who signed on then. Then we put that up on the web and by now we have I don't know how many tens of thousands of signatures from around the world.

Tacey Ann Rosolowski, PhD
0:30:41.8
Why was it important to put forth a list of a rights of patients at that time?

Gabriel Hortobagyi, MD
0:30:52.8
Well, part of it was that we wanted this to be something of true international impact. Cancer in most of the world—certainly outside of the U.S.—you could say perhaps outside of Western Europe—is still a dirty word. It's still a taboo about which nobody talks. In consequence, it a stepchild in the public health budget of most countries around the world. So cancer patients go untreated, mistreated, ignored. In consequence, the differences in mortality rate in different countries are huge—are enormous. To give you an example, the US has a population of 300 million people or so. This year we will have unfortunately about 40,000 women die of breast cancer. Around the world we have 7 billion people. All right. That would be roughly fourteen, fifteen times the population of the US But mortality from breast cancer is much higher in proportion, especially considering that life expectancy is much shorter in most of the other parts of the world. Breast cancer being largely a disease of the aged, it should have a lower frequency, lower incidence. This is a big issue. While one could think that in modern times the declaration of human rights should be something that everybody is familiar with, that's just not the case. A definition of the rights of patients and cancer patients we thought would have a greater impact. In fact, eventually the UACC adopted our Charter of Paris as the UACC's credo for cancer patients' rights. And more recently in Ireland last year, there was a major meeting of the World Health Organization about non-communicable diseases—so chronic illnesses of the heart, lungs, diabetes, and cancer. They adopted the same declaration as the basis for continued deliberation and how this should twist the arms of governments throughout the world to think about what they needed to do in order to address this. Because this is, of course, as countries—even the poorest countries—grow and their economy improves, the life expectancy of their citizens will

improve, and they will increasingly face this time bomb of cancer for which they are very poorly prepared. That was a very long digression.

Tacey Ann Rosolowski, PhD
0:34:28.6
No. Not at all. The last time after we turned the recorder off you had mentioned that you had wanted to address international outreach issues as part of one of the subject areas you wanted to make sure we covered, so we've embarked on that now. I'm sure we'll come back to it. It's also a great example of thinking outside the box, too. I'm wondering if you could maybe talk a little bit about some instances in either the research you did for the breast cancer research—under the Breast Cancer Research Foundation grants or in other areas where you, yourself, went through that process but with a research focus.

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Chapter 18
A: The Researcher
Therapy to Block Angiogenesis

Story Codes
A: The Researcher
C: Discovery, Creativity and Innovation
A: Overview
A: Definitions, Explanations, Translations
C: Professional Practice
C: The Professional at Work
D: On Research and Researchers
D: The History of Cancer Research and Care
D: On Pharmaceutical Companies and Industry

Gabriel Hortobagyi, MD
0:35:18.5
Following this initial example with Dr. Hung, then it became increasingly clear to me, on my side as a clinician, that this same scientific epiphany that I had gone through really needed to happen to my other colleagues in the clinical area and similarly needed to happen to other basic science investigators in the institution—the colleagues of Mien-Chie Hung. So we talked briefly about this project of doing an inventory of what was going on in breast cancer research and the institution at that time. Then from that we put together some of the most exciting projects into the first application for SPORE. Then from then on, I sort of acquire this responsibility—some of it self-inflicted, some of it sort of rubber-stamped by those who worked with me—that one of my roles was to cheerlead this group and continuously develop this pattern of translational research. I felt and continue to feel very passionate about the fact that this is a process—a process that if not successful will put significant brakes on the development of important diagnostic and therapeutic approaches to cancer and that the only way we are going to really get to conquer this group of diseases is if we all wanted to learn more about them and wanted to really understand all aspects of it, not just our little world—our little slice of the world. So that went on and with each additional project that I shared or collaborated with Dr. Hung on, this became more of a passion. It became more of a challenge for me how to communicate my enthusiasm to my colleagues.

00:37:53
So after the E1A project, then we went on to the BikDD project. The BikDD project actually continues. In fact, we have reformulated the project a number of times based on newer

discoveries and improvements and tweaking of various aspects of it. We are planning to go on with an investigational new drug application to the FDA. This has to go through a special committee called the RAC—the Recombinant DNA Advisory Committee—because every gene therapy project that has some even theoretical risks of affecting our genes—our gene pool—has to go through this thing that was imposed on us by some previous government that was absolutely frantic about *Nineteen Eighty-Four* and some futuristic dangers to mankind. So that's continued. Then our next projects with Mien-Chie were—again, it started out as a conversation—a loose conversation—about various things. That takes us back to the beginnings of angiogenesis as an area of research. At the very beginning of angiogenesis, there was this great hypothesis, which of course goes back to this pediatric surgeon from Harvard who came up with the idea that cancers needed to grow their own blood supply in order to survive and grow. Then many investigators contributed to that field, including several from our institution, including Dr. [Michael] O'Reilly from radiotherapy, Josh [Isaiah. J.] Fidler, Lee Ellis, Mien-Chie Hung, and many others. One of the first realizations was that, again like for apoptosis, there were a number of proteins. There was this very large family of proteins that had either angiogenesis stimulating effects or angiogenesis inhibiting effects and that it was the balance of these various pro-angiogenesis and anti-angiogenesis proteins that eventually determined whether in a particular tissue a particular group of cells was able to or unable to elicit the formation of new blood vessels. One of the early anti-angiogenesis substances that was identified was something called endostatin. As the name suggests, it is something that inhibits the development of endothelial cells—endostatin. Endostatin was actually taken to the clinic. Someone purified it or synthesized it—I don't recall—and we did some Phase 1 and Phase 2 trials. It was a bust. It was a bust to a large extent because the half-life of endostatin once you inject is so short that it just doesn't stay around. Within just a few minutes it is gone.

Tacey Ann Rosolowski, PhD
0:41:46.0
Just like in a comparative sense, what's kind of a time frame for the creation of a blood supply to a growing tumor? Or is that hard to characterize in a general way?

Gabriel Hortobagyi, MD
0:42:01.5
No. So the concept is that when a cell that has developed the ability to grow to a certain extent uncontrolled by the surrounding control mechanisms and suppose it has metastasized to the liver, lung, or what not. It can divide and grow its little colony of cells, and it can absorb from the extracellular environment nutrients and can sort of dump the residues of that. But it cannot do that beyond—after reaching a certain size because there's just—the cell itself, from the outside of this collection, will be an obstacle for those on the inside to obtain nutrients and get rid of their debris. So once it reaches that size—and very arbitrarily we've been talking about one cubic

millimeter, and one cubic millimeter, of course, takes a whole lot of cells. We are talking about probably a million cells or more. So once it reaches that size, this colony becomes sort of stationary. It cannot grow any further because even though the cells on the outside can divide because they have direct access to the extracellular fluid around them, those on the inside die because they have no way to eat, drink, or prosper. So it's at that time when they—it is thought that they start to release in increasing amounts these proangiogenic substances that then disseminate through the extracellular area and start to attract endothelial cells. The process must be fairly quick—measured probably in days or just a very few weeks—because otherwise cancer wouldn't happen the way it happens. But I don't know that anyone has actually determined in a human model what the timeline is. It is a very difficult experiment to design.

Tacey Ann Rosolowski, PhD
0:44:50.9
Uh-hunh (affirmative).

Gabriel Hortobagyi, MD
0:44:52.2
In fact, I know that there are experiments in animal models. But animal models are so artificial and so idiosyncratic—depending on what animal and what cancer and where you put it—it's not terribly reliable. But if you inject a proangiogenic substance, like VGF for instance, I'm sure that within hours you will start to see some effects of that. Now how long will it take for an endothelial cell to leave an existing blood vessel and sort of move to where the cancer cells are? And do they actually move or do they just start building buds and the buds get longer? That part is less well understood. So endostatin was one of the first ones. There was another one called angiostatin. That was a bust, too. Those sort of went—

Tacey Ann Rosolowski, PhD
0:46:03.6
For the same reason?

Gabriel Hortobagyi, MD
0:46:04.6
Yes. So there was some disappointment, and then those sort of disappeared. Then the field of angiogenesis didn't revive until Genentech came out with what is called Avastin today—bevacizumab—which is a monoclonal antibody that binds to the vascular endothelial growth factor or the EGF. Being the monoclonal antibody it is, it has a very long half-life measured in weeks. For the first time there was some measurable effect in human tumors. There were some objective regressions of breast cancer and colon cancer and brain tumors and so on. Then the entire field sort of got very enthusiastic. But very early on it became apparent that bevacizumab,

while it had some therapeutic effects, it also had some side effects and toxicities that were not desirable.

Tacey Ann Rosolowski, PhD
0:47:21.1
I'm sorry. I missed the name of that drug.

Gabriel Hortobagyi, MD
0:47:23.0
Bevacizumab or Avastin.

Tacey Ann Rosolowski, PhD
0:47:25.4
Oh. Okay. Yeah. That is the name—

Gabriel Hortobagyi, MD
0:47:27.4
Bevacizumab is sort of the generic name and Avastin is the commercial name. So then Mien-Chie and I started to think about, well, this drug is good but at the same time it can have some nasty effects. It can drive your blood pressure through the roof. It can make you bleed. It can make you have clots. So all kinds of problems with it. We said, "Well what can we do with endostatin so as to make it more of a functional drug?" At that time, Mien-Chie came up with a construct where you could use endostatin bound to something else—not to use it as a drug but to use it as a taxi, as a vehicle because there are receptors for endostatin in endothelial cells. So then we said, "Well, then we would use that just as a guide, but we still have to kill the cells with something else." Then from that eventually emerged this very clever construct in which we took an enzyme that—we took a prodrug. A prodrug is a chemical substance that has no activity on its own because it has to be processed by an enzyme to remove some of the inactivator parts. So we said, "Let's take this prodrug and link it to the endostatin. The endostatin will take it to the area where the tumor cells and the tumor vasculature is. Then independently we will administer an enzyme that will go to the same place and affect the activation of the prodrug." So that sounds very complicated but it works beautifully—at least in the test tube. There are actually precedents for it in other areas where you put together this package that targets the organ system or tissue where you want it to go, and then you administer this activating enzyme and that accomplishes two things. Virtually all of the therapeutic activity you are looking for happens at the target—

Tacey Ann Rosolowski, PhD
0:50:26.7
Right there.

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Gabriel Hortobagyi, MD
0:50:28.2
—tissue and nowhere else, and by not happening anywhere else you prevent all of the side effects—the non-target effects of that treatment. So this became the Endo-CD project with which we are still working. CD stands for cytosine deaminase, and cytosine is a purine that it is related to 5-Fluorouacil, and 5-Fluorouracil is one of the cytotoxic drugs we use for breast and colon and many other cancers. Cytosine is not known to be a therapeutic agent, but with the process of this enzyme that can activate, we hope it will become so. That is one of the latest projects that the BCRF is funding us with. Again, this is not strictly speaking gene therapy. It is very high-profile molecular biology in which you are modifying a molecule in vivo—in the live patient—and not in the laboratory, not in the pharmacy. So those are sort of the projects we have been working on with BCRF's support and in collaboration with Dr. Hung's lab. This has been happening while at the same time we were conducting clinical trials with Avastin. So I was on both sides of that discovery part. Unfortunately, Avastin didn't quite live up to expectations. While it is an active agent, it is not the magic bullet. It is not as effective as we were hoping for. So it does produce shrinkage of breast cancers in maybe one in ten, one in fifteen patients. When added to chemotherapy, it increases the tumor shrinking ability of chemotherapy substantially by about fifty percent. It prolongs the duration of control of the disease but at the end of the day doesn't make most patients live any longer. The problem, of course, is that it has the toxicities that I mentioned and that a lot of people not used to this drug are unaccustomed to and afraid to. We think today that while it is effective, it is effective only for a relatively small subset of patients with breast cancer or colon cancer and other cancers. The problem is that despite trying very hard over the past ten, fifteen years, nobody has been able to come up with a biomarker that can actually identify those patients who benefit and those patients who do not benefit. Something that complicated matters with Avastin is that the company that produces it decided that this was a great cash cow. So they priced it at something like—if a patient were to receive it for a full year that would be roughly $100,000 before administration costs and before any other additional costs to the patient or her insurance would have to cover. So that became a political football and eventually the FDA withdrew—the breast cancer withdrew the breast cancer indication for Avastin. It is still on the market for many other cancers. I think it works for breast cancers, but it has some issues.

Tacey Ann Rosolowski, PhD
0:54:53.9
Uh-hunh (affirmative).

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Gabriel Hortobagyi, MD
0:54:55.5
So we were working on that. The more Avastin got into trouble, the more we got interested in our Endo-CD project because it seems like it has some possibilities that Avastin will not have any time soon.

Tacey Ann Rosolowski, PhD
0:55:13.3
As you kind of look ahead to the next step, where do you see the interesting intellectual points coalescing to suggest what is the next project you are going to try to be working on?

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Chapter 19
A: The Researcher
A New View of Breast Cancer and Research on HER2 Positive Breast Cancer

Story Codes
A: The Researcher
C: Discovery and Success
A: Overview
A: Definitions, Explanations, Translations
C: Discovery, Creativity and Innovation
C: Professional Practice
D: The History of Cancer Research and Care

Gabriel Hortobagyi, MD
0:55:31.7
Okay. To answer that, let me go back about fifteen, twenty years. I'm talking about the early part of the 1990s.
Tacey Ann Rosolowski, PhD
0:55:44.9
Uh-hunh (affirmative).

Gabriel Hortobagyi, MD
0:55:46.7
So up until then we really thought of breast cancer as a disease of the breast—cancers that may grow into different morphological appearance and microscopic image. But they were essentially just breast cancer. Then while the estrogen receptor was discovered probably twenty years earlier, there was a lot of argument about the value of the estrogen receptor in the 1980s and even into the 1990s, in part fueled by technical difficulties in measuring it appropriately and testing for it and by poorly designed research projects that led many to conclude that it had no value. But then several things came together in the early 1990s. One was that we increasingly became confident that the estrogen reception and secondarily the progesterone receptor were truly important and that those breast cancers that expressed higher quantities of estrogen receptor were a different animal from those that did not. Simultaneously, in coming in part from work related to some of the early work that Dr. Mendelsohn had done with the epidermal growth factor receptor, there were observations about HER2. HER2 was another biomarker. It is also a cell surface receptor. That suggested that those tumors that had a lot of HER2 on their surface or that had many copies of the HER2 gene inside the nucleus behaved differently. They were much more aggressive than those that did not. They tended to be estrogen receptor negative. So that

then came up with a—like a third different type of breast cancer. While there was not a single date when we decided that breast cancer was no longer a single disease, it was again this dawning of this insight of we no longer think of breast cancer as being as single disease and all treatment—one treatment fits all. This happened somewhere during the '90s. I remember some of the times when I started to talk about this in public as I was invited to give lectures and grand rounds and whatnot. It was a gradual evolution.

0:58:55.3
The people at the beginning started to look at me like, where did you get that from? And it was only within the smaller club of breast cancer experts where this sort of became an understood thing. But it wasn't something that anybody really discovered. It was that just slow coming together of concepts from different sources. Then in 2000, of course, came the completion of the Human Genome Project. In the mid-1990s, Dr. Pusztai, and Dr. [Robert C.] Bast and Dr. [Gordon B.] Mills and I started to work on an exclusive collaboration with a company called Millennium. These were the early days of gene expression profiles. It was sort of revolutionary, but we were just taking the first steps of this and trying to figure out what to make of it. That also underlined the importance of the estrogen receptor, and it wasn't just the estrogen receptor. But it became apparent that those breast cancers that express or overexpress the estrogen receptor also had a different expression of some 600-700 other genes from the estrogen receptor negative tumors. So then we had much more ammunition all of a sudden, and I'm talking now about the last 1990s before the Human Genome Project results—that there were these differences—these fundamental differences in the biological underpinnings of these various breast cancers and that we needed to think differently about them. In the meantime, of course, we developed newer hormonal therapies, so the aromatase inhibitors came around, the LHRH analogs came around. Then on the other side for the HER2 positive breast cancers, Herceptin came around. Then lapatinib came around. So then it was an entirely new ball game. Then soon after the Human Genome Project, some scientists—at that time it was in Stanford, but the lead scientists moved to UNC—published a very influential paper in which they looked at several dozen primary breast cancers, and they looked at the latest technology and gene expression profiling and were able to identify four or five fairly different breast cancers based on their gene expression profile. Among those five were the three that we had sort of become comfortable with, which was the estrogen receptor positives, the HER2 positives, and those that expressed neither the estrogen receptor nor the progesterone receptor nor HER2. Then was another category there that nobody knew what to do with—and even today we don't know what to do with—which was a normal-like thing, which is probably an artifact of the technology or the way we obtain tumors. So then that now gave us sort of two overlying or overlapping ways to look at breast cancer: one by gene expression profiling and one by looking at simple pathological techniques, such as immunohistochemistry and FISH. We identified very similar subgroups of breast cancer—subtypes of breast cancer. From the mid-2000s—I'd say 2003, 2004, 2005—there has been this explosion of knowledge

and understanding about what these subtypes mean. And we clearly think of breast cancer today as very different syndromes—very different diseases that just happen to start in the breasts' tissue, but they are biologically different. They behave differently. Their sensitivities to existing treatments is different. So it's quite a revelation. So that was another emerging paradigm. Then more recently, these small versions of that start to pop out more and more frequently, in part because the enormous investment of money that this country has made in the war on cancer and the enormous investment that pharma has made in developing new therapeutics for cancer—is just starting to come to fruition, and there is this incredible proliferation of knowledge and publications and new drug candidates and new test candidates that I think is going to be enormously influential in what the future of managing breast cancer is. So it's very, very exciting.

Tacey Ann Rosolowski, PhD
1:04:37.3
How do you see your own research path coalescing within that or out of this new context?

Gabriel Hortobagyi, MD
1:04:50.5
Well, in several different ways. First of all I was very much involved in the early development of the HER2 story.

Tacey Ann Rosolowski, PhD
1:05:06.5
Uh-hunh (affirmative).

Gabriel Hortobagyi, MD
1:05:07.4
And the development of Herceptin. In fact for about ten, fifteen years—very early on I organized every year a translational research meeting about HER2 and about Herceptin and similar anti-HER2 drugs. During that time, these were small meetings by invitation only—about fifty of the cream of the crop of breast cancer investigators. During that time, we generated an incredible number of collaborations and joint projects and research areas that are still producing incredible consequences.

Tacey Ann Rosolowski, PhD
1:05:51.4
Can I ask you just—is it accepted now in the field that breast cancer is more than one disease?

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Gabriel Hortobagyi, MD
1:06:00.3
Yes. Absolutely.

Tacey Ann Rosolowski, PhD
1:06:01.3
Okay. You had said when you first began to talk like this people looked like deer in the headlights or something. I'm wondering what was that process and how long did it take?

Gabriel Hortobagyi, MD
1:06:13.9
The process of repetition, the process of generating more and more evidence in support of that. By now the evidence is just overwhelming for that. It's not unique to breast cancer because it's like—it's certainly—the lymphomas and leukemias preceded the solid tumors impact, and we've known for probably a good fifteen, twenty years—perhaps longer—that even the acute leukemias come in different flavors and types. Chronic leukemia is the same, and the lymphomas by now—I've lost track of how many different types of lymphomas there are.

Tacey Ann Rosolowski, PhD
1:06:53.2
Uh-hunh (affirmative)

Gabriel Hortobagyi, MD
1:06:53.2
Breast cancer was sort of one of the first solid tumors—if not the first—where this eventually took place. But it's happening in lung cancer. It's happening in sarcomas. It's happening in colon cancer. It's going to happen in prostate cancer. It's going to happen in every single one of our malignancies when sufficient amount of research is done—

Tacey Ann Rosolowski, PhD
1:07:20.0
Uh-hunh (affirmative).

Gabriel Hortobagyi, MD
1:07:21.7
—and when these differences become relevant. So these differences would not be terribly relevant in breast cancer if all we had was chemotherapy. All right? But since we have now treatments that are very specifically targeting a subtype of breast cancer—they don't work in

other subtypes of breast cancer—these differences become highly relevant. Now that is starting to happen in other solid tumors.

Tacey Ann Rosolowski, PhD
1:07:53.4
I interrupted you—I'm sorry—with my question. You were talking about how you were involved in creating the HER2 story—studies of Herceptin—

Gabriel Hortobagyi, MD
1:08:05.8
Yes. So that has turned out to be a very exciting story because the HER2 positive breast cancer—the subtype used to be the worst prognostic subtype. Today it is starting to be one of the best. We have made an incredible amount of progress in a very short number of years with that. Simultaneously with that—and because some of the individuals involved in that little think tank I used to organize had other areas of investigation that were very exciting, and some of my own colleagues here in the institution were starting to look at other areas—I became involved in the development of other targeted therapies. But my role had changed because over the past let's say fifteen years, increasingly as my department grew and as my research grew it was less and less about my own research and more and more facilitating and coordinating and sort of guiding the research of others. That is an interesting transformation because it's frightening to some extent because you are departing from your own area of strength and moving into an area where you are much less comfortable.

Tacey Ann Rosolowski, PhD
1:09:40.4
Uh-hunh (affirmative).

Gabriel Hortobagyi, MD
1:09:41.8
Yet it has to happen because there is so much to do and so little time to do it that—unless you go through that transforming process—you end up becoming totally ineffective or you end up limiting yourself to just what you can accomplish yourself. Also, in the meantime, of course, I was taking other roles nationally. First I became much more involved with my specialty organization with ASCO and the AACR and eventually joined the board and became president of ASCO. Before that, I had become president of the International Society of Breast Diseases and was on the board of the International Association of Breast Cancer Research. Of course, that also takes time and effort away from your own research. You have to rearrange your resources and your activities. More recently, somewhere in 2005, I joined the Southwest Oncology Group and within a couple of years I became the chair of the breast committee. So that is a very large

organization of about 2000 members. Now my role there is to coordinate the research of that large breast cancer group and to try to serve as the conduit, if you wish, for our own research here to be translated into national or international level research through SWOG—the Southwest Oncology Group. It's an important role because there are some things that we can do very well here within the institution. Certainly most laboratory research can be done extremely well here. We have outstanding scientists and that's great. We can do early clinical trials very well. In fact, at any one point in time we have 100 to 120 phase 1 or early clinical trials. But once you go much beyond that, the institution is too small, ironically, to do that. So for instance, now through SWOG, we are leading two clinical trials, one that requires 9400 patients and one that requires 4500 patients. Even though we are a very large group and we see about 3000 new breast cancer patients per year, when you really have to identify a small and homogenous subgroup of those, it would take us several decades to collect that number of volunteers to contribute to those clinical trials. Through SWOG, we are recruiting about fifty patients per week for each of these clinical trials. So in a question of about three years, we are going to finish the recruitment. That would not be possible without such an organization. You have to give up something in order to get something else. Being part of SWOG and working very closely with the NCI has also given me the opportunity to get some of my younger faculty members involved in getting the positions of leadership within national and international trials that will advance their careers and that will serve us. SWOG serves as an amplifier, if you wish, to our own research.

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Chapter 20
A: The Administrator
Breast Cancer Service at MD Anderson in the Late Seventies

Story Codes
A: The Administrator
B: MD Anderson History
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
B: Growth and/or Change
C: Understanding the Institution
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care

Tacey Ann Rosolowski, PhD
1:14:09.9
Well, you are beginning to address the next real subject area that I wanted to talk about, which is your roles within—first what was the breast medical oncology as a service and then the shift when it became a department and, obviously, that involved a whole other set of skills and roles than working in the laboratory and collaborating with other experiments—also where you kind of entered into this subject in an unusual way. So I wonder how do you want to tell that story. Do you want to go back in time and kind of trace it chronologically? Or would you like to talk now about the facilitative coordinating roles specifically? How would you like to proceed?

Gabriel Hortobagyi, MD
1:15:05.6
To go back in time briefly because I think it is important to look at that. So initially—I might have mentioned in an earlier conversation—breast cancer was seen as part of the Department of Medicine at a time when there was developmental therapeutics in medicine. There was virtually no breast cancer seen in Developmental Therapeutics. So even though I trained in Developmental Therapeutics, I had to cross over to the other side in order to have access to breast cancer patients and research.

Tacey Ann Rosolowski, PhD
1:15:44.8
As I was just taking notes about the organization, it was Division of Medicine and then the Department of Medical Oncology and the Breast Medical Oncology Service was within that. Is that correct?

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Gabriel Hortobagyi, MD
1:15:56.8
There was no Division of Medicine.

Tacey Ann Rosolowski, PhD
1:15:56.7
Oh. There was no Division of Medicine?

Gabriel Hortobagyi, MD
1:15:57.8
At that time, this was called MD Anderson Hospital and Tumor Institute.

Tacey Ann Rosolowski, PhD
1:16:06.4
Uh-hunh (affirmative).

Gabriel Hortobagyi, MD
1:16:09.9
There were no divisions. So there was a—I guess there was a Department of Developmental Therapeutics. There was a Department of Surgery. There was a Department of Radiotherapy. There was a Department of Medicine. The relative structure of these various organizations to each other was not very clear.
Tacey Ann Rosolowski, PhD
1:16:38.3
Uh-hunh (affirmative).

Gabriel Hortobagyi, MD
1:16:40.2
Clearly, Developmental Therapeutics and Medicine were competing. They were artificially separated, but it was that way because it was the only politically acceptable way to bring in new people who would certainly antagonize those who had been here before; and in fact, they did. There was a lot of turmoil during that time within medicine. Within the Department of Medicine, there was this small thing—I guess we were a section. I don't know how formal that was, but we were called Medical Breast. Nylene Eckles was the—I guess the section chief before I arrived, and George Blumenschein became the section head when Nylene stepped down, probably about six months before I arrived. So George—by the way, George Blumenschein's son—also called George Blumenschein—is now a faculty member here in the Head and Neck and Thoracic Oncology. So his father was a hematologist by training, and he did a year or so at the NIH

looking at coagulation. It is my understanding that when he finished that he was looking for a job and his father-in-law, who was the dean of medicine at the University of Chicago, knew Lee Clark. So he put in a call and said, "Lee, my son-in-law is looking for a job. Do you have any openings there?" He was recruited pretty much fresh out of his fellowship at the NIH in clotting. He was recruited as a section chief for breast cancer and as director of education for MD Anderson. I won't even speculate about how that happened and what—but that's the way things happened at that time.

Tacey Ann Rosolowski, PhD
1:18:56.6
I'm remembering when we first had a conversation about the institution. When you arrived, there was a very real problem about there were no mentors in breast cancer for you, and this is another story to indicate how there was that vacuum.

Gabriel Hortobagyi, MD
1:19:13.3
Right.

Tacey Ann Rosolowski, PhD
1:19:14.1
So how did it all happen then? (laughing) How did treatment and diagnosis and all those things happen in this environment?

Gabriel Hortobagyi, MD
1:19:25.6
Well we still had Nylene Eckles around, and she was helpful, if nothing else, in giving us the example. Then we had a group of very good surgeons who were focused on breast cancer—Charlie [Charles M.] McBride and Marvin Romsdahl and Ed White and a couple of others—and they knew a lot about breast cancer. There were a couple of radiation therapists who were really outstanding: Eleanor Montague, who has since retired; Gilbert Fletcher, who was the head of Radiation Oncology; and Norah Du Tapley. These three were truly outstanding radiation oncologists. They were entirely focused on breast cancer, and they knew a lot about it. Dr. [Aman U.] Buzdar and I started on the same day as fellows in the breast service. We knew dramatically little about breast cancer, so we had to sort of learn on the job because there were no classes about breast cancer. Nobody lectured us about this is Breast Cancer 101, and this is the way you diagnose it, and this is the way you treat it. You sort of picked up pearls left by the center. So we learned about our colleagues in the other disciplines. By the time we arrived, George Blumenschein had been here for about six months, so he had learned a little bit and transmitted whatever he knew. He was a very good communicator. Nylene Eckles was still

around, so she served as an example. Then there was another guy called Charlie Tashima. Charlie Tashima was an older guy. I think he was from Hawaii. He's still around. I think he works out of Park Plaza. That's in private practice. He was a good solid medical oncologist who had experience with breast cancer. He enjoyed serving as sort of a more senior faculty member. We could ask him questions and whatnot. But it was largely an empiric process of watching and learning and reading and learning on the job.

Tacey Ann Rosolowski, PhD
1:21:59.8
Uh-hunh (affirmative).

Gabriel Hortobagyi, MD
1:22:01.7
Fortunately, both Dr. Buzdar and I had a major interest in becoming involved in research, in part because of our ignorance. So we spent a good part of our fellowship developing research projects and starting to write papers and trying to pick brains from whoever was willing to make them available to us. By process of trial and error, we sort of came up with what we are today.

Tacey Ann Rosolowski, PhD
1:22:42.8
Uh-hunh (affirmative).

Gabriel Hortobagyi, MD
1:22:47.0
At that time, we didn't know any better. I think we could have shortcutted that process enormously had there been individuals who sat down with us and said, "Now let me walk you through the process." There were several other people on the faculty who sort of semi-mentored me: Jordan Gutterman, Evan Hersh, Bob Livingston—even J Freireich. But they were not really the hands-on mentors. They would sort of say, "Why don't you do this?" And then you were on your own. Fortunately, both Dr. Buzdar and I are pretty much self-starters. We don't need people looking over our shoulders, so we would just say, "I have no idea how to do this, but I'll figure it out." We did eventually.

Tacey Ann Rosolowski, PhD
1:23:39.9
I was curious. As you compare the section in the late '70s and early '80s at MD Anderson, I imagine that when you compare it to peer institutions there were other institutions that had more of a critical mass of individuals who did specialize in breast cancer. But given that difference, how would you compare the treatment that was offered to patients? Then I was also thinking—

do you think that the lack of or the vacuum enabled you and Dr. Buzdar and others to be more creative perhaps here than you might have been elsewhere?

Gabriel Hortobagyi, MD
1:24:29.1
Yes. So I think of this process in a way similar to the way I think of the development of the state of Texas in the 1800s. The early part of the 1970s was really the Wild West in oncology. There were a few centers that were starting to organize themselves and certainly Memorial in New York had been around for a number of years. They had outstanding surgery. But medical oncology was not a developed specialty. There were training programs and only a handful of organizations. We have something like 150 medical schools in this country, give or take a few. When I started looking for a fellowship in the early '70s, there maybe four or five places that had a formal training program—Rochester, New York. There was Boston. Harvard had a very small program. Boston University had a somewhat larger program. Actually, it was Tufts. Memorial had a program. MD Anderson had a program. The NIH had a program—NCI. But these were all very small. I didn't know of any others that actually had a structured training program. Training didn't have the same meaning as it has today. If you compare how we train our fellows today—how much time we spend with them, how much time we spent structuring their curriculum and their rotations, and all of that—that's a far cry from—people would come here and train, and eventually they would be told, "Today you work there." Why? Because there's nobody else working there, so it's like a good idea. But it wasn't like, "We are going to teach you about lung cancer," and "Why don't you sit here today and the next several days, and we'll give you every day a lecture about a different part of lung cancer, and you'll learn and you can ask questions." No. And it wasn't only here. I think it was everywhere because that was the state of the art. In fact, medicine—even in the 1970s—was largely a process of apprenticeship. It was not a systematically taught thing, expect for the basic medical school part. Beyond that, it was largely an apprenticeship. So in that setting, I took my boards of internal medicine because you had to take that in order to qualify for the boards in oncology. I took my boards in oncology in 1977, and I was the second class that took the boards. The boards in oncology did not exist before 1975. The first boards were in 1975 and the second in 1977, so it wasn't really a modern organized discipline. It was not recognized until just a couple years before as a subspecialty of internal medicine. We had very few drugs, so there was very little to do except give morphine and symptomatic control and hope that people would die in peace and without too much suffering. In the breast cancer area when I started, we did not see patients with primary breast cancer because the surgeons cured them all according to them, of course. There was no need nor was there any reason to see that type of patient because they were cured by mastectomy or whatnot. It was only over the next several years after I started that we started to be involved in the treatment of primary breast cancer. We started to develop neoadjuvant and adjuvant chemotherapy and hormonal therapy, and eventually we got to where we are today. But that was

a process and a very slow process. By the same token, in the institution—most of the healthcare institutions were much less structured at that time. You had much more freedom to do things because there were fewer regulations. There were fewer rules. There were fewer guidelines, so to some extent you could do many creative things. You didn't have to get seventeen signatures to go to the bathroom. So that, of course, had great advantages for a budding researcher. I guess it had some disadvantages in the sense that there was not as much control over things.

Tacey Ann Rosolowski, PhD
1:30:18.3
Uh-hunh (affirmative).

Gabriel Hortobagyi, MD
1:30:19.0
But for the time I think it was the right approach.

Interview Session:3
Interview Date: January 23, 2013

Chapter 21
B: An Institutional Unit, Program
The Breast Cancer Service: From Section to Department

Story Codes
A: Professional Path
A: Contributions to MD Anderson
A: Career and Accomplishments
B: Growth and/or Change
B: MD Anderson History
C: Leadership
C: The Administrator at Work
D: On Leadership

Tacey Ann Rosolowski, PhD
1:30:23.9
Now from 1979 to 1984, you were alternative chief of the Breast Medical Oncology Service and then in 1984 and until 1992 you served as chief of the Breast Medical Oncology Service. So I wonder if you could tell me how you came to take on that role and what it meant ultimately.

Gabriel Hortobagyi, MD
1:30:53.4
Today when we look for someone in an administrative position we go through a search. We consult everybody and his uncle. We go through interviews. We go through a search committee. We go through deliberations. Then we make an offer and the person comes back with requests and this, that, and the third. Eventually there is a formal appointment, a formal announcement, and the person takes possession of his or her new position. Well none of that happened there. So we were—George Blumenschein, Charlie Tashima, Aman Buzdar, and I, and then eventually we recruited a couple of other junior people—but Buzdar and I were doing essentially all the research in the department. Buzdar even then was known to be a little bit more abrasive. I was a little bit more diplomatic, so George Blumenschein, who was the section chief, relied very much on me for a variety of things. Eventually he started talking about me as the alternate section chief. So when he left town, it was sort of understood that I would cover for him and I would take care of those things that needed to be covered. I'm not sure that there was ever a process of would you like to, or what does that mean, and what are the expectations, and you get a salary increment of X, or these are your duties. One day I just started to be referred to as that, and I guess the next year in my contract there was a one-liner that said I was that. In 1984, Dr. Blumenschein, I think, got into a tussle with Dr. LeMaistre, who was the president, and was

eventually removed as section chief. So on a Friday afternoon, I was called in by the then head of medicine because by then we had—so prior to that, sometime in the late ’70s, the then physician in chief and VP for patient care—

Tacey Ann Rosolowski, PhD
1:33:31.3
Was that Dr. Cox? James Cox?

Gabriel Hortobagyi, MD
1:33:32.7
No. No.

Tacey Ann Rosolowski, PhD
1:33:33.9
Oh, that must have been before.

Gabriel Hortobagyi, MD
1:33:34.1
It was [Fred] Conrad.

Tacey Ann Rosolowski, PhD
1:33:35.7
Oh, okay.

Gabriel Hortobagyi, MD
1:33:36.8
Conrad. He preceded Jim Cox. So Conrad was a flight surgeon from the Air Force. He was a very organized, very bright oncologist who had flown I don’t know how many missions in Vietnam. He was appointed as VP for patient care and physician in chief, and he picked me and appointed me as associate vice president for patient care. I lasted in that for about—I don’t know—maybe six months, maybe a year. I didn’t like the job, and it was just piled on to whatever else I was doing without any real benefit. So I essentially stepped down and moved on. But my first—one of my first tasks was to merge the two training programs: developmental therapeutics and medicine. That was the first step—to merge the two departments. So around that time, they also recruited Irv [Irwin H.] Krakoff. For Irv Krakoff, they did an administrative reorganization in which they removed the department chairs from developmental therapeutics and medicine and created a new structure called the Department of Medicine or the Division of Medicine—something like that. They appointed Irv Krakoff as the head, and when Irv Krakoff—under the orders of Mickey LeMaistre [Dr. Charles LeMaistre]—removed George Blumenschein

from his section chief position, he called me in Friday afternoon at 4:30 saying, "I just fired your boss. You are going to be the section chief from now on." I said, "Irv, please think about it over the weekend." He says, "Well. No not really." (laughing) So I was it.

Tacey Ann Rosolowski, PhD
1:36:01.4
I am not asking for indiscreet disclosures, but I'm curious. Was the difference of opinion between George Blumenschein and Dr. LeMaistre—did that have something to do with decisions about the section?

Gabriel Hortobagyi, MD
1:36:16.2
Oh, absolutely.

Tacey Ann Rosolowski, PhD
1:36:17.6
Is there something that's relevant to an understanding of how the section evolved? As I said, I don't want you to be indiscreet. But I'm just curious if there is information that—

Gabriel Hortobagyi, MD
1:36:26.6
In that sense, no. It had nothing to do with the section. Dr. Blumenschein—remember he was also the director for education.

Tacey Ann Rosolowski, PhD
1:36:36.9
Oh, okay.

Gabriel Hortobagyi, MD
1:36:38.4
He was a very outspoken person. I think what happened is that somewhere in public he either challenged or said something that Dr. LeMaistre was not very happy about.

Tacey Ann Rosolowski, PhD
1:36:56.9
Uh-hunh (affirmative).

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Interview Date: January 23, 2013

Gabriel Hortobagyi, MD
1:36:58.9
It had nothing to do with the internal functioning of the section.

Tacey Ann Rosolowski, PhD
1:37:05.6
Uh-hunh (affirmative). So that following Monday when you suddenly came to work and were (laughing) section chief—

Gabriel Hortobagyi, MD
01:37:11
I was it.

Tacey Ann Rosolowski, PhD
01:37:12
—how did you think about that role? Because suddenly you have a different kind of mandate to make decisions.

Gabriel Hortobagyi, MD
1:37:20.8
Well, yes and no. Again, today when we recruit—for instance, we are recruiting for my replacement as a department chair. So there is a thoughtful group of senior faculty members who are a search committee. We request applications from all over the country. They come for visits. They make presentations. They interview with dozens of people. They have a job description about what is expected of them. They have a number of resources that are given to them. These are the positions you can recruit to. This is space you have. These are areas where we would hope you could work to improve the department and build out these. This is what the future looks like, but we also want you to give us your ideas about where you would like to take this department. That didn't happen in 1984. We just told them, "You're it." There was not a job description. There were not a these are the resources you have. The resources I got were what was there. There was no discussion of, "Would you like some more space?" or "Would you like more secretaries?" or "Would you like an additional position?" None of that was—that was not discussed. Even later in 1990-something when we were made from a section into a department, that was sort of Dr. Krakoff's swansong before he retired. He made us into a department, and he made us into a department because of political reasons not because he was necessarily thinking of us. So at that time in the executive committee of the medical staff, there were five or six surgical departments but only one Department of Medicine. So whenever a vote came—or that was controversial—the surgeons sort of drowned the voice of medicine. So he said, "I can deal with this by making many of our sections departments." And in fact, at that time leukemia

became a department, sarcoma became a department, GI became a department, GU became a department, lung became a department, and breast became a department. All of a sudden, there were more medical departments than surgical departments, so we gained a little bit of greater balance within the staff leadership or the faculty leadership in the institution. But were we asked as section chiefs, "What are your needs?" or "This is your job description. This is what I expect from you." None of that. It was just a change in name.

Tacey Ann Rosolowski, PhD
1:40:19.4
Uh-hunh (affirmative).

Gabriel Hortobagyi, MD
1:40:20.5
We were in the same office, in the same clinic space. No more positions. No more salary. No more nothing. It was just a change—an administrative change.

Clip
A: The Administrator
A: Professional Path
A: Contributions to MD Anderson
A: Career and Accomplishments
B: Growth and/or Change
B: MD Anderson History
C: Leadership
C: The Administrator at Work
D: On Leadership
B: MD Anderson History
Learning to Lead Breast Medical Oncology

> ***Tacey Ann Rosolowski, PhD***
> **1:40:30.4**
> Where I want to go with this is how you feel within the various roles that you served—within the section, within the department—whatever that is—how you felt you've worked to kind of reshape breast medical oncology administratively or functionally within the department to make it stronger in all of the ways. How would you characterize how your role evolved? Even if no one was giving it to you, you were kind of making it up as you were going along.

Gabriel Hortobagyi, MD
1:41:08.9
Initially when I eventually became—what was that word—alternate section chief?

Tacey Ann Rosolowski, PhD
1:41:16.3
Yeah. Alternate section chief. Uh-hunh (affirmative).

Gabriel Hortobagyi, MD
1:41:19.6
Well, I was so junior I had no concept of where this was going and what I was supposed to do. I understood that my role was there when the boss wasn't there and that I had to carry on. Then as you mature, you realize that you have different ideas about how the group should grow. As you start to understand the size of it better and as you become more confident about your role as a physician and as a specialist, you start to be productive, and you start getting feedback both from inside and outside the institution. You become more self-confident. Your horizons open up. Then you start proposing changes and proposing improvements. I did that even as an alternative chief. I was the first one to recruit a research nurse—in fact, the first three research nurses—because I was at that time essentially the only one who had grant funding. Then I was the first one to recruit—well, first of all, Dr. [Robert S.] Benjamin, who is the chair or the ex-chair—past chair of the Sarcoma Department—and I worked with the Texas legislature to pass a bill that approved the concept of nurse practitioners and physician assistants. We were then the first to recruit a physician assistant to work in our respective departments or sections at that time. So then this opens up, and then you realize that in order to support your research nurses you need to grow to a certain minimum size because you need a certain number of grants in order to support the extra expenses. The only way you can do that is by increasing your volume and getting more grants. Then you start understanding the administrative intricacies of this. Then you start to understand better the interactions with the other departments. Then you start visiting other places. You see how they function. You see those things that they do better. You see those things that they don't. Gradually you develop a better-rounded idea of what a breast center should look like.

When I came here, even though we had a very strongly collaborative approach where we developed that, we didn't think of ourselves as a breast center. The breast center concept came later. But it came, again, as a gradual awakening of, you know, we are not doing this for ourselves. We are doing this for our patients. Therefore, let's rethink this process in a patient-focused manner. That's how eventually over several iterations of the breast center, it evolved. Because at the beginning, the breast surgeons worked in one area. The

breast radiotherapists worked in another area of the building. The medical breast worked—in fact, our first clinic in medical breast—we were just in a hallway, and we had one of those down-foldable shelves on which we wrote notes, and there was a phone. That was our clinic. Eventually we had a nicer one with rooms dedicated just for what we did. There was at least a conference room, which doubled up as a working room. Then we grew to a larger size and then we helped to design that one. And eventually the fourth or fifth medical breast or breast medical oncology clinic was more according to our specs. What happened here at the Mays Clinic was entirely developed by us as a joint effort. We essentially requested and required all of the things that are there. So it was the first time that we actually had all the resources and all the tools at the right place, and we were truly working in a joint enterprise with all of the specialties needed to achieve that. So that evolves gradually. At first you start to understand what you need in terms of patient care because that's how you are trained as a physician. Then you start making improvements for that. Then because of my interest in clinical research, I started to identify those areas where I thought we could do a better job or could make our research work more efficient. Then you start to expand the educational part. Then you organize the training of fellows and residents and visiting scientists. Then the last part was—in my evolution, I guess—the integration of translational research and the longstanding struggle to actually recruit some laboratory-based investigators within the department, within the section of the department. And only within the past ten years was I really successful in getting a critical mass of translationally thinking physicians into the department. So it's an evolution. If I could start my academic life over with everything I know, I'm sure that process would be much shorter. But I was learning on the job.

Tacey Ann Rosolowski, PhD
1:47:57.9
Well, I notice we are at 3:00, and so our official time is over. Would you like to close off for today? We do have another session scheduled.

Gabriel Hortobagyi, MD
1:48:07.7
Let's do that because I have to take care of few things this afternoon.

Tacey Ann Rosolowski, PhD
1:48:12.1
All right. It's one minute after 3:00, and I'm turning off the recorder.

1:48:16.2 (end of audio)

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Gabriel Hortobagyi, MD

Session 4—January 28, 2013

[Note: Recorder is turned on during a conversation –in-progress.]

Chapter 22
B: MD Anderson Past
Creating a Patient-Centered Breast Service

Story Codes
C: Patients
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
B: Growth and/or Change
A: The Clinician
C: Understanding the Institution
B: The Business of MD Anderson
B: The MD Anderson Brand, Reputation
C: Professional Practice
C: The Professional at Work
C: The Clinician at Work
D: On Care
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care

Gabriel Hortobagyi, MD
0:00:00.0
We did that, and it turned out that this poor patient had to walk miles and miles towards the institution in order to go through all of her appointments for radiology and for the lab and to see the surgeon and to see the medical oncologist. It was a huge undertaking. It was a huge undertaking for a healthy person. Just imagine what it was for someone who was ill because of her cancer or because of some comorbid conditions. So that underlined the fact that we were not

really patient centered, but we were bureaucracy centered because it was convenient to have all of the surgeons here. And we just happened to have space for the radiation oncologist there, and I do not think it was an intentional decision—to hell with the patient. No, I do not think it was that. It was just the thoughtless evolution of bureaucracy, you know? So with that in our back pocket, we then were more successful in getting our recommendations listened to, and they were incorporated into the plans of the Mays Clinic, and some if it was incorporated into the plans for this building.

Tacey Ann Rosolowski, PhD
0:01:27.8
Can I ask you about the timing? You said that there was a certain moment when in the previous location you became too large.

Gabriel Hortobagyi, MD
0:01:37.4
Right.

Tacey Ann Rosolowski, PhD
0:01:39.2
What was the increase in patient load? And why was that increase happening?

Gabriel Hortobagyi, MD
0:01:47.0
Well, the increase was the result of the fact that MD Anderson was coming out of its infancy. It was becoming better known not only locally but nationally and internationally. And then more and more patients were looking for our services, and this is a complicated phenomenon. Sometimes institutional leadership doesn't understand this well. One way you grow is because you take good care of people. That patient goes and tells friends how happy they were with their treatment at MD Anderson, that spreads the news, and people come back because of patient satisfaction. That's one thing. And another one is that as you do research, you publish research results, you present them to meetings. Other physicians listen to that, and the next time they see a patient who's relevant to that meeting or to that presentation or the next time they see a patient with breast cancer they remember, "Oh, yes. There was that guy from the breast service at MD Anderson, and he seemed to be right on the ball in presenting that. So let's get a consultation here." So that's another source of expanding the referral. And sometimes institutions think cheaply about how much research is costing us. But research, in reality, is what drives our growth. It is what drives patient access to this institution because people don't come to get what they could get very well three blocks from here in a private office. It's much easier to drive to their private physician's office where there is plenty of parking. They don't have to put up with

this maze that the medical center is. And they are in and out in minutes, and they get done. They come because of our reputation, and our reputation is based on our research. And then the third part of it that is very important is that every year we have thousands of trainees of all sorts—physician trainees, technician trainees, nurse trainees. I think we train something like 3000 or more trainees every year between undergraduate students and postgraduate students and doctoral candidates and all of that. And many of those are from outside our community, of course. And when their friends, relatives, family members, and colleagues think of where to refer someone they say, "Ah, I trained at MD Anderson. It's the greatest place on earth." So all of those things contribute, and it's sort of a geometric expansion.

Tacey Ann Rosolowski, PhD
0:05:17.3
I was wondering, too, just about timing because wasn't it 1994 that the breast cancer gene was discovered?

Gabriel Hortobagyi, MD
0:05:23.8
Uh-hunh (affirmative).

Tacey Ann Rosolowski, PhD
0:05:25.2
And I know I talked with Dr. Strong—Louise Strong—about how that had a considerable impact in at least the conversations about who was going to be handled here and what kinds of services were going to be provided. Was that a factor at all?

Gabriel Hortobagyi, MD
0:05:41.4
A very small one probably, and to a large extent it is because the breast cancer genes are responsible for less than five percent of breast cancers, and second because we did not discover the breast cancer gene here. We contributed to the literature that led to the discovery of the breast cancer genes, but we did not actually do that ourselves, so we cannot claim credit for that. Now what I think did attract people is the conglomerate of research—the results that were emerging at that time. So that was the time in the late '80s, early '90s when we were starting to see the results of a lot of research in basic biology. And we were starting to understand better that, and eventually ten, fifteen years later came the completed Human Genome Project, the oncogene gene story, the monoclonal antibodies, tyrosine kinase inhibitors, and all of these new drugs. So all of that started in the later part of the '80s, and among that I am sure would be that BRCA1 and BRCA2 mutation became part of that story. A little bit before that the p53—they discovered p53 and the cloning of that—so every scientific discovery adds to what we know. How much

each individual scientific discovery contributes to our referral is much harder to determine unless there is a clear sign that the discovery happened here, and it's given a lot of press. But I was always interested in finding that discoveries have indirect effect, too—at least in patient referral. So suppose that I or one of my colleagues stands up at a meeting, and we say, "We just found that we have this great treatment for patients who are blond and under age twenty-five with breast cancer. And we have this great thing, and this is our experience, and this is the result of our research." So this gets great press. It is written up by Gina Kolata in the *New York Times* and it is misinterpreted, as usual. So the next day—or the next Monday—you get this torrent of phone calls from physicians and patients about either wanting advice or wanting to come to be seen. And only a tiny minority of those calls come from or are relevant to patients who are under age twenty-five and are blond. The rest are totally unrelated to it, and it's just a visibility issue. "Oh, ah ha. I read this very interesting thing about MD Anderson and breast cancer and women under the age of twenty-five and with blondes and what not. But I've got this patient who's got sarcoma and has chronic obstructive lung disease. Let me call MD Anderson." And it's the most bizarre association, but it happens every single time. And most of the calls we get as a consequence of publicity are just more calls but not necessarily relevant to what we just published.

Tacey Ann Rosolowski, PhD
0:09:55.0
Have you gotten to the point where you anticipate that?

Gabriel Hortobagyi, MD
0:09:57.0
Oh, yes. Absolutely. Absolutely. So we know that anything that gets us in the public eye—unless it is really something very bad—will just generate phone calls; and more recently, of course, it generates emails. But it is not necessarily focused on what was important at that moment.

Tacey Ann Rosolowski, PhD
0:10:23.9
So tell me about what happened when the breast center was moved into this new service where everything was pretty much close, you pretty much got what you wanted, and you had a real model of a center that was patient centered. What did you observe?

Gabriel Hortobagyi, MD
0:10:42.3
Well, yes. That was very nice. And then we saw this retrenchment from all parties. It was interesting because we had this great opportunity to actually work together, but everybody wanted his own little corner. And then there were discussions about which part should be the

surgeons and which part should be the medical oncologists and which part should be—you know. We had to push very hard to convince people that this was not about us, and it was not about establishing a new private property there. But this was about sharing, and this was about sharing for the benefit of the patients that we were there to treat.

Tacey Ann Rosolowski, PhD
0:11:29.2
So help me understand how this was so different from those meetings where people began to see perspectives change. What was so threatening?

Gabriel Hortobagyi, MD
0:11:44.3
You have to realize that you might change people's behavior to some extent without necessarily changing their underlying reactions. And people would—at the beginning of this breast center, individual physicians still wanted their name on a room—on an examining room. Not literally, but they wanted to know that they were the ones who'd always see patients in that room. And that was their room, they wanted it furnished exactly to their specifications, and they didn't want anyone else to fool with that room even though they were there half a day a week or two half days per week. And we had to push very hard. And at the beginning we were able to sort of comply with that a little bit, but I didn't want to because that was giving the wrong message, because the message was we are going to share this entire space. And we are going to have to—as we grow, we will fill this, and we can't afford to have a room reserved for Dr. X simply because Dr. X wants it. And that process actually took years, and it wasn't really completed until the past—I would say three or four years.

Tacey Ann Rosolowski, PhD
0:13:18.4
Really?

Gabriel Hortobagyi, MD
0:13:19.0
Yeah.

Tacey Ann Rosolowski, PhD
0:13:20.7
So—and just to be clear—you moved into the center in the Mays Center [Mays Clinic or Ambulatory Clinic Building]. What was the year when the breast center opened there?

Interview Session: 4
Interview Date: January 28, 2013

Gabriel Hortobagyi, MD
0:13:28.0
I think 2002 probably.

Tacey Ann Rosolowski, PhD
0:13:30.3
Wow. So we're talking a decade.

Gabriel Hortobagyi, MD
0:13:32.1
Yeah. Yeah. So it took growth to get us to the situation where we could no longer afford to have any room unoccupied at any time of the day during the week, but we had to sort of move people around so as to use and occupy rooms whenever they became available. And it was only last year that my original vision of—because I remember when we moved in. I talked to the then head nurse or clinic administrative director and said, "You know, whenever I go out to the airport I look at this board—this electronic board—in every airport, and it shows all the flights. And it shows all the gates, and it shows times in and out and what not. And when I pull up my reservation online I can see my name there, and I can see where I sit. And presumably others can do the same thing, and presumably the airline can see where all of us sit. And they fill planes, and they have food, and they remove food and beverages, and this whole thing is an enormously complex puzzle. Why can Continental Airlines do it and MD Anderson can't? So let's put up one of these electronic boards, and let's feed the information." My God, it's as if I had threatened to murder someone's mother, you know? "No, you can't do that, and you can't share that information with anyone." And so we struggled with that for years—probably for the best part of about five years—until we were finally getting to the point where I started to ask for more space for the breast center. They said, "Well, we have no more space. We would have to build another building, and we don't have the money to build another building." So I said, "Okay, then you need to play ball, and we need to use technology to improve our room utilization." Because when we moved—well, even five years ago, the average number of patient visits per room—per examining room—in the breast center was about three.

Tacey Ann Rosolowski, PhD
0:16:03.5
That is remarkably low.

Gabriel Hortobagyi, MD
0:16:04.9
Oh, it's horrible. Yeah.

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Tacey Ann Rosolowski, PhD
0:16:07.0
I'm shocked.

Gabriel Hortobagyi, MD
0:16:08.1
If you go out to Intercontinental Airport, probably each gate gets used—I don't know—fifteen times a day, twenty times a day depending on the turnaround and whatnot. And the actual patient contact in each room is probably ten, fifteen, sometimes twenty minutes. A very complicated situation may take an hour occasionally, but we don't see that many in any particular day. So finally last year, after millions of consultations and millions of conferences and millions of interactions and discussions and getting engineering to look at our efficiency and getting time studies—finally we put up these electronic boards where you can now see who checked in, where is that patient—is she in the lobby, is she sitting in a room—whose patient that is, who's the nurse responsible for that, where is that going, how long has the patient been sitting there. And the patients on the outside—to some extent, I think—can see where they stand in terms of their waiting and all of that.

Tacey Ann Rosolowski, PhD
0:17:30.9
So does it have the patient's name or is there a number or—?

Gabriel Hortobagyi, MD
0:17:34.4
I have to look at the waiting room because there would be HIPAA considerations on the outside. From the inside, of course, we have number and chart number not name.

Tacey Ann Rosolowski, PhD
0:17:44.4
I am just thinking because in a lot of DMVs you get a number and you're waiting to do something with your driver's license, and your number comes up, and you know where to go, and you're being tracked.

Gabriel Hortobagyi, MD
0:17:57.3
We have also proposed what a number of restaurants do today. You walk in with your reservation, and they give you a beeper, and they say, "Go to the bar and have a drink, and when your table is ready we'll beep you." No name necessary. No privacy issues violated. You go and

have your margarita, then this thing starts lighting up, and you go and have your room or your table.

Tacey Ann Rosolowski, PhD
0:18:30.7
Yeah, I have had that actually in radiology services.

Gabriel Hortobagyi, MD
0:18:32.8
Yeah.

Tacey Ann Rosolowski, PhD
0:18:33.3
Yeah.

Gabriel Hortobagyi, MD
0:18:33.9
Yeah. And I think—I'm very private, and I hate it when I go to a doctor's office and the nurse comes out, "Hortobagyi!" You know—and everybody turns around and says, "Who is that?" I really dislike that. It's not that I have anything to hide, but it's nobody's business that I'm there. You know?

Tacey Ann Rosolowski, PhD
0:18:55.6
Yeah. Yeah. And in a situation where you're maybe frightened and—

Gabriel Hortobagyi, MD
0:18:59.1
Right. Right. Right. Right.

Tacey Ann Rosolowski, PhD
0:19:00.2
—you're ill. You don't—yeah.

Gabriel Hortobagyi, MD
0:19:01.0
Right. Right. Right. So finally we got to that point. So that's a long evolution of all of this. Right now we are in a situation where we are in these pods, and each pod consists of several specialists. And we work sort of side by side. And I can just finish seeing a patient of mine, and

if I need a surgical opinion I just walk next door. I say, “Hey, would you mind taking a look at this patient? It’s a very simple issue. I’ll send you a formal consultation later. I just need your very simplistic ballpark view so that I can plan.” And that shaves weeks off the workup and getting ready and then making decisions. And that is working out very well. And we also then have an immediate—the immediate ability of saying, “You know, I hear you, but I don’t think that’s a good idea because of A, B, and C. Have you considered that?” And then instead of waiting three weeks to get to that point and then having to make an extra phone call and then playing phone tag with the other doctor, we just resolve this over just a few minutes.

Tacey Ann Rosolowski, PhD
0:20:32.5
So what do you think made the difference when you had—when you first moved in and there was all this retrenchment and people feeling threatened? You know—what broke the dam? What enabled people to move into this mindset of sharing?

Gabriel Hortobagyi, MD
0:20:47.6
Well, first the fact that we kept on sharing information with them. Your private property, your room is being used on the days you are there only three times per day. The days you are not there it’s not being used at all. In the meantime, there are physicians who are clamoring for rooms because they can’t—they don’t have space to see patients. And then we kept on hammering on the same idea. We need to share. We are a team. We need to share. We are a team. And repetition often serves to get a message eventually across. So that was that part. The research part was—research is always an evolving issue, and probably our very first research activities we did in breast medical oncology were the development of clinical trials. And we mentioned in one of our earlier conversations the combination of chemotherapy with the FAC regimen and the locally advanced and inflammatory breast cancer protocols. And then we got more and more into new drug development, so we started to do Phase II and Phase I clinical trials with new drugs. And that provided us with some resources because most of those drugs came from industry—pharmaceutical industry that had developed drug A, B, or C—and we would get access to that for doing a clinical trial, and the company would pay for the cost of doing that clinical trial. And you usually overestimate your costs a little bit so that you can be sure that the hospital doesn’t get shortchanged for that. And then sometimes there is a little bit of money left, and then you use that for reinvestment into research. And most of the costs of clinical trials are based on making sure that everything that the clinical trial calls for actually takes place and that all of the data are collected prospectively in the cleanest and most accurate fashion. For that you need research nurses, you need data managers, so much of the cost is related to personnel. And as the number of clinical trials we performed increased we had, of course, the need to have more and more personnel for that. So eventually we built out a group at the beginning—one and then two and

then three—and eventually we got up to what we have now which is about fifteen or eighteen research nurses and about ten data managers and whatnot.

Tacey Ann Rosolowski, PhD
0:23:55.0
Wow.

Interview Session: 4
Interview Date: January 28, 2013

Chapter 23
A: The Administrator
Regulations on Clinical Trials and New Research Projects in Breast Medical Oncology

Story Codes
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
B: MD Anderson Culture
B: Growth and/or Change
A: The Clinician
C: Understanding the Institution
B: The Business of MD Anderson
B: The MD Anderson Brand, Reputation
C: Professional Practice
C: The Professional at Work
C: The Clinician at Work
D: On Care
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care

Gabriel Hortobagyi, MD
0:20:47.6+
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Tacey Ann Rosolowski, PhD
0:23:55.0
Wow.

Gabriel Hortobagyi, MD
0:23:55.3
And that allows you to then be a little bit more flexible about how you use those individuals and how you do that. In the meantime, of course, research became much more complex. The regulatory requirements became much more complicated. The actual complexity of the clinical trials became much more intense. Translational research became an integral part of clinical trials that required much more to do—additional biopsies, additional tests, additional imaging. So when we started, I remember the first nurse was able to handle eight, nine, sometimes ten different clinical trials at the same. Today one of my nurses can handle two trials at the same time. She's a hero because it's a much more labor-intensive effort and intensive activity. And then HIPAA came in of course, and many of the regulatory aspects of informed consent and how you manage the data and the external audits and the FDA audits. All of that was sort of each an added layer of activity on this.

Tacey Ann Rosolowski, PhD
0:25:31.4
What's your view of that? I've talked to people who have felt that regulations have gotten out of control. What's your view of that? Are they a necessary burden? I mean—is it too burdensome?

Gabriel Hortobagyi, MD
0:25:47.9
Well, on some of my worst days, I would like to be a dictator and go after the thirty or forty people around the country who are responsible because of their irresponsibility or malfeasance for the rest of us being punished with regulation. Because what has happened over the past forty years is that everything was going well, and then someone decides to be either sloppy or dishonest. And then in order to prevent that event from taking place again, there is a burden of regulation on everybody. And that has happened a number of times, so when you add up each individual—so each individual regulatory aspect may not be huge, but when you add twenty-five then the conglomerate of the twenty-five adds a huge amount of work, none of which actually

improves the efficiency of research nor does it make delivery of effective treatment or diagnostic faster to the patient who is the only person important in this thing. And we do so many things to protect the bureaucracy that sometimes we forget why we do research, and it is a huge problem. It is a huge problem, but it is always the issue of the sins of the few end up punishing the many. So I don't know where you stand on the gun controversy, but it's not very different there, even though it's both qualitatively and quantitatively a different controversy. But you get a mass murderer who takes an AR-15 or whatever that thing is called and goes out and kills twenty kids. Everybody in the country has to now think of gun control. Well, I happen to think that we do need some more strict rules, but in reality if nobody did that—if there were no mass murderers—we would not care that much about having 300 million or 400 million or 200 million guns in the country. Now unfortunately we have to care because these things keep on happening. And the same thing is in research—in medical research. Someone fakes a piece of research—everybody else pays. And we've been paying. We've been paying very heavily. When we started to run clinical trials we would get roughly a grant for—oh, the equivalent of maybe $400 or $500 per patient for running a Phase II clinical trial. Today it's not unusual for a company to pay us—despite much more stringent review of the real cost—$25,000, $30,000 per patient. And when you talk to drug company folks when they have a new drug and they're going to run the definitive clinical trial of whether the drug is or is not worth FDA approval, that company sets aside $200 million, $300 million for that single clinical trial. And much of that is to answer all the regulatory requirements.

Tacey Ann Rosolowski, PhD
0:30:23.0
What do you think is the broader effect of that? When each clinical trial is so expensive, how does that change how research is done? I mean at the level of the institution.

Gabriel Hortobagyi, MD
0:30:36.9
Well, it slows it down tremendously and requires—if we did today research and patient care the way we did it in 1973—so what is that? Forty years ago? We could probably do it with forty percent of the personnel we have on board today—maybe even less. So that gives you an idea of what the additional regulatory aspects of research and patient care and HIPAA and dealing with insurance companies and Medicare and Medicaid and whatnot has added to our ability to run an institution. It is a huge amount of extra—and in my mind—largely unnecessary cost. So Congress screams and yells about how expensive medical health care is. And we as private citizens see these costs escalating. But nobody thinks about how much of this is the effect of the laws passed by Congress and the regulations passed by government agencies and the doings of insurance companies. And of course it never ends because nobody takes ownership and nobody takes responsibility for this now. So it is—and even more than money the amount of time and

effort of many of our brightest and best investigators that goes into these things that add no value to their research is a huge waste. Because instead of having—I don't know—ten discoveries during their lifetime, they may have three or four because they have to spend so much time doing piddly stuff.

Tacey Ann Rosolowski, PhD
0:32:59.8
I was reminded, too, when you were talking about those enormous costs, and I think in one of our previous conversations you talked about how the tendency for granting was actually—money is granted in a fairly conservative way, and I am sure those spiraling costs increase the conservatism as well.

Gabriel Hortobagyi, MD
0:33:18.7
Absolutely.

Tacey Ann Rosolowski, PhD
0:33:19.1
You don't want to take risks—

Gabriel Hortobagyi, MD
0:33:20.5
Absolutely.

Tacey Ann Rosolowski, PhD
0:33:20.8
—when there is that much money at stake.

Gabriel Hortobagyi, MD
0:33:20.3
Absolutely.

Tacey Ann Rosolowski, PhD
0:33:23.4
Yeah. Now when you were and have been thinking about how to develop all of these elements of patient-centered care—the research, and we haven't talked about education and the translational piece yet—but when you are thinking about all of that and how to get all the post pieces of the puzzle rising at the same time, did you—how long did it take you to understand how connected all of those things were in a program such as what is happening here at MD Anderson?

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Gabriel Hortobagyi, MD
0:34:11.6
I don't know. I never thought of it in those terms.

Tacey Ann Rosolowski, PhD
0:34:15.4
Or maybe you thought of it in a different way.

Gabriel Hortobagyi, MD
0:34:17.3
The understanding of that develops gradually and develops in part because you look back at what you have done and what you have not done, and you look at the missing pieces and you say, "Gee, I should have done that, or I could have done that, or it's time to do that." And the other part of that is that as you become more clearly responsible from an administrative perspective to get many things done and developed, then you realize what it takes. Because while you are just thinking about doing your research, you think of what you need immediately to get that done. But you don't necessarily think of what the optimal structure of a research infrastructure should be. All right? So as our research group was developing, well, I would discuss on a weekly basis or sometimes more often with my research nurses what our needs were, where we are short, where we were short of something, what more resources we needed to put in place, how could we be more efficient doing something. You think of different models of utilizing research personnel, and that's what you do. And then as budgets become tighter, you really start to deconstruct the whole thing and start thinking about what other ways there are to build this out. So in that sense, that sort of underlies what we discussed earlier about the lack of the business orientation and training of physicians. And yes—what is that called? The executive development program—well, it was wonderful but that was a few weekends for a few months as opposed to a full MBA or as opposed to full training, as I'm going to be an executive in IBM or GM or Apple or something like that where you would from day one be used to thinking of this programmatically in the sense of I'm going to build the best and largest—I don't know—racecar or the best and most efficient computer, and for that this is the way the business should look.

Tacey Ann Rosolowski, PhD
0:37:44.4
Well, and I'm even thinking, too, that there's an additional piece because you're not just interested in creating the best and most impactful breast center. You want a breast center that's going to be an engine of producing more knowledge about breast cancer.

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Gabriel Hortobagyi, MD
0:38:01.1
Absolutely.

Tacey Ann Rosolowski, PhD
0:38:01.6
So there's a strategic piece there, too.

Gabriel Hortobagyi, MD
0:38:04.3
Well, and there's the multitasking. Because if I'm the vice president for—I don't know—new truck development at Ford, I focus on developing that new truck. And I've got some engineers working here and some marketing people and some people who are looking at cost and whatnot, but all of my focus is on that. Right? Here we have our focus on—we take care of a very large number of patients. And as a supervisor—as a department chair—I need to make sure that the quality of care is as high as can be, that all of my faculty members are providing the same or higher level of quality, that all of the support personnel—nurses and et cetera—are working in that direction, that my interactions as a department with the breast center—which is not directly under my control—is such that I can influence the development of the breast center. I am responsible for all of the research activities, making sure that the research productivity of the department is as high as can be and is the highest quality as it possibly can, making sure that the research enterprise breaks at least even and it doesn't go in the red too often, making sure that I have the support research personnel that we need. I need to make sure that all of our research activities are actually coordinated and that there are no independent republics reinventing the wheel every so often. I need to make sure that each of my faculty members has a research activity so that their careers can be developed and that I can get them promoted, and I can get them rewarded for what they do. And I can hold them accountable for what they do. I need to make sure that we educate the next generation of physicians, that we mentor our younger faculty with the resources and knowledge of the older faculty, and that ultimately our entire budget as a department fits into the budget of the division and within the vice president—the line vice president of the institution. And during all of this I am writing papers, I am running my own research. I'm making presentations thirty, forty, fifty times a year around the globe; so the multitasking is quite considerable. You're like the juggler—keeping as many of those objects in the air as you can.

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Chapter 24
A: The Administrator
Mentoring, Career Support, and Education in Breast Medical Oncology

Story Codes
A: The Administrator
C: Professional Practice
C: The Professional at Work
C: Leadership
C: Mentoring
D: On Research and Researchers
D: On Leadership
D: On Mentoring
B: Building/Transforming the Institution
B: Institutional Processes
C: Understanding the Institution
D: On the Nature of Institutions

Gabriel Hortobagyi, MD
0:38:04.3
Well, and there's the multitasking. Because if I'm the vice president for—I don't know—new truck development at Ford, I focus on developing that new truck. And I've got some engineers working here and some marketing people and some people who are looking at cost and whatnot, but all of my focus is on that. Right? Here we have our focus on—we take care of a very large number of patients. And as a supervisor—as a department chair—I need to make sure that the quality of care is as high as can be, that all of my faculty members are providing the same or higher level of quality, that all of the support personnel—nurses and et cetera—are working in that direction, that my interactions as a department with the breast center—which is not directly under my control—is such that I can influence the development of the breast center. I am responsible for all of the research activities, making sure that the research productivity of the department is as high as can be and is the highest quality as it possibly can, making sure that the research enterprise breaks at least even and it doesn't go in the red too often, making sure that I have the support research personnel that we need. I need to make sure that all of our research activities are actually coordinated and that there are no independent republics reinventing the wheel every so often. I need to make sure that each of my faculty members has a research activity so that their careers can be developed and that I can get them promoted, and I can get them rewarded for what they do. And I can hold them accountable for what they do. I need to make sure that we educate the next generation of physicians, that we mentor our younger faculty

with the resources and knowledge of the older faculty, and that ultimately our entire budget as a department fits into the budget of the division and within the vice president—the line vice president of the institution. And during all of this I am writing papers, I am running my own research. I'm making presentations thirty, forty, fifty times a year around the globe; so the multitasking is quite considerable. You're like the juggler—keeping as many of those objects in the air as you can.

Tacey Ann Rosolowski, PhD
0:41:08.7
What support do you have in doing all of that? And obviously, you don't do it alone. What do you rely on?

Gabriel Hortobagyi, MD
0:41:16.0
Well, so you rely heavily on your immediate support, which is quite limited in terms of the support the institution provides. As the department chair you get an executive assistant. And your executive assistant deals with your schedule and your travel and your meetings and making sure you do not commit to things that you cannot accomplish and that your schedule is kept fairly coordinated. But with the evolution of technology, you end up doing much of what secretaries used to do in the past. I write all of my papers. I do not dictate anymore. I make all of my slides. To a large extent, I don't rely on the travel agency to pick up the best schedule because I know the schedule with rare exceptions as well or better than the travel agency, especially to places where I go with some frequency. I know I need to take the 6:50 flight to Washington because that gets me there at 11:15 and gets me to the hotel in time so that I can get a good night's sleep and get up by 6:00 the next morning—just as an example. And for all of the research activities, I have to generate resources and funds so that I can get an infrastructure for research. The institution doesn't pay a penny for that. Education—well, it depends on how much we want to do in terms of education. Certainly for mentoring our younger faculty—as a department chair you get a little bit of funds from PRS for that. The fellowship program pays for some of the fellows if the fellows are involved with research with the department. We need to provide those resources to them if they are fortunate enough to have a paper accepted for presentation. We have to generate those resources so they can travel and they can do that. Those are just additional activities that you have to be involved in to generate the resources to run the group. And then many of the grant applications that you send out—which are multi-specialty, multi-disciplinary—you do that in part to enable your group to do the research, but a very important secondary objective is to bring people together. So you actually use the process of application to force people to work together. Well, force is the wrong word—to entice, to encourage, to foster interactions. And it works better that way than if you send out an edict that nobody will follow. And one of the first principles of leadership is never to give the order that someone will not

follow. You have to be careful about how you go about managing or coordinating especially bright people. It is very—it's very challenging because it's—and especially academic centers do not work on dictatorial principles.

Tacey Ann Rosolowski, PhD
0:45:13.2
What are some of the other strategies you've found for successfully leading very bright people—enticing them rather than sending down edicts?

Gabriel Hortobagyi, MD
0:45:29.1
Well, probably the most effective one is to empower them—to figure out what their strengths are and build on their strengths. So in my early years, for instance, I tried to set expectations for all of my faculty members, which was good, and I still do that. But I tried to set sort of one-size-fits-all expectations, and I expected everybody to take care of patients, everybody to do research, everybody to teach, and everybody to do service to the institution in the same measure. And it didn't work, of course. There were some of my faculty members who were and still are wonderful physicians, but they do not have the knack for—or the interest for doing research. And trying to force them to do research was a disaster because every year during their evaluation I would end up with this heated discussion about I asked you to do this and you didn't do—I didn't have the time because I was—it was a totally nonproductive thing. So after a while I figured out that I had to recognize that different people have different strengths, and we all have weaknesses. And there was no point in harping on weaknesses when I could build on their strengths. So to the person who did not want to do research but was a good doctor I would just say, "Okay. So let's make a deal. You do fifty percent more or a hundred percent more patient care than your colleagues who want to do research. And I will be very happy for that." And they were very happy for that. That allowed me to empower the others—who really wanted to spend more time on research—to do research, less patient care, and have a little bit more protected time. And similarly for those who wanted to spend more time on education—great. I have some colleagues who are great at committee work—fabulous. And then for as long as the unit, the overall department, and the overall faculty accomplishes what we as a unit want to do or as we as a unit are expected to do—for instance financially—I'm happy. So I think that's an important part of it—building on people's strengths. The other part is to become a good listener and really try to understand what is behind issues. What really drives two people to go at each other? What is their disagreement and what is the disagreement based on? And what are potential areas of commonality that they can come together on and sort of reduce the tension on the disagreements by building on the agreement. So that's an important part. The third part is to continuously challenge people in a positive way. Challenge them to stretch, to reach for things that they don't think they can reach. An example is someone comes and shows you a review paper they have

written. You read it, and you say, “This is very nice but I think you can do better than this by doing X, Y, Z.” Or someone who wants to come see you with a project and says, “Can you get me some money to do this project?” And you say, “Yes, I can, but I think it would look a whole lot better on your CV if you applied for a federal grant and you got it. Furthermore, that would allow me to give you a little bit more protected time so that you can spend it on this wonderful project. If I give you the money, that doesn’t help you. It just—it’s a short-term Band-Aid. So why don’t you apply for that grant?”

Tacey Ann Rosolowski, PhD
0:50:15.4
So that’s really mentorship by showing people how to look at the big picture—how to fit into the big picture of their career.

Gabriel Hortobagyi, MD
0:50:25.2
And all of those things are important ways to make people—to deal with personalities, deal with the faculty and to recognize that each of your faculty members—and for that matter each of your office personnel—is a unique individual. And the more you know about them the more you understand them, the better able you are to keep peace. And more than peace, make the group as productive as possible. So that works. And the other part of it is transparency so that all of the decisions that have an impact on your faculty or your office personnel come with information. So it’s not just you are going to say, “As of next week, you’re going to work twice as hard as this past week because I say so.” But you say, “You know, we need to increase the number of patients we see because we need to recruit more patients in our clinical trials to pay for our research infrastructure; otherwise, we’ll have to let several research nurses go. Or we need to see more patients because we are behind budget, and this what we put in the budget. This is what we were requested to produce, and we are twenty percent behind.” People understand that, and for as long as that is a continued process as opposed to coming out of the blue, that’s something they understand. And especially when you explain to them why—while all of them are treated individually—this is sort of the standard. And for instance, I tell every year to my faculty, “If you are here on a full-time clinical contract, my expectation is you spend three full days in the clinic. You are expected to see this many patient visits, this many new patients and consults, and generate in charges this amount. If you dedicate seventy-five percent of your time to research and you have the grants to support that, then I prorate my expectations from the full-timer down to this. And everybody who spends seventy-five percent or more in research gets that same expectation. And if you are fifty-fifty because you have a huge committee assignment and administrative tasks and whatnot, then the prorate means this.” And then everybody has a clear idea of what is expected of them and why.

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Tacey Ann Rosolowski, PhD
0:53:51.2
It is not personal and arbitrary.

Gabriel Hortobagyi, MD
0:53:53.2
It's not personal. It's not arbitrary. I'm not taking it out on you. It's not that I don't like you or that I like that person better. It has nothing to do with it. These are the expectations. I estimate we will reach these calculations on the basis of our budget and on the basis of last year's productivity and based on the previous year and it's transparent. So my faculty now get every month the numbers of where they are. And of course at the beginning of the year, they have their expectations that they signed on, that we discussed, so halfway along the year they know that they are ten percent ahead or five percent behind or thirty percent behind. And if they are thirty percent behind they know that they are going to be in trouble unless they pull up their socks because the expectations are not going to change. So transparency in that sense is better. The same with promotions. The same with who gets to go to meetings. There are three meetings throughout the year where everybody wants to go, and of course not everybody can go because someone has to stay here and take care of patients and take care of patient service and be here to answer the phones and whatnot. So one day many years ago I said, "Who should have the first priority for going to the meeting?" Well, obviously someone who has an oral presentation and has a very prestigious presentation of research done within the department. Everybody agreed. Who should be the second priority? Well, someone who has a poster presentation—again, for the same reason. Who should have the third priority? Well, someone who has important business connections and needs to interact with colleagues and representatives of the NCI and the pharmaceutical companies so that we can get more resources for research and more collaborations and whatnot.

Tacey Ann Rosolowski, PhD
0:55:55.9
So this was actually a conversation you had at a meeting.

Gabriel Hortobagyi, MD
0:55:58.1
Right. Absolutely.

Tacey Ann Rosolowski, PhD
0:55:59.8
So it was really—it was one of those consensus moments where people were generating those priorities themselves.

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Gabriel Hortobagyi, MD
0:56:04.8
Right. Right. Who should be the lowest priority? Well, the person who just wants to go there and sit in the audience and do nothing except learn. That's a worthy thing, but when push comes to shove that person will have the lowest priority.

Tacey Ann Rosolowski, PhD
0:56:18.6
Right. How are we distributing resources?

Gabriel Hortobagyi, MD
0:56:19.8
That's right.

Tacey Ann Rosolowski, PhD
0:56:19.9
Yeah.

Gabriel Hortobagyi, MD
0:56:22.3
And that worked beautifully, so two months or three months before any of those meetings, the executive assistant circulates a table saying, "I need to know who wants to go and what are the reasons you want to go and what days you want to go." Then on the basis of that, we get a list of people who want to go and why they want to go. We prioritize it. Only those who really need to be there want to go, and there are six or seven people who want to stay. There's no problem. If everybody signs up because they want to go then some at the bottom will be cut off and say, "Sorry, Charlie. You need to stay home because someone needs to mind the cash register—or the equivalent in the breast center. So transparency is very important. And I bet you that it's no different in any enterprise. There are many other enterprises different from academic organizations that tend to be top down; and while in the short term they might work, they probably don't work as well as if you really got buy in from everybody who works in the group. In academic organizations it's even worse. And physicians—by training—throughout history have been fiercely independent. And it's very hard to lead physicians from the top down by telling them, "Thou shalt do this because I say so." And, "Thou shalt not do this because I prohibit you from doing that." Because they will just do it exactly because they want to show that they are independent, and you don't rule their lives.

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Tacey Ann Rosolowski, PhD
0:58:26.9
And is that an intellectual thing? Or is it something that this specialty selects for in personality?

Gabriel Hortobagyi, MD
0:58:35.3
Both. So if you think about that, to get into medical school you have to do—you have to be at the top of your classes. Essentially you have to do very well on your MCAT. You have to do very well starting from high school in order to get into the right college. And then there's a selection process throughout that. And throughout training you are encouraged to compete. And when you compete, of course, the emphasis is looking out for number one. I don't necessarily think that's the best way to choose candidates for physicians, but that's the way it has been. And to some extent, I think that came from the civil rights movement and trying to avoid discriminatory behavior and selection. So because of that, instead of the classical personal interview and trying to figure out who has the humanistic qualities that would best fit a physician, we select on the basis of grades and the basis of test performance. And I don't—that might be great for an engineer, but I'm not sure that that's great for people in service professions where they need to actually serve human beings. But that's the rule of the land at the moment.

Tacey Ann Rosolowski, PhD
1:00:26.3
We have about five minutes before our time today is over. And I do have additional questions. I know that you have spent a lot of time with me. I'm hoping maybe we can schedule one more session to finish up.

Gabriel Hortobagyi, MD
1:00:39.8
Okay.

Tacey Ann Rosolowski, PhD
1:00:40.6
Okay. Would you like to close off for today, and then we can resume next time?

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Interview Date: January 28, 2013

Chapter 25
A: The Administrator
Education in Breast Medical Oncology

Story Codes
A: The Administrator
A: Personal Background
A: The Educator
A: The Leader
A: The Mentor
B: Education
C: Education at MD Anderson
D: On Education
D: On Mentoring
C: Education at MD Anderson
C: Professional Practice
C: The Professional at Work
C: Collaborations
C: Leadership
C: Mentoring

Gabriel Hortobagyi, MD
1:00:46.0
All right. We didn't talk much about education.

Tacey Ann Rosolowski, PhD
1:00:50.9
No.

Gabriel Hortobagyi, MD
1:00:51.2
Education is a critically important part of our specialty and medicine in general. And education has two different very important components. One is sort of the technical part of it—the acquiring knowledge and acquiring the knowledge of finding where to find more knowledge, which with today's technology it has been somewhat easier. And I think that part is very important because while you don't—as a physician in training, you don't need to learn absolutely everything there is nor can you. You do need a certain basic amount of information that is clearly at your fingertips at all times—that's stored up here. You can't just Google

everything. You have to have a really in-depth knowledge of medicine in order to be a physician of any sort. And then beyond that, some of the intricacies and some of those things that change rapidly—there are many, many tools that you can use—electronic tools that are wonderful. And you just have to make sure that you consult those that are legitimate as opposed to the crazy ones. Perhaps an equally or more important part of medicine is the mentoring part, and the mentoring part is very important in part because it provides an example to those who come behind you and to show how you organize your life—how you behave, how you interact with people, with patients—and what is the right way to keep a balance between life and work and all of those things. And second because mentoring can really shortcut a number of very time-consuming, decision-making processes.

Tacey Ann Rosolowski, PhD
1:03:26.0
Such as?

Gabriel Hortobagyi, MD
1:03:33.7
For instance, in academic medicine—where am I heading with my training? Some people come to train with us and they know exactly what they want to do. Others are much less certain. They don't know what's on the other side of their training program. So sitting down with those people and going through their thinking process and the advantages and disadvantages of what would happen if they went out to private practice or if they stayed in an academic environment—what happens if they became physician educators, what happens if they became physician scientists, what happens if they got some additional training? What if in addition to a degree in medicine they got a degree in law or a degree in public health or a degree in something else? And it's very hard to do that on your own without the experience and the knowledge and the resources of someone who has ten, twenty, thirty, forty years ahead of you. So that is an important part. And if you are involved in research, not all of us start with a full knowledge of all of the research techniques and what we do with all of the pitfalls of doing a certain type of research. So it helps very much for someone who is helpful enough and critical enough to point out what you're doing right and what you're doing wrong—and at the same time not competing with you.

Tacey Ann Rosolowski, PhD
1:05:13.8
Uh-hunh (affirmative). I had an interesting conversation with people in faculty development a while ago, and they were talking about how mentoring has changed so much because the time demands on every individual has increased so dramatically.

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Gabriel Hortobagyi, MD
1:05:27.6
Yeah. Yeah.

Tacey Ann Rosolowski, PhD
1:05:28.7
And how maybe even that the mentoring of someone—stopping in to somebody's office, sitting down, having a coffee or going out for a drink, and having an hour-long discussion—that those days maybe are gone. And how do you see that? And how do you see mentoring—ideally how it takes place—and then maybe how mentoring has to change, given people's responsibilities and time demands?

Gabriel Hortobagyi, MD
1:05:57.7
Yeah. So the environment is clearly changing. And I think eventually we will—as a community—need to rethink the process of who and under what circumstances should fund medical education—especially postgraduate education because your undergraduate, to some extent, is no different than going to law school or going into any of the other professions. The student pays for the privilege of being educated. But after graduation, most of the funds today come from either the federal government—Medicare, to a large extent—or some funds that institutions—academic institutions—carve out from other somewhat obscure sources that I call robbing Peter to pay Paul. And it's not a tenable model in the long term because Medicare is going to continue to cut back on reimbursements, which means that most of the institutions will end up subsidizing Medicare as opposed to getting something out of it for medical education. And yet it is critically important to maintain and, in fact, enhance mentoring because if you—probably fifty, sixty years ago, if you finished medical school and went out to practice, you were reasonably well prepared for the time. But today that is not true. Today that's not true. And in fact, our fellows—and remember, a fellow in medical oncology at this institution finishes and has already had six or more years of training after graduating from medical school and still is green behind the years—you know? And so additional training and mentoring is really critically important unless we really want to compromise our level of care and our level of research and our level of commitment to the education of the next generation.

Tacey Ann Rosolowski, PhD
1:08:32.4
So what does and what should mentoring look like that will preserve the highest quality of care and research?

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Gabriel Hortobagyi, MD
1:08:42.3
A mentor should be an experienced individual who is willing and able to dedicate sufficient time to serve as a sounding bar—to advise, to listen, to critique both the good and the bad—and who should be committed to the professional development of the other person. It can't be just a casual thing where someone shows up in your clinic and sees your patients and then adios. So there has to be some time carved out. There has to be some time dedicated exclusively to mentoring independent of other joint activities. And there has to be some thought given to that perspective, and you need to understand what the other person is struggling with, what the other person is trying to decide, where they are heading. Have they even figured out where they were heading?

Tacey Ann Rosolowski, PhD
1:09:56.3
What was a watershed moment for you when you received some really key pieces of mentoring or instances of mentoring?

Gabriel Hortobagyi, MD
1:10:20.0
Actually the watershed event was not about what I got or I did not get but what I saw in some of my colleagues who—how should I say this—who under the guidance and with the support of a strong mentor were able to succeed in a more direct manner and in a shorter period of time. I just wrote a letter in support of a colleague and a friend who is about—probably ten years younger than me and who is being promoted to distinguished professor of something at a different institution. And this person—graduating from a relatively small program in oncology—was just catapulted up the ranks because that person had three or four truly strong and outstanding and dedicated mentors who made sure that they moved this person ahead. And it made a huge difference. It made a huge difference. And I have seen that in several of my successful colleagues. I don't think that that ever happened to me to that level. All right. And I'm not complaining. I have done very well, so I can't complain. But some things would have been much easier for me had I had someone who was looking over my shoulder saying, "I can open the door for you." And so that's where I saw how important this was. And then later with that knowledge I have been able to sort of push ahead some of my own junior faculty, and it is wonderful to see that—how they succeed.

Tacey Ann Rosolowski, PhD
1:13:14.7
Well, I will turn off the recorder now so you can—

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Gabriel Hortobagyi, MD
1:13:18.1
All right.

Tacey Ann Rosolowski, PhD
1:13:19.2
—speak to your next person. And I'm turning off the recorder at 3:39. Thank you very much, Dr. Hortobagyi.

Gabriel Hortobagyi, MD
1:13:26.8
Thank you.

1:13:27.0 (end of audio)

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Gabriel Hortobagyi, MD

Session 5—March 15, 2013

Chapter 00E
Interview Identifier

Tacey Ann Rosolowski, PhD
0:00:04.3
Okay. So we are recording, and I'll just put the quick identifier on. This is Tacey Ann Rosolowski, and today is March 15, 2013. The time is about 1:18. I am interviewing Dr. Gabriel Hortobagyi for our fifth session together, so thank you for agreeing to this final session.

THE UNIVERSITY OF TEXAS
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Interview Session: 5
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Chapter 26
B: An Institutional Unit
A Brief History of Breast Medical Oncology

Story Codes
B: MD Anderson History
B: MD Anderson Culture
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
B: Growth and/or Change
B: The MD Anderson Brand, Reputation
B: Institutional Mission and Values
C: Giving Recognition

Tacey Ann Rosolowski, PhD
0:00:04.3+
I wanted to ask you a couple of questions to recapture some material that was lost on the last interview. We were talking about the development of breast medical oncology. It's really the first phase of that that we needed to recover. You had begun talking about the complexity of the process of bringing together all the components to create patient-centered care in breast medical oncology. You started your reflections on how that process really began with the biweekly meetings. So I wonder if you could talk a little bit about those biweekly meetings and then how that process of developing patient-centered care evolved from that.

Gabriel Hortobagyi, MD
0:01:22.5
In the early days, it became apparent that we needed to communicate better and more in real time in order to work out the best sequence and combination of treatments for individual patients and also to avoid patients wasting their time. Because when you do consultations in a sequential mode and you depend on each individual's schedule, then if you need four or five specialists involved, it can take literally weeks until everybody gets to see the same patient. So we developed these meetings where all of the relevant specialists were in the same room at the same time, and we would present a small number of patients for discussion including their imaging and their pathology, and the opportunity for the physicians in the room to briefly examine the patient, if that was needed. Then at the end of that conference, one would be able to come up with a—hopefully with a consensus, but certainly with a majority view as to what needed to be done. That was a little bit challenging to implement because at the beginning various dominant specialists felt that they already knew how to treat breast cancer, and they really didn't need anyone else telling them how to do it. It took a little bit of overcoming resistance by showing the actual benefit of multidisciplinary programs.

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Tacey Ann Rosolowski, PhD
0:03:42.4
And how did that show itself?

Gabriel Hortobagyi, MD
0:03:44.5
Well, sometimes there were heated discussions and resistance from one side to someone else's idea about how to integrate various treatments. Sometimes people would get hot under the collar and walk out of the room. Sometimes individuals who were supposed to implement the consensus decision refused to do so. There were a number of different ways when that happened, and it took really years until this smoothed out. But the patients were very happy and grateful for having the opportunity to access multiple specialists at the same time. It saved them time, and I think they had figured out even before their doctors that getting their doctors to talk was a good thing. And then, I guess, we also figured out that in addition to being a tool that would benefit patients, it also became an educational tool and an instrument for cultural change and that gradually even the most vocal opponents of change would relent. So the old saying—if at first you don't succeed, try and try again—was clearly in play here because we continued to have these meetings, and often we would have the same discussion time and time again about different patients but the same topic. Should surgery come first? Should chemotherapy come first? Should we use radiotherapy? Should we use radiotherapy before surgery or after surgery? What was the role of hormones, et cetera? While we started out—at least our surgeons and radiation oncologists started out—with pretty fixed positions because they had really been in charge of managing breast cancer at this institution for the previous several decades, slowly the medical oncologists and the imagers and the pathologists started to have some inroads into the discussion. And after a number of patients had responded favorably to interventions by medical oncology and their surgeons and radiation oncology started to see those results, then things started to change. Of course, the more they changed, the more rapidly they started to change because once you establish some degree of credibility, it is easier to reinforce that credibility.

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Chapter 27
A: The Researcher
An Overview of Research Issues

Story Codes
B: Controversy
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
B: Growth and/or Change
B: Research, Care, and Education in Transition
A: The Clinician
A: The Researcher
C: Professional Practice
C: The Professional at Work
D: On Research and Researchers
D: The History of Cancer Research and Care
D: Ethics

Tacey Ann Rosolowski, PhD
0:06:53.2
And what was the piece with research, too? Because you had trials at a certain point that were being run, were you able to—were those research results becoming part of that discussion as well?

Gabriel Hortobagyi, MD
0:07:08.2
Yes. So part of these discussions was that sometimes you could get to some agreement about the specific area of controversy, and sometimes you couldn't. And when we couldn't, we took advantage of that, and instead of a head-on confrontation and screaming and yelling we would propose—all right, so we have two different opinions about this. Well, this is a perfect opportunity for a clinical trial, and lets have a clinical trial to resolve the issue, and let's figure out who is right and who—and more importantly, what is of greater benefit to patients. And if it doesn't make any difference, we should also find that because then we would have two equivalent approaches to a particular problem. With that in mind, then we started to develop clinical trials. Some of our earlier clinical trials were just to integrate chemotherapy into the overall management of advanced breast cancer and inflammatory breast cancer. Later we developed clinical trials to figure out how much benefit radiation therapy brought into the equation, how much benefit immunotherapy with BCG and *Corynebacterium parvum*, and other nonspecific immunotherapy agents would contribute. Then we started to look at different types of surgery, and eventually from those discussions—which were initially thought to solve internal

problems—we eventually became some of the leaders of breast cancer management throughout the country. That was very gratifying. Some of those treatment approaches that were developed here took a decade, sometimes two decades to be adopted elsewhere throughout the country. But essentially everything that we had proposed and everything that we developed and published on has survived the test of time, which is, I think, encouraging. It just reflects well on the—at the risk of sounding self-serving, the really genuine intent of those in those conferences to try to do better and to try to figure out how to best treat patients.

00:10:10
The development of clinical trials and protocols then also pointed out that in order to do this well, we needed to collect data well and accurately and dispassionately and without the vested interests. So that led us to the recruitment of research nurses and data managers. And in fact, it was our department that developed the concept of research nursing.

Tacey Ann Rosolowski, PhD
0:10:52.9
How did that take place?

Gabriel Hortobagyi, MD
0:10:55.7
Well, eventually we realized that we didn't have the time to make sure that every patient on a clinical trial did what needed to be done according to the protocol. The principal investigator didn't have the time to do all of that, especially in larger trials that had several hundred patients. We needed someone who could babysit each protocol. We couldn't—we didn't have the resources nor could we find physicians who would do that fulltime, but we could find trained registered nurses who were ready for the challenge. Eventually they developed the techniques, and they developed the job descriptions, and they helped us develop forms to collect the data, and we developed the standard operating procedures. And then we found funds to pay for them, which was an important consideration, and we haven't stopped since then. At the very beginning, we had one research nurse for a couple of years, and now we have—I don't know—fifteen or twenty. Of course throughout the institution, now there are hundreds of research nurses because it's a critically important task.

00:12:32
At that time forty years ago, there was not the concept of conflict of interest. Nobody talked about conflict of interest. While the public and politicians talk about conflict of interest in monetary terms, I think that that is just the tip of the iceberg because physicians make a decent living, so it's hard to have a physician become biased by giving him $2000 honorarium or something like that. But a principal investigator has a vested interest in the success of his clinical

trial and unconsciously can do a number of things that will compromise the factual outcome of a clinical trial.

00:13:36
The second role of a nurse or a second person who doesn't have that vested interest is to provide that sort of unbiased approach to data collection and data management. It also makes sure that it is not the principal investigator who actually collects data and perhaps would have the opportunity to alter the data. It is a totally unbiased person who just collects that data and protects that data. Because soon after we started to recruit research nurses, we also came to the agreement that before the trial is completed, the investigator shouldn't actually look at the data except for what needed to be attended to on a day-to-day basis. I think it was an early development in clinical trials that was very important.

Tacey Ann Rosolowski, PhD
0:14:44.1
And the reason for that was—was what—not to have a look before the trial is created—completed?

Gabriel Hortobagyi, MD
0:14:53.5
In the 1970s there was a major discussion—a major controversy in oncology about how to do clinical trials. Some oncologists—many oncologists, I would say, especially many statisticians—considered that the only reliable way to get information was to do randomized blinded clinical trials because that would avoid the assignment of treatments based on physician bias or perhaps patient bias and preference and whatnot. And there was another side, and we were part of that within this institution, and several of the leaders of the institution at that time considered that doing a randomized trial was sort of unacceptable, and it was an unethical use of patients, and they could do that very well without the control group because they were unbiased, and they were pure anyway.

00:16:14
During those discussions, many of which were very public discussions, it became apparent that it is actually difficult to be unbiased because we all are led to some extent by our belief systems and our cultural background, and that much of science is based on evidence, but much of science is not. Sometimes when you develop a hypothesis, you come to believe that hypothesis even before you have proven it. If your career depends on the success of your hypothesis, then it's very easy to be misled and to fool oneself into accepting a conclusion before reaching that conclusion. Since I was much younger at that time and I still hadn't completely accepted either of those positions, I started to see some of the weaknesses of each argument, especially the weakness of the absolute embracing of either side. But I did see—and so did some of my close

colleagues—that there needed to be some protection of the process of generating the best evidence because we are all imperfect human beings, and with the best of intentions we can actually mislead ourselves into areas that we didn't want to go.

00:18:02
That led us into the process of trying to develop data management and data collection methods that wouldn't be viewed as unimpeachable by outsiders. It didn't happen overnight, of course. Some of the earliest research I did based on retrospective studies—with what I know today I would say, "My God, how did I do that? How come I didn't know better?" But it was done with the best of intentions at that time. And I know that others within the institution who are passionate about their research also did it with the best of intentions. At that time, certainly scientific misconduct hadn't been talked about or discovered. Today it is a fairly prominent aspect of what we talk about because there have been some very highly publicized cases of fraud—scientific fraud or misconduct. At that time, I don't think it was much of a topic of conversation either because it hadn't been discovered or it was uncommon or because there were actually far fewer scientists. There was less competition for resources, and perhaps people didn't feel the need to misquote or develop erroneous things. So that's how we developed our research group.

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Chapter 28
A: Overview
Physician Extenders and a View of the Coming Physician Shortage

Story Codes
A: The Researcher
A: The Administrator
B: Beyond the Institution
B: MD Anderson and Government
D: Cultural/Social Influences
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care
A: Contributions
A: Activities Outside Institution
A: Career and Accomplishments

Gabriel Hortobagyi, MD
00:19:50
Then also in that process, we developed physician extenders. I may have talked about that earlier, but Dr. [Robert S.] Benjamin and I helped the Texas Legislature to pass a bill that would structure the roles and utilization of the services of physician assistants and nurse practitioners. Then eventually those two groups of highly skilled people became very important in this institution, and today we have hundreds of them employed in a variety of roles throughout the institution, and as we go into the future of medicine in general—and oncology in particular—they will play an increasingly important role—in part because they can focus in a narrow area and develop extraordinary high quality skills and in part because we expect to have a fairly serious problem with physician shortage in the county, especially in those specialties that deal with chronic illnesses like cancer, diabetes, arthritis—a variety of these conditions that in the past had no real treatment or few effective treatments. Today they have increasingly effective treatments and many options for treatment.

Tacey Ann Rosolowski, PhD
0:21:36.7
What's the source of that shortage? What's created it?

Gabriel Hortobagyi, MD
0:21:42.7
Well, it's a complicated problem, and it's a multifactorial problem. But I became sort of a pseudo-expert in that because when I was president of ASCO we commissioned a study—a workforce study—for oncology which was done. It came up with projections that by 2020 we

would have a shortage of something like a third of the physician hours that would be needed to serve the population. Part of the reason is the continued growth of the US population, and that growth rate is higher than the growth rate of physicians. The increase in the life expectancy of the population, and of course, cancer in general is—the frequency with which people develop cancer is in direct proportion with age. So the older you get the higher your chance of developing cancer. So if you die at age thirty, your chances of developing cancer are rather low. If you live to age eighty-five then—if you are a man, you have a one-in-two chance of developing cancer. If you are a woman, you have a one-in-three chance of developing cancer, so the incidence is huge. And of course, we projected that the life expectancy of the average American citizen will continue to increase.

00:23:52
Then there were all the successes of other specialties. As cardiovascular causes of death started to drop—and they have dropped by, I believe, half over the past half a century; but of course you have to die of something—and then cancer has become a much more prominent cause of death. It was also related to the successes of cancer research. It used to be—just to give you an example, when I started working with breast cancer we had about four or five drugs that were worth something. Once you used those up—at least in metastatic breast cancer—you had nothing else to offer. You just used symptom control, and that was all you could contribute. So the number of visits per patient was much more limited, and the survival of patients with cancer was much more limited. Now we have improved the survival of most cancers—of patients with most cancers so people live longer. We have dozens of active drugs for most of the cancers. There is much more to do for oncologists. In addition, we are treating with drugs the bulk of patients with primary breast cancer who in the past were only treated with surgery, for instance. So instead of me seeing only patients with metastatic breast cancer—who arguably represent maybe twenty-five percent of all breast cancer patients—and seeing them for six, eight visits throughout their lifespan, now I see virtually all patients with breast cancer—with primary and metastatic. Those with primary I might see forty, sixty times over their lifespan, and if they develop metastatic disease, then many more. A single patient has occupied or is now occupying a much greater fraction of the oncologist's time than it used to.

00:26:27
And then there are the regulatory issues. We are much less efficient now than we used to be forty years ago. We see fewer patients per unit of time than at that time because we spend a lot more time documenting and justifying our existence, filling out forms, making phone calls, dotting i's and crossing t's, and doing a lot of stuff that doesn't add much value to what we do. But that's what's happening today.

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Tacey Ann Rosolowski, PhD
0:27:02.7
We are only seven years away from that 2020 landmark. What do you feel in the intervening years since that report came out that we are indeed on track to that one-third hours of shortfall, and what's the effect going to be?

Gabriel Hortobagyi, MD
0:27:22.8
Clearly we are on track for that. You probably won't notice it now, but a good segment of the population is already noticing it. If you are on Medicare and you have cancer, you have far fewer options. If you are looking for a physician, it might take you a year to a year and a half to find a physician who will treat you. Now that's in part because Medicare doesn't reimburse very well so physicians pick and choose but also because there are so many other patients that can fill the average physician's appointment template that they don't feel the need to bring in those on Medicare and Medicaid and whatnot. That represents maybe thirty-five percent or maybe forty percent of the population, and as the population continues to age it will compound the problem. And also we notice it less because there are many more physician extenders now doing what physicians used to do.

00:28:49
But since we undertook that workforce study, there has been very little change in the number of training positions for oncology or for postgraduate training in medicine. It takes—from the moment you make the decision, suppose that today the powers that be decided they are going to increase training positions for oncology by thirty percent. Well, the earliest you could make a difference would be about eight years from now because it would take that long to get people through a pipeline. None of that has happened. I think that is going to be a serious issue. How we deal with that will, I think, define us as a society. But of course, one way to define that or to solve the problem is to say, "Well, we're just going to have to ration care. That way it will be cheaper." And then if insurance companies, Medicare, and Medicaid disallow about half of the stuff we do as physicians, we will have more time on our hands. I don't think it's the right way to do it. It's something similar to the sequester, but it is one option. Some insurance companies are already doing something like that, so it's going to be a complicated future in terms of that. And it's not unique to oncology. Rheumatology, for instance, is in a very similar situation. When I went to medical school, there was very little you could do for lupus or for scleroderma or for a variety—for rheumatoid arthritis, osteoarthritis—and today there are multiple treatments for all of those conditions. The lifespan of patients with those conditions—and most importantly the quality of life of those patients—has improved enormously. But they also take up a much greater fraction of the rheumatologist's time than they used to, so they are also going to face a shortage.

00:31:27

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Diabetes—you know, when we started—when I started in medical school, we had two different types of insulin, and we had maybe one or two oral anti-diabetic agents. We didn't have very good ways to keep blood sugar under control, and we were not that sophisticated about the long-term effects of diabetes, so we didn't do as many things. Well, today management of diabetes is a science in and of itself. It keeps endocrinologists and internists occupied almost fulltime. It is a much more complex and a much more demanding branch of medicine than it used to be. As we learn more about each of the diseases we treat as physicians, I think that is going to be reflected in our efficiency and what we are able to do. And how we react as a society to that, I think, will be important.

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Chapter 29
B: An Institutional Unit
The Evolution of Breast Medical Oncology and the Breast Center

Story Codes
C: Understanding the Institution
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
B: Growth and/or Change
B: Critical Perspectives on MD Anderson
B: Institutional Processes
A: The Clinician
C: Professional Practice
C: The Professional at Work
C: Collaborations
B: Institutional Mission and Values
D: On Care
C: Leadership
C: Mentoring

Tacey Ann Rosolowski, PhD
0:32:40:8
I would like to go back in time again and focus on breast medical oncology and that history again and kind of go from the point where—I don't even know if I asked you where breast medical oncology was actually located in the beginning.

Gabriel Hortobagyi, MD
0:33:04:2
Breast Medical Oncology used to be at the ground floor of—what is that called today? It's not the central core but the Bates-Freeman Building, I think. So it is a long hallway that goes to the old library—the old library that used to be at the bottom of the Yellow Zone. It was in that hallway. The breast clinic was—have you seen those changing tables that are in public bathrooms that you just fold down?

Tacey Ann Rosolowski, PhD
0:33:50.2
Oh, they fold down from the wall?

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Gabriel Hortobagyi, MD
0:33:52.8
So the Breast Clinic was one of those—or maybe two of those—side by side in the hallway.

Tacey Ann Rosolowski, PhD
0:34:01.8
I'm sorry, I shouldn't be laughing. It's just a terrible image.

Gabriel Hortobagyi, MD
0:34:04.5
Well, it is funny. It's a terrible image, but that's the way we did it. So there were two nurses, and there were the three or four physicians, and we had about four examining rooms. While some physicians were in the examining room seeing patients, the rest of us were writing longhand in these charts standing in the hallway with these fold-down trays. And then—well, I don't remember where our offices were. I am sure we had offices somewhere. I remember later we graduated to offices on the ground floor, which is now the second floor, actually. But at that time it was the ground floor of that same area between the area where the old library was and where medical photography used to be. At that time, the Yellow Zone Building didn't exist. I remember my office was a corner office that looked out on—what is the name of that street that goes between what is garage two and garage five and the old prevention building? What is that? I guess that would be the Mickey [Charles A.] LeMaistre building.

Tacey Ann Rosolowski, PhD
0:35:46.9
I'm not as familiar with the streets here since I—and I have an office on campus.

Gabriel Hortobagyi, MD
0:35:50.3
It was there. And then—

Tacey Ann Rosolowski, PhD
0:35:55.2
How many patients did you see per year at that time?

Gabriel Hortobagyi, MD
0:36:02.1
Probably about 800 or so, but it kept on increasing gradually. Then from there we moved further down—still on the ground floor. I guess it would be approximately where the Anderson Network office is now in the central core. Then our offices also moved, and my office went up to the tenth floor of the newly built—it wasn't the Lutheran Pavilion, it was what became the Pink Zone or

the Rose Zone. And from there we went down to the sixth floor of the same building. From there our offices moved across the street to the first faculty tower, but our clinic remained in the Rose Zone, and then eventually we moved here.

Tacey Ann Rosolowski, PhD
0:37:25.2
To here?

Gabriel Hortobagyi, MD
0:37:26.2
Both the offices and the clinic.

Tacey Ann Rosolowski, PhD
0:37:29.6
Now when you made the move over to the Rose Building and the Lutheran Pavilion, to what degree did you have input into what that all looked like—you know, what your facilities were going to look like? Zero?

Gabriel Hortobagyi, MD
0:37:47.0
Yes.

Tacey Ann Rosolowski, PhD
0:37:47.5
Yikes.

Gabriel Hortobagyi, MD
0:37:48.2
Yeah, zero. Certainly our first couple of moves we had no input whatsoever. The third one—when we moved up to the sixth floor—Dr. [George] Blumenschein and I sat down with the architects and with hospital administrators, and we gave them a number of things that were on our wish list and what would be a good organization—physical organization of the clinic because we were less concerned about our offices. It was mostly to make our breast center more functional and more patient friendly. And then all of that was ignored. So they did whatever they pleased, and then we moved in.

Tacey Ann Rosolowski, PhD
0:38:44.4
How did the facilities compare? I mean, were there improvements?

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Gabriel Hortobagyi, MD
0:38:47.5
There were improvements. Certainly we got a very substantial increase in real estate, so we had more examining rooms and a bigger waiting room, and we had little workrooms where we could write and dictate and fill out forms and do things—and chat and discuss cases and meet with the nurse and that. So it was—in that sense it was improvement. It was also improvement that our offices—when we moved to the sixth floor of the Rose Zone—were immediately next to the breast clinic. That was very helpful because it made jumping up to the clinic for a moment to take care of an emergency or something that needed to be done at that moment—it could be done without too much disruption to the other things we were doing. So that was helpful. But this is the first center where we really had a great deal of input.

Tacey Ann Rosolowski, PhD
0:40:00.2
And so what was that process when you knew you were going to be moving to this building?

Gabriel Hortobagyi, MD
0:40:06.8
By that time Dr. [John] Mendelsohn had been here for some time, and he was very good at getting input and getting buy in. So he requested that the relevant administrators and the administrators that head the development of the Mays Clinic and the [Cancer] Prevention Building were to really make an extra effort to take it as project managers, and all of the future occupants should have a say in how the building was designed. And we took several months to actually go through that process, and it was a fairly public process and a fairly transparent process. We got much of what we requested.

00:41:00
I had greater ambitions. I was hoping that in addition to getting all of our offices and all of the clinics and surgical suites and radiology and radiation therapy in one building that we could also build a large enough building so as to include all of the laboratory-based research relevant to breast cancer, and that was shut down. And I understand it now because it is much more expensive to build a building to the specifications of a highly sophisticated modern lab than to build an office building. This is just a cube, and you just need four walls and a door and a window, and you've got an office. You don't need to do anything terribly sophisticated. If this was a wet lab, then you would need to comply with a number of extra regulations. You would have to have much more plumbing, ventilation, much more electrical stuff. Yeah, so it's much more expensive and complicated to do that, so I understand that. I was still disappointed because I wanted to have my way, but that wasn't to be the case.

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Tacey Ann Rosolowski, PhD
0:42:21.1
So what—what were some of the details? You said—maybe I should ask it differently. What was the logic behind putting all of these things together and what ended up taking place in the breast center?

Gabriel Hortobagyi, MD
0:42:43.7
As you create the concept of multidisciplinary care, there is this gradual shift in your thinking that takes place—and not only in mine but in everyone else's that works with you. And as you increasingly see the benefit in truly working together in a collegial manner and developing the patient-centered approach, you realize that it is not just a state of mind but that the geography also contributes to that. As long as the medical oncologists were on the ground floor, the surgeons were on the fifth floor, the radiation therapists were in second basement, and the radiologist was on the second floor, we were like independent republics and that we really didn't get that feeling that esprit de corps of we are all in this together for one single purpose.

0:44:13.4 (end of audio 1a)

0:00:00 (begin audio 1b)

Gabriel Hortobagyi, MD
0:00:01.9
And then gradually you start to figure out that gee, wouldn't it be nice if I didn't have to send my patients up to the sixth floor but that I could just flag down Joe Blow and say "Hey Joe, would you mind taking a look at Mrs. Smith?" But from that initial realization—I can't tell you exactly when that happened, but it started to happen within the first few years, and as we tried to influence the development of the second then third breast center without much success, part of what we were thinking was wouldn't it be nice if we could bring the clinical disciplines together in the clinic? And initially our thought was really just the surgeons and the radiation therapists. And the surgeons, in principle, were easier because yes, they needed to go to the OR for their surgical act. But in the clinic it didn't matter where they were, so if there was space for both the surgeons and the medical oncologists, that was easier. With the radiation oncologists it was more complicated because their equipment requires insulation. It requires protection from radiation, so in most centers radiation therapy is in the basement for a very good reason. It simplifies the issue of preventing radiation from hitting innocent bystanders, the rest of the hospital staff, and patients. And then much of what they do has to deal with their equipment and with their nurses who have to be on site. So the radiation oncologists have to be on site much of the time, so it's not terribly practical for them to be away in a different floor, in a different clinic. And at that time, we were not even thinking about how important the pathologists and the radiologists were.

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And the radiologists, of course, also have the issue that where the equipment is that's where the radiologist needs to be in practical terms to read. Now today they can do it much more functionally because they can read x-rays being 200 miles away through the Internet. The same for pathologists, although that hasn't caught on as much. And it was the development of translational research that eventually led us to the realization of how important the role of the pathologists and the imagers was to what we did. And until that realization became really a strong realization, I guess we thought that the main members of the team were the surgeons, radiation oncologists, and medical oncologists, and that the other two disciplines were sort of auxiliary to this. And of course today we think that they are central to everything we do and that every member of the team is equally important in order to do this well. So that's how it sort of developed.

00:03:48
But the first time we could actually implement that well was here in the Mays building, because it really takes long-term planning. And you need to take all of the cultural and specialty needs into consideration from the ground up, from the moment you start planning the building, in order for this to work. So you can't just design a generic building and say, "Okay, we're just going to herd all of you guys in there and you figure out how you're going to work." So it took a concerted effort to do that, and then it took a concerted effort for us—who were the small leadership group of the breast center—to distribute the space in a way that would actually force people to interact. All right? Because the initial instinct was—and this is now three decades after we've been practicing multidisciplinary care—the initial instinct was for the surgeons to say, "Okay, these two hallways are ours and then you guys can go there." And we said, “No, that's not the way it is going to happen. We are going to be all intermixed, and we are going to be elbow-to-elbow every day all day because that will force us to actually realize that we have much more in common within the breast center than the breast surgeons have with the colorectal surgeons and I have with the leukemia doctors across the street.” Because it's much more important for me to interact with the breast surgeons than to interact with the leukemia doctors. It's not that it's not important for me to learn what the leukemia doctors do and for them to learn what I do, but it's secondary to some extent, because for my principal mission the other members of the breast cancer team are the critical relationships.

Tacey Ann Rosolowski, PhD
0:05:58.5
What still needs to occur, do you think, to bring that collegiality and that esprit de corps to an even more perfect form, if you will?

Gabriel Hortobagyi, MD
0:06:11.7
Well, perfection is the worst enemy of good. You realize that. So I think we are very close to

about eighty to eighty-five percent of perfection, and the next fifteen to twenty percent will take a huge effort, and I'm not sure it is likely to happen anytime soon. So what it would take—it would have to start from medical school to lay the foundations of interspecialty interaction and the realization and the active teaching of that's the way people need to function. And that's not how physicians, and especially specialists, are trained today. Specialists are trained within just the specialty, and they are taught everything within that specialty almost to the exclusion of what other specialties do. And I think it's important to break down those barriers. The second thing is that something that has helped us enormously in this institution to achieve what we have accomplished in multidisciplinary care is our compensation system, that until recently didn't depend on how many patients we saw and cared for. And the stark contrast is, for instance, with another great institution with is Memorial Sloan-Kettering, where physicians are actually compensated based on their volumes. And being a private hospital Memorial, of course, wants to incentivize the generation of revenue. So with much logic, the administrators say, "You know, if we give a certain commission for each individual patient or unit of service or something to the physicians, they will react to that by increasing their volume," and especially younger physicians who have kids going to college or they're building a house or they're buying a new car—I don't know.

Tacey Ann Rosolowski, PhD
0:09:03.4
Med school debt?

Gabriel Hortobagyi, MD
0:09:04.5
Yeah. And so it incentivizes that type of behavior at the cost of interactions because then you're competing with your colleague next door for patients, because the more patients you take perhaps the fewer patients are left for your colleague. And then there's competition between the various specialties. And perhaps most importantly for the mission of this institution and what should be the mission of Memorial, too, it competes with your dedication of effort and time to the other missions, especially research and teaching. Because of course, if you spend fifty percent of your time in patient care and fifty percent in research and education that's one thing. But if you spend eighty percent of your time in patient care, guess how much you're going to spend in research and education? So while we maintained a delicate balance about keeping all our missions at an equivalent level, I think we did very well, and those were the golden years of this institution. In recent years for a variety of reasons, there has been much more emphasis placed on increased generation of revenue, and this past couple of years our administrative leadership has implemented some steps that will incentivize individual physicians to increase generation of revenue. And I think that is a major mistake. It's a major mistake, and it will translate on the long term in a major change in our culture, and it will be to the detriment of our research and education.

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Chapter 30
A: The Administrator
Stepping Down as Chair of Breast Medical Oncology

Story Codes
C: Evolution of Career
A: Professional Values, Ethics, Purpose
B: Critical Perspectives on MD Anderson
D: The History of Health Care, Patient Care
A: Character, Values, Beliefs, Talents
A: Personal Background
A: Professional Path
A: Inspirations to Practice Science/Medicine

Tacey Ann Rosolowski, PhD
0:11:22.1
I wanted to ask you a few questions about leadership and about the administration, so I'll kind of go through those in sequence. The first one was you left the position as head of the division, and when did that happen? And I wonder if you could comment on why you left that position.

Gabriel Hortobagyi, MD
0:11:47.0
So it happened on August 31 at midnight. I actually wanted it to happen a year earlier, but I was requested to put in an extra year. Why? Well, multiple reasons but probably the major reason is that I had reached a point in my mind where I realized that I no longer wanted that leadership position so badly as to justify for me to continue. That's probably the most candid way to express it, but there are many details to that as to why. Part of it was because over the years I have noticed that as the institution grew, it had gradually made the transition from a healthcare institution into a corporation. And in that transition it went from a physician- and scientist-led institution. It converted into a business people-led institution where physicians and scientists stopped being important members of the employee group, and they just became interchangeable cogs in the machinery. We are no longer called physicians. We are called providers or we are called some other—for me—offensive term. And I became increasingly disenchanted with that. Also as part of the process and part of that, of course, comes from pressures from outside the institution.

00:14:29
Medicine is in a profound state of disarray. This country has one of the most dysfunctional healthcare systems in the world, and if you have, first, best insurance and if you have lots of money, you are likely to get very good care. But if you are not—and especially if you are not

very careful about how you go about getting healthcare—we provide healthcare that is inferior to most industrialized countries. And this is reflected in statistics. Our infant mortality rate puts the US in, I think, number sixteen in the world. Our average life expectancy is nowhere close to the top. We have a number of other countries from Europe—including North America and Canada—where life expectancy is several years longer than here. And we have a very large proportion of disenfranchised citizens who have no insurance and who get really very poor care. And the entire system is based on the whim and caprice of for-profit organizations who have taken over the decision making about how we treat patients. And it's largely for-profit hospitals and for-profit insurance companies right now. Some of the hospitals call themselves not for profit, but they are still making a profit. I assume you read [Steve] Brill's article in *Time* magazine? Yeah. So that's just scratching the surface. Actually, despite protestations to the contrary from a number of CEOs including ours, it is largely true. And it is much worse than what he managed to uncover. So that has gradually come to grate my enthusiasm. And the reaction of our own institution has been not to fight for changing the system but to say, "Let's figure out how we can function most optimally in the current system. And for that, we need to continuously increase the revenue." So for the past I don't know how many years, I have been asked every year to increase the generation of revenue by—I don't know—ten percent or fifteen percent—mostly unrealistic levels. And it was—it has become my task to force my colleagues to do something that they didn't really want to do. And there was not much joy in doing that, especially when I didn't agree with the process.

00:18:07
In many organizations in the world, you generate your yearly budget by realistically looking at your capabilities and at your missions and say, "What should be our goals for next year based on that?" In our institution as of late, we get a figure that comes up from the top, that someone pulls out of their hat, saying, "We have this much debt in terms of our capital campaign. And our buildings—we need to pay for those; therefore, we need this amount of money for next year. Therefore let's just distribute it to our various units so they can generate the money that we need." And I think that's the world upside-down. And that's not the purpose of an institution—a healthcare institution—so I was unhappy with that. And then deep inside my mind, for many, many years has been that what you learn in your—I remember in our Rice course that most leaders should not remain in their position—in the same position for more than about ten years. And of course, I had been a department chair for about twenty years and the leader of this group for about thirty, so I thought I had overstayed my welcome by much. And I thought that our department would be best served by opening the position to someone who is truly hungry to make an impact and to take the department to the next level. So all of those were sort of influences.

00:20:08

And on a personal level, I have many outside interests. I'm passionate about music. I'm passionate about literature and poetry. I'm an avid reader. I love history. I love to travel, and my work is now—despite the fact that I travel a lot professionally, my schedule truly interferes with what I would like to do in terms of travel. And I've also become a whole lot more interested in policy, and the more I have to deal with the nickel and dime stuff of every day, the less I can think of policy. And then there are a number of other personal interests that have grown over the years, and when you get to the point where—at the beginning of my career, it was clear that virtually everything that counted for me was my profession and what I did in my profession. And my private life was, to a large extent, irrelevant. It wasn't completely like that because, obviously, I've been happily married now for almost forty years and that was important. But now I realize that my private life is just as important and perhaps much more important than my professional life. And that's again a transition. It's a gradual transition. And now that I'm starting to have grandchildren, I realize that I have the opportunity of watching them grow, which I missed, to a large extent, with my own children because I was constantly either here working or reading or writing grants or papers or traveling somewhere. And then as you get older, you think about your own mortality and you say, “Well, I'm more than likely past my fifty percent point. In fact, I might drop dead at any moment. Why not give it a little bit more prominence and enjoyment for the rest of my life?” So those are considerations that—every time you go to sleep, I'm sure the wheels are whirring and turning and considering that. So it was the right time to do it. I was very content and happy with that decision. My wife and I discussed it over several years, and I had discussed it with [Waun] Ki Hong and eventually with John Mendelsohn. So it was one of the most satisfying decisions, especially after I took it.

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Chapter 31
A: Professional Service beyond MD Anderson; Contributions to International Policy Issues

Story Codes
A: Contributions
A: Activities Outside Institution
D: Global Issues –Cancer, Health, Medicine
C: Professional Practice
C: The Professional at Work
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care
C: Patients, Treatment, Survivors

Tacey Ann Rosolowski, PhD
0:23:20.2
I wanted to ask you. You had mentioned at one point that your international work was very, very important to you, and I'm wondering if you would talk a bit about that. I'm curious if that dovetails with some of these policy interests you were mentioning as well.

Gabriel Hortobagyi, MD
0:23:40.2
Well, that's sort of another aspect of my schizophrenic life or mind. We talked about the fact that I spent my earlier years in Hungary. Of course I maintained or developed a number of professional relationships in Hungary and throughout Europe over the years—over the last few decades. So many of the European oncologists consider me as European. All right? So I'm very frequently invited as a guest speaker, as a visiting professor, as a coordinator or chair of meetings and sessions, as a co-leader of international studies in oncology, and so on. Then I spent another part of my youth in South America, and because of my languages, the South Americans or the Hispanics throughout the world also consider me as part of them. So I have the same relationships with them. And of course, part of that means that I frequently get called about could you come as a consultant to the Ministry of Health or to such-and-such campaign, or could you help us develop guidelines for our country or whatnot. So over the years, in addition to my work in North America and my involvement in a number of organizations within this country and Canada, I have had similar involvements—mostly at the level of policy but also at level of education and research—in Europe and in Latin America. I have some other activities in Asia, but they are less prominent there and less involved. So as a result of that I am very familiar with what is going on in that part of the world—so Europe, North and South America. And then you start to work with organizations such as the WHO, the UICC, UNESCO, so on and so forth, and then you meet people from less privileged areas of the word—Africa, Southern Asia, et cetera.

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00:27:01
So then two different things happened almost as an outgrowth of that, and we talked about the development of the Charter of Paris in one of our sessions and about the rights of patients with cancer and the hope to influence policy in a variety of regions around the world to enhance the level of care for patients with cancer without necessarily a direct intervention, hands on. Then from a different perspective, I was one of the founders of what has come to be called the Breast Health Global Initiative. And we did that initially with the support of the Komen Foundation and with a dear colleague and friend, Ben Anderson, who is a surgeon from the University of Washington and the Hutchinson Cancer Center in Seattle. Our purpose was to develop this as a demonstration project and to bring together the constituencies to develop guidelines for treatment of breast cancer in various parts of world, taking into consideration the reality of the resources available in different parts.

00:28:51
So when I'm invited as a guest speaker to—I don't know—let's say India and they ask me to tell them about the state of the art of managing breast cancer. Well, I give them a science fiction presentation which would be pretty normal in Atlanta or in Chicago or in St. Louis or whatnot. But for India it is totally unattainable except for the very highest socioeconomic stratum because I talk about drugs that cost $100,000 per person per year, interventions, and machinery that costs a couple million dollars. And the healthcare budget of a country like India—which is not poor but of moderate resources dedicated to healthcare—and it's a fraction of what we spend in this country. So we realized that it was unrealistic for us to do this, and we were not doing a service to anyone except perhaps the fantasies of the physicians and scientists who were listening to us and who were dreaming about maybe one day we can do this. So we brought together a large group of individuals from different parts of the world—most of them representatives of something—either a professional organization or an international agency or a political decision-making organization that influenced healthcare, et cetera. So we brought together about fifty different people and set ourselves the task of dividing the world into three layers based on socioeconomic considerations, and for that we used essentially the WHO's classification of countries of limited, moderate, and high resources. Then based on the expenditures per capita for providing healthcare in each of those regions or groups of countries, we set out to create guidelines as to what would be a realistic minimum level of care for someone with breast cancer. How do you diagnose? How do you treat locally? How do you—what is the minimum you should be able to do as a society to really be able to claim that you provide breast cancer care services to your community?

00:31:55
After a series of discussions and whatnot, we came out with some guidelines which were published in the periodical literature and broadly distributed throughout the world to

governments and eventually have been adopted by a number of organizations. We have had three successive editions of this. In the process we continue to raise funds to try to maintain this organization—on a shoestring, by the way—and also to develop the type of research that nobody else does, which is to develop pilot projects of implementing these guidelines. So are there cost-effective—truly cost-effective methods for diagnosis in a country that doesn't even have a single pathologist? How would you deal with the situation like in some African countries where if you have a lump in the breast, the diagnostic procedure is that if you go to a surgeon, he'll do a mastectomy as a diagnostic procedure and send the breast on ice to the next country where a pathologist will eventually see it, and you'll get a pathology report back six months to a year later. So we have now about eight or ten of these pilot projects—some of them associating a prosperous institution with a very poor institution in a target country—developing new diagnostic processes that are cheap where individuals who don't necessarily have a medical degree can be trained to do this well and hopefully try to disseminate that. And if successful we might be able to do that on a larger scale.

00:34:19
We are trying to develop healthcare extenders—so screening not with mammography but simply with physical examination for earlier diagnosis of breast cancer—and we are trying to educate and train women from the local communities in a country to try to supply workforce where it doesn't exist or there are no physicians for hundreds of miles around. Similarly, there are a number of other proposals and projects, and it has been fascinating to develop this. While it is not satisfying to settle for the minimum you can do, we hope that at least it will force governments who feel that it is more important to spend their money on F-16s and B-1 bombers and AK-47s than on the healthcare of their population—it forces them to rethink that they have some obligations to their population. So we are disseminating this not only through the government—because the governments that are guilty of such an approach, of course, will not disseminate this—but also through professional societies: UNESCO, WHO, UICC, and so on. So we hope that this will start to have an effect, and both Ben and I are pretty passionate about that. When I talk about breast cancer in the US, we talk about the tragedy of 230,000 women developing breast cancer and 40,000 of them dying. But the reality of breast cancer is that around the world there will be 1.6 billion breast cancers this year and probably close to 600,000 will die of breast cancer. So compared to that, 40,000 is peanuts. Not to take anything away from the tragedy of the 40,000 dying, but this is a much bigger problem than our provincial problem within the US. So that's the type of issue that I'm very much interested in and hope to have some impact on.

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Chapter 32
B: Key MD Anderson Figures
The MD Anderson Presidents

Story Codes
C: Portraits
C: Funny Stories
C: Personal Reflections on MD Anderson
C: Human Stories
C: Offering Care, Compassion, Help
C: This is MD Anderson
B: MD Anderson History
B: Building/Transforming the Institution
B: Growth and/or Change
B: Obstacles, Challenges
B: Controversy

Tacey Ann Rosolowski, PhD
0:37:09.2
I wanted to ask you about—to reflect a bit on leadership—your own and then also you've worked with three MD Anderson presidents.

Gabriel Hortobagyi, MD
0:37:19.2
Four.

Tacey Ann Rosolowski, PhD
0:37:20.7
Four? Ah, okay, yes. Well, maybe we could start with the presidents then—just some commentary on their leadership styles, the mark they left on the institution, and kind of a critical view of them.

Gabriel Hortobagyi, MD
0:37:38.0
Well the first one was R. Lee Clark. Lee Clark was, I think, a flight surgeon. He was the first and founding president of MD Anderson, and he was instrumental in really the very beginnings. When he was recruited MD Anderson didn't exist. He went through the transition of when MD Anderson was in a couple of disabled railway cars, the first buildings, and he recruited virtually every one of the first faculty members at MD Anderson. When I came in 1974, we were then constructing, I guess, the third and fourth buildings of MD Anderson which were the Lutheran

Pavilion and what is now the Rose Zone. Because at that time the central core existed and the one that is parallel to that—I guess it's the Bates-Freeman Building. I no longer remember those names because I no longer use them. Lee Clark was an amazing character with a great deal of charisma, a great deal of social graces in the sense of people skills. The joke used to be that Lee would go up to Austin when the legislature was meeting, and he would present the MD Anderson budget, and there would be dead silence. And then someone would timidly ask, "But Dr. Clark, are you sure that's all you need?" (laughs) So he had a great deal of influence in Austin, and he knew how to use that influence and how to use that power. He made some extraordinarily good recruitments. He recruited a very strong first chairman for radiation oncology in Gil [Gilbert H.] Fletcher. He recruited a very good surgeon, Ed White. He recruited a number of internists, and I never met the first head of Internal Medicine, but certainly there was a strong cadre of individuals. The first group of radiologists was outstanding. The first group of pathologists was outstanding, and Lee Clark had an incredible vision.

00:40:48
Just put yourself in the situation of Texas in 1941. This was a backwater town, and how people lived here without air conditioning and in a swamp that had endemic malaria and yellow fever in a very primitive state—we are still a somewhat backward state culturally but light years ahead of what this was at that time. And he had to struggle nationally with the perception from the Brahmins from the northeast—who thought and still think that they are superior human beings—that he was going to develop a competitive, first-class cancer center in the middle of Texas. You have to have incredible vision and courage. Not only did he do that, but in a very short period of time he managed to put this institution on the map. He managed to get some national financial support, and he continued to recruit people. He had a great administrative style. I don't know if I mentioned to you that when I was a fellow here, I would walk through the hallways going from point A to point B and I would cross Dr. Clark who was, of course, the great god. He would know who I was, and he would greet me by my first name, and he would know what I did. "How is your project with x, y, or z? Are you working hard enough? I don't like the tie you're wearing today" or something like that. He was very personable. When we took call, there were no quarters for the house staff to sleep, so there was a couch in Dr. Clark's office. So we would sleep there whenever circumstances permitted, and there was a shower in his bathroom. But he would come in early and he would sort of nudge you and tell you, "Get out because I've got a meeting in about ten minutes." (laughter) And that was on the top floor of the central core. That's where his office was.

00:43:51
So, in his own way, without being a scientist—because he never presumed of being a scientist nor was he really a scientist. He didn't have the training for that, but he was apparently a very good surgeon. And he had this vision and the political skills and the people skills, and he built this institution from scratch. So in some ways it is of much greater merit than the subsequent

presidents. Without taking anything from the other three—each of whom has enormous merit—but Lee Clark was sort of the founding father. He also had the vision to develop incredible international relationships. Lee Clark was very much involved with the UICC. He invited a number of very prominent cancer specialists over the years to come to MD Anderson to talk, to visit, and he had numerous interactions. So MD Anderson was pretty well known around the world—perhaps even better than inside the US—by the time I came here. That's the reason I took that. We were training a large number of international students. Today in many parts of the world, the leaders of their cancer community or cancer research community were trained in the US—certainly true for Japan, certainly true for much of Western Europe, but also true for South America and parts of the Middle East and North Africa and Asia and whatnot. So he was very, very influential, and he left a huge mark on the institution.

00:45:49
Then when he stepped down—and I think he stepped down because he reached the age limit—then Mickey [Charles A.] LeMaistre was recruited. I think Mickey had been—he was not a cancer researcher. He was a pulmonary specialist, and his specialty was, in fact, tuberculosis. But he became interested in the problem of tobacco and its relationship to lung cancer, and that's how he came about towards cancer. But he was really—I think he was selected as president of this institution because of his role as chancellor of the University of Texas. He never presumed of being a cancer research specialist. I think his major skill was the political interactions both with the University of Texas and the Board of Regents and the higher education establishments throughout Texas. He was very, very good at that. By the time he took over, of course, Nixon had signed the war on cancer thing, and we had become an NCI-accredited cancer center. We were one of the first three. So by then MD Anderson was on the map. Mickey was also very effective at raising funds—not as much as Mendelsohn—in part because we didn't need it as much. In the mid ’70s the legislature was throwing money at us, and we had plenty of money. In fact, we didn't have a development office at that time. People who wanted to contribute just wrote a check, and I guess they sent it to Mickey's office or to Lee Clark's office. But Mickey was a much more reserved administrator. I got to know him much better after he stopped being president than while he was president. I seldom saw him walk around the institution. He sort of focused on his inner circle and worked with them. He worked also very much with potential donors, but it was just the big picture as opposed to really developing that.

00:48:46
Then came John Mendelsohn, and John was—the last few years of Mickey LeMaistre's tenure were painful because it was around the time when managed care started to make a dent in Texas. To prepare for that, there was this apocalyptic vision that this would be a terrible scene, so they hired some consulting organization. As you know, consultants are people from out of town with a business card. So they came, and they gave us a horrible report. They charged us probably a million dollars to tell us that we would go belly-up, and there was no way we would survive

because being a freestanding cancer center we had no referral base. So Mickey and his administration took that very seriously. We laid off something like 2000 people; and at that time we were much, much smaller than now, so that represented probably a quarter of our workforce. It was enormously painful, and we lost a lot of very valuable employees at a time when we were just recovering from the 1988 Wall Street crash, so a lot of people got hurt. It turned out that it was totally unnecessary. The advice we got was junk. Pretty soon we had to rehire a number of people because we were growing, and we had no way to take care of individuals. But it left—it sort of dampened the spirit of the institution, and when Mickey finally stepped down, the faculty were demoralized, and the employees were fearful of when were they going to be RIF'd. That was a term—RIF—reduction in force.

00:51:13
So then John Mendelsohn came in, and John Mendelsohn came in and his first act was to give grand rounds and go on record saying, "We are doing fine. We are going to be the best cancer center in the world. We are going to be doing that on the basis of research-driven patient care and the best education we can provide to our students, our faculty, our patients, and our community." And it was so invigorating that he really just lifted the spirits of the institution within a question of hours. He was, of course, and is a scientist—a card-carrying scientist who has contributed in a major way to what we know about cancer. He had been a cancer center director before in San Diego. He was a department chair at Memorial in New York. He ran a large lab in New York. So he had many, many skills and something that we didn't know that he also had: he turned out to be a monster in terms of fundraising. He has been, without doubt, the most successful fundraiser I have ever known. He's now seventy-six or seventy-seven, although he doesn't look his years. But from the moment he arrived until now, he has this incredible innocence that is transparent. He never got a big head like many very prominent and famous people—especially scientists and physicians—so he has this ability to have this very candid and down-to-earth conversation with anyone—with you, with me, with the donor who wants to give five dollars—and he makes everybody feel comfortable. It has been amazing to me to watch this man communicate with a variety of people but especially with those who are extremely wealthy. Many of the wealthy ones—not all of them but many of them—are very sophisticated people. They have been around for a long time. They have made a lot of money. They have had the ability to interact with a lot of other sophisticated people. They are well traveled, and some of them are well read. Most of them are well educated, so you can't just pull the wool over their eyes. And John just links up with them without any effort and without trying to sell them a bill of goods. He just has this uncanny ability to convince them that what we are doing is inherently good, that what we're doing is important, and that they need to contribute.

00:54:22
He was really the one who started our Development Office. I believe there was a development office before he came, but the development office before he came was essentially an office with

one person and a secretary, and I think they just processed the checks that came in without anybody asking for it. Since Memorial at that time had a very effective—and they still have an enormously effective development office, John sort of imported that concept, and he recruited a professional fundraiser. Today our Development Office is one of the most successful development offices in the country. We're still not as good as New York, but we are very good. Could we do better? Of course, but our development efforts have been very good and as a result you see all of what you see around us, and at least much of it—not all but much of it—has been paid for with philanthropy, and that's very largely John's contribution to the institution. John also contributed a lot to recruiting some good people, but he is a profoundly good human being. I don't think he has a mean fiber in his body, which to some extent is a disadvantage for a CEO and for a president because presidents frequently need to make painful decisions, and some of the painful decisions that would have been and probably are still necessary for this institution were not made during his tenure. He made some, but he left some others unmade.

Tacey Ann Rosolowski, PhD
0:56:48.2
Can you give me an example?

Gabriel Hortobagyi, MD
0:56:52.9
Examples. Over the years, a number of individuals on our faculty stopped being productive. They stopped getting grants. They stopped writing papers. They stopped working hard or trying, and they continued to be carried on with the institution paying for their salary, providing for their office, their secretaries, all of their maintenance, providing them laboratory space, and resources, and whatnot. That was just all going down into the black hole, and the decision to trim the deadwood was never made. Ever since I've been here, we've been fighting for laboratory space. There's never enough laboratory space. So during John's tenure—and of course when you walk around the institution, you walk through labs that are full of cobwebs, and a human being hasn't been sighted for years, but they belong to someone. Finally when it was obvious that this thing of we don't have enough lab space was ridiculous, the administration under John put together this committee that would assess the productivity of each lab. So they sent around questionnaires that every department chair had to fill, and then they visited all the labs, and then they came up with a scoring system. There were some labs that got all ones. There were some labs that got twos and threes. There were some labs that got fours. And there were a few labs that got fives, meaning they weren't doing a damned thing. Never. There was never any repercussion to that. No follow through, nothing that said, "Listen you guys, you got straight five. What are you going to do about it? We're going to repeat this in one or two years, and if you're still below, let's say, the average, your lab space is gone." It never happened. So that's the type of hard decisions that were not made.

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0:59:44.2 (end of audio 1b)

0.00:00 (begin audio 2)

Gabriel Hortobagyi, MD
0:00:01.6
I understand it's very hard to do that. It's very hard to confront someone who—especially someone who has a strong feeling of ownership and tell them, "Charlie, you're out of luck. I need that lab space and I'm going to give it to Smithie." So that tarnished a little bit the last few years of John's tenure. The other thing that towards the end of his tenure happened was that he became increasingly enclosed in his inner circle, surrounded by the chief financial officer and the chief legal officer and the vice president for the physician-in-chief and vice president for hospital and clinics. He was less available to the rest of the faculty, and I think that was problematic because he became isolated. During the last few years before Ron DePinho arrived, the administration clearly lost touch with the faculty. I'm sure you will hear that from many others in the institution, because it was so obvious that it was painful. Of course, you can understand part of that because the institution grew enormously under his leadership, and the larger an organization is the harder it is to stay in touch because there are so many things to attend to.

Tacey Ann Rosolowski, PhD
0:02:00.9
It was also a really rapid growth.

Gabriel Hortobagyi, MD
00:02:02
It was also a really rapid growth.

Tacey Ann Rosolowski, PhD
00:02:04
And managing that shift in such a short period of time—

Gabriel Hortobagyi, MD
0:02:09.9
Absolutely.

Tacey Ann Rosolowski, PhD
00:02:08
—enormously complicated.

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Gabriel Hortobagyi, MD
00:02:08
Absolutely. And then there were lots of recruitments, and there were reorganizations here and there and restructuring and—so there are many explanations but—so that's how I remember sort of the good and the not so good from that administration. Then our fourth president, who was a little bit of a surprise to all of us—not because he's not an outstanding scientist. He is, but he has never been in charge of a healthcare institution, and he doesn't have the experience of leading a patient-care-related organization. That requires very different skills from running a lab or from being a brilliant scientist. I just hope that he picks up those skills or that he recruits individuals who have those skills, because currently we don't have them in the upper structure of the institution. I hope that we get to a point where there is—we go back to the balance—that perfect balance where our four missions are all at the same level. And right now we are not at that point. I think it would be very important for us to keep that because that's what got the institution to where it is now—not where it is now but what we have become. You can argue whether we are indeed the number one institution in the country or not. That's a little bit of an artificial thing because of the way it is done by that magazine, whatever that is called. I think we are very good, but we can always be better.

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Chapter 33
A: View on Career and Accomplishments
Fostering Collaboration and Collegiality

Story Codes
A: Career and Accomplishments
A: The Leader
A: Character, Values, Beliefs, Talents
A: Professional Values, Ethics, Purpose

Tacey Ann Rosolowski, PhD
0:04:06.5
May I ask one more question? We're at three-o'clock, and I don't want to take too much of your time. I wanted to ask as you look back over what you've contributed to the institution, what is it that you're most gratified by?

Gabriel Hortobagyi, MD
0:04:36.8
You know, that's hard because there's not one thing. I've done many things. I've worn many hats in the institution. But if I were to pick one, it is probably bringing together this group—the entire breast cancer group—in a way that it is a collaborative, collegial, and productive group with enormous diversity—enormous at originating interests, backgrounds, and passions—but everybody focused on moving the field forward. Of course, in order to do that you have to do some research. You have to talk to a lot of people. You have to continuously press. You have to teach. You have to train. You have to cajole, twist arms, do all kinds of things. But that's probably my—in retrospect that's, I think, my major contribution to the institution.

Tacey Ann Rosolowski, PhD
0:05:47.3
How would you characterize your own leadership style?

Gabriel Hortobagyi, MD
0:05:54.9
(laughing) Imperfect in every way you can imagine. Some I might have mentioned in previous conversations I'm sort of a reluctant leader. I enjoy seeing other people grow and succeed and accomplish things. I'm pretty good at organization, but I'm impatient at doing things that I don't like to do. I think that's clearly a shortcoming, but there's nothing I can do about that.

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Tacey Ann Rosolowski, PhD
0:06:45.5
Are there some leadership principles that you've focused on or come across in your experience over the years?

Gabriel Hortobagyi, MD
0:06:55.4
Well, yes. So there are some pretty no-brainers. Number one, I think, is to have goals and to focus on those goals and not go bunny trailing—just continuously focus and not let others distract you with side trips to nowhere—so that's very important. The second is that leadership is, to a large extent, a service, and you don't do it for yourself. You do it for everybody else. Yes, you benefit from it yourself in many ways, including the satisfaction of having accomplished something. But it is a service. It's like being president. You don't do it because you want to have a big head, but you are serving the country. So those are very important principles. The third one is to be very respectful of others because you learn something every single day, and sometimes you learn from the most unexpected source. The fourth I would say is to never give an order that someone will not follow. And while that sounds totally ridiculous, you really have to have that sense of where the limits of your power are. And sort of a corollary of that is that it is much better to accomplish things by persuasion than by obligation. Getting buy in and getting consensus are very important activities to indulge in. There are some other things that are secondary: the organizational skills, dealing with money, dealing with crisis management, and that type of stuff. But I think those first four are probably the more important ones. And of course, giving example—giving a good example to people—not expect that people will do stuff that you are not willing to do yourself.

Tacey Ann Rosolowski, PhD
0:09:39.7
Is there anything else that you would like to add? We didn't touch on awards or anything like that, but I wanted to give you the opportunity to see if there's anything else that I've missed that you'd like to say about your roles.

Gabriel Hortobagyi, MD
0:09:54.1
No, I think that's pretty well enough. Awards are nice recognition that other people give you. I never expected any, never looked for any. I'm happy whenever I get one, but I always realized that I look a whole lot better because of the people I work with than because of myself. I have a number of colleagues—not in this institution—but a number of colleagues who call me periodically and ask for either a nomination or a letter of recommendation because they are seeking an award. I find that mind boggling because then it becomes totally meaningless. If you're nominating yourself for an award, it's because others have not nominated you. The whole

point of an award is that someone else recognizes that you have contributed to some extent to something. Otherwise, it's sort of a joke. So I never indulged in that nor am I planning to. But people have been kind to me, and that's nice.

Tacey Ann Rosolowski, PhD
0:11:21.1
Is there anything else you'd like to add?

Gabriel Hortobagyi, MD
0:11:24.2
Well, it's been a good run. I'm enjoying my senior statesman role, and it's fun. I just look forward to the next several decades.

Tacey Ann Rosolowski, PhD
0:11:43.3
Thank you very much for all the time you've taken with the interviews, Dr. Hortobagyi. I really appreciate it.

Gabriel Hortobagyi, MD
0:11:47.3
My pleasure. Thank you very much.

Tacey Ann Rosolowski, PhD
0:11:50.6
I'm turning off the recorder at fourteen minutes after 3:00.

0:11:55.3 (end of audio 2)