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REPORT TO PHYSICIANS

JULY/AUGUST 2003 Vol. 48, No. 7/8

OncoLog



Researchers Explore Possible Applications of Nanotechnology in Cancer Treatment

by Ann Sutton

In his book, *Engines of Creation*, K. Eric Drexler postulates a world in which tiny robots are unable to control their own self-replication and eventually engulf the earth. Such doomsday scenarios reflect a common misunderstanding about nanotechnology. Most scientists agree that nanorobots will not be developed for many years, if ever. Instead, current research in nanotechnology is focused on nanomaterials, tiny particles of organic and inorganic matter.

(Continued on **next page**)

Dr. Michael G. Rosenblum, a professor in the Department of Biimmunotherapy, holds a model of a buckminsterfullerene molecule, or buckyball. Dr. Rosenblum and his colleagues are studying the use of buckyballs, nanoparticles composed of 60 carbon atoms in the shape of a soccer ball, to deliver chemotherapeutic drugs to cancer cells.

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Researchers Explore Possible Applications of Nanotechnology

(Continued from page 1)

These particles and their potential uses in the treatment of cancer are being investigated at The University of Texas M. D. Anderson Cancer Center. Specifically, researchers are looking at ways in which nanomaterials might be used to deliver targeted treatments to cancer cells.

Nanotechnology refers to materials, devices, and systems created through the manipulation of matter on a nanometric scale and the exploitation of novel phenomena and properties that occurs at that scale. At 1/80,000th the width of a human hair, a nanometer is the length of 10 hydrogen atoms placed end to end. The possible applications of nanotechnology are innumerable, but medicine and computer science are expected to be among the first fields to yield viable products and techniques. Nanotechnology is already in use in a few commercially available products, including sunscreen and wrinkle-free pants.

Nanomaterials are created using either a “top-down” or “bottom-up” approach. The top-down approach refers to etching and molding materials into smaller and smaller components and is applicable to computer technology, whereas the bottom-up approach involves assembling structures atom by atom or molecule by molecule and is therefore more suited to medical research.

Gravity exerts control over such things as an ant, a person, or a red dwarf star. However, material smaller than a nanometer is governed not by gravity but by the laws of quantum mechanics. Nanomaterials exist between these two worlds, resulting in odd but exploitable behavior. “Nanotechnology is kind of a test-tube wonder in search of an application,” said Michael G. Rosenblum, Ph.D., a professor in the Department of Bioimmunotherapy at M. D. Anderson.

Working with such small materials in medicine poses unique problems. Nanoparticles are so small that they can be cleared out of the body before they complete their mission. They also have large surface areas relative to their volumes, which allows for easier manipulation but means that friction can be a problem.

Specialized nanoparticles called nanoshells are the focus of a research collaboration between John D. Hazle, Ph.D., chair (ad interim) and associate professor in the Department of Imaging Physics at M. D. Anderson, and engineers at Rice University in Houston. Nanoshells, which are hollow spheres made of silica and sometimes coated with gold, were invented by Naomi Halas, Ph.D., a professor of electrical and computer engineering and chemistry at Rice University. Antibodies can be attached to the surface of nanoshells, causing the shells to target certain cells. Laser light directed onto the shells from outside of the body would cause them to superheat, destroying tumor cells but leaving healthy cells unaffected.

This application of nanoshells is especially attractive in the treatment of prostate cancer; the prostate is near the surface of the body and therefore more easily accessible than other tumor sites. “You could theoretically spare most of the gland and just kill the part of the gland that has the tumor cells,” said Dr. Hazle.

Coating the shells with gold has distinct advantages; gold colloids have been used in medicine for years and are known to have low toxicity. “It’s very inert, but you can also do the chemistry needed to bind antibodies and other biomolecules to the gold. These nanoshells can mimic gold colloids; the body doesn’t know that they’re shells instead of particles,” said Dr. Hazle.

Dr. Hazle expects that the use of gold nanoshells in tumor ablation will enter clinical trials in three to four years. “What we’re focusing on is the best way to target cells and get them in a high enough concentration to either directly damage all of the surrounding tumor cells with heat or coagulate the microvasculature and starve them [the



Dr. John D. Hazle, chair (ad interim) and associate professor in the Department of Imaging Physics, is collaborating with engineers at Rice University to research the use of nanoshells for tumor ablation.

tumor cells] though a lack of blood and oxygen,” he said.

Nanoshells also could be filled with a drug-containing polymer. Heating the shells would cause the polymer to change shape, squeezing out a controlled amount of the drug.

“The shells that were activated would either burst or become permeable enough that the drugs would be able to escape into the local environment, so you could do more of a locoregional therapy and get a much higher local tissue concentration of a drug than you would be able to get systemically,” said Dr. Hazle.

Physicians have no way to accurately control the release rate of time-release drug implants, and patients who need regular doses of a medication must go to the doctor’s office often to have the drug administered. Using drug-filled nanoshells would allow for a more accurate rate of drug release and for patients to release the drug themselves by heating the implanted particles with an infrared light.

Dr. Rosenblum is studying another type of chemotherapeutic drug delivery system by applying nanotechnology’s most famous discovery, buckminsterfullerene, or the buckyball. A nanoparticle composed of 60 carbon atoms in the shape of a soccer ball, the

buckyball earned its discoverers, Sir Harold W. Kroto, Ph.D., of the University of Sussex, UK, and Robert F. Curl, Jr., Ph.D., and Richard E. Smalley, Ph.D., both of Rice University, the 1996 Nobel Prize in Chemistry.

“We’re trying to put chemotherapeutic agents on the surface of these particles so that they will be active when they are delivered to the target cell,” said Dr. Rosenblum. The current method of attaching drugs directly to antibodies has not been successful because each element in the pair adversely affects the other. A buckyball could carry separately the drug and the antibodies needed to target a particular cell. It also could deliver more than one kind of drug simultaneously.

“What these particles will allow us to do is to link these drugs together on the surface of the sphere in a combination that is synergistic, hopefully delivering that combination punch to the target cell with our antibodies,” said Dr. Rosenblum.

Dr. Rosenblum’s group is also evaluating whether buckyballs can safely and efficiently deliver radioisotopes to cancer cells. Calculations suggest that, in most cases, the radioisotopes will not escape their carbon cages before they reach the cells. Buckyballs could potentially deliver currently unusable radioisotopes, such as radon and actinium-225, to tumor cells. “It has the potential for holding radioisotopes for which there is no known chelator, that is, no way to link these isotopes to carrier molecules,” said Dr. Rosenblum.

Research into these techniques is still confined to the laboratory and, according to Dr. Rosenblum, there is no way to predict when they might be tested in clinical trials. “Before we do it, there’s no way of knowing how it is going to work,” he said. “We don’t even know what the challenges are at this point, but all of the things we are going to find out are going to be new; that’s the interesting part.” ●

FOR MORE INFORMATION, contact Dr. Rosenblum at (713) 792-3554 or Dr. Hazle at (713) 792-0612.

Sharing the Burden: Palliative Care Team Helps Patients, Families Through Difficult Times

by Karen Stuyck

Even as they try to cope with the physical consequences of their disease, patients who are dying of cancer have a host of other concerns: Will the money from my life insurance policy be enough to take care of my family when I am gone? How will my death affect my children? When the time comes, will I be able to face death with peace and dignity?

(Continued on page 4)



Members of the palliative care team (left to right)—**Thuc Nguyen**, a clinical nurse, **Marlene Lockey, M.S.W.**, a senior social work counselor, **Dr. Fadi Braiteh**, a fellow in the Department of Symptom Control and Palliative Care, and **Dr. Ahmed Elsayem**, an assistant professor in the Department of Palliative Care and Rehabilitation Medicine—greet patient [REDACTED] before sitting down to discuss her treatment.

Palliative Care Team Helps Patients and Families

(Continued from page 3)

Helping patients and their families through this difficult time requires a team as diverse as the problems and issues that arise at the end of life. At The University of Texas M. D. Anderson Cancer Center, physicians, nurses, nutritionists, social workers, chaplains, and counselors work together to help critically ill patients “express their maximal physical and psychosocial potential for as long as possible,” said Eduardo D. Bruera, M.D., professor and chair of the Department of Palliative Care and Rehabilitation Medicine at M. D. Anderson.

The entire palliative care team makes regular visits to each patient’s room, listening to concerns and offering solutions to help the patient have the best possible quality of life and remain as autonomous as he or she can be. The family is encouraged to attend these visits, or they can hear the team’s recommendations on an audiocassette. On a typical visit, the palliative care group makes more than a dozen recommendations, said Dr. Bruera.

“These issues vary enormously from one person to another,” he said. In addition to dealing with the patient’s medical concerns, the group might be asked to help someone obtain medication coverage, make a will, reconnect with a religious community, or contact an estranged relative. Resolving these personal issues can bring the patient great peace of mind, Dr. Bruera said. Sometimes, patients at the end of life appreciate just having the opportunity to speak frankly about the things that are distressing them—without worrying about burdening a family member.

Most patients are referred to M. D. Anderson’s palliative care program while they are receiving treatment, so palliative care is integrated with the primary cancer therapy. The palliative care staff tries to tailor their approach to each individual patient. One patient, for instance, might choose to be very actively involved in his or her care, while another wants the physician to make the end-of-life care decisions.

“We cannot take a one-size-fits-all approach to communications and decision-making,” Dr. Bruera said.

“Our number one goal is the comfort and well-being of the patient, and our number two goal is the comfort and well-being of their family.”

**– Eduardo D. Bruera, M.D.,
chair, Department of Palliative Care
and Rehabilitation Medicine**

A patient’s style of decision-making is highly personal and may change as his or her illness progresses. “As caregivers, we need to be sure that we understand where that particular patient wants to be in the discussion today and then tailor our communication approach,” he said.

The palliative care team tries to incorporate the family’s needs into the treatment plan, not only because family members are usually responsible for taking care of the patient but also because the patient feels better when the family is helped and supported. The team makes sure that each family member has a chance to ask questions, understands what is happening with the patient, and knows what to do if things go wrong, Dr. Bruera said.

“Our number one goal is the comfort and well-being of the patient,” Dr. Bruera said, “and our number two goal is the comfort and well-being of their family.”

Taking care of the family extends to offering counseling. According to Estela A. Beale, M.D., a patient’s main worry often is, “What will happen to the children when I die?” Dr. Beale, a child and adult psychiatrist and associate professor in the Department of Neuro-Oncology, works with the children of patients receiving palliative care. She typically meets first with the entire family and then once with just the parents and again with each child. She helps the family deal with practical issues, such as who is going to take care of the children after the parent dies, and with the emotional aspects of the loss, such as helping the children to

comprehend that their mother or father is dying.

If the patient and child can discuss with each other their worst fears about their mutual loss, Dr. Beale said, they can “take advantage of the time remaining to recoup memories of their time together and create new memories.” Sometimes, for instance, the parent and child will make photo albums together, write a diary, or plan some event that they’ll both enjoy, such as playing a game or watching a movie.

The palliative care staff tries to remain a presence in the family’s life even after the patient dies. Dr. Beale and other staff visit each bereaved child six months and then a year after the parent’s death to see how the child is dealing with grief and if he or she could benefit from additional help.

Signs of trouble at the six-month visit, Dr. Beale said, include school problems, symptoms of depression, intense sadness, and withdrawal and isolation from family and friends. Some children seem to do well initially but then experience problems associated with bereavement later on, sometimes on the anniversary of the parent’s death. “If we intervene at the first anniversary, we hope the children won’t have problems again later,” Dr. Beale said.

The Department of Palliative Care and Rehabilitation Medicine also has less formal programs for connecting with bereaved families. When a patient dies, the family receives a card encouraging them to contact the palliative care staff for counseling or grief support. Also, patients and their caretakers, as well as bereaved families, are all invited to the department’s Friday afternoon teas, where they can talk to one another and to social workers, counselors, and volunteers. “Over the years, we’ve found that this informal approach is very effective in bringing in people who wouldn’t come to a more formal support group,” Dr. Bruera said. “People have tea and cookies and mingle with each other and chat.”

Discussions regarding the end of life or the incurability of an illness are never easy, Dr. Bruera said. “However,



Dr. Estela Beale, an associate professor in the Department of Neuro-Oncology, helps children and families cope with the illness of a loved one. In a recent session with Dr. Beale (left), [REDACTED], sister of a patient, selects puppets from a variety of toys, designs a short play, and assigns roles to her mother, [REDACTED] and Dr. Beale.

there are specific techniques doctors and nurses can use to make sure that patients receive the information in the way most effective for them to understand it and also feel comfortable and supported.”

But how can physicians who haven't had the benefit of formal end-of-life training learn these techniques? Most oncologists care for dying patients on a regular basis, but numerous studies indicate that they often feel ill prepared for this emotionally difficult job.

“End-of-life care is a daily issue for any oncologist,” said Dr. Bruera. “Unfortunately, most cancer training programs do not emphasize how to deal with the physical and psychosocial problems and family issues associated with advanced illness.”

A 2001 survey published in the *Journal of Palliative Medicine*, for example, found that fewer than 53% of fourth-year medical students from six U.S. medical schools believed that their education had prepared them for treating dying patients. The students from the two medical schools that had a formal end-of-life curriculum, however, felt significantly more prepared than their peers at the other four schools.

M. D. Anderson offers training in end-of-life care to doctors, nurses, and

other health-care professionals through the Department of Palliative Care and Rehabilitation Medicine. Participants learn how to treat their patients' pain, fatigue, and other physical consequences of cancer, as well as how to help dying patients deal with the psychological distress, confusion, spiritual concerns, and family issues associated with end-of-life care.

Dr. Bruera said that health-care professionals also come to M. D. Anderson to observe the palliative care team in action and learn how to relate more effectively to dying patients. Physicians often visit the department for a few days or even a few weeks at a time. When health-care professionals are able to “see the techniques used with patients, ask questions, and participate, they can really feel much more comfortable and effective in communicating with patients who are near the end of their lives,” Dr. Bruera said.

“The good news,” he added, “is that our ability to serve patients who are dying of cancer is much, much better than it was only 10 years ago.” ●

FOR MORE INFORMATION, contact Dr. Bruera at (713) 792-6084 or Dr. Beale at (713) 792-7546.

Palliative Care Internet Resources

Journals

- Journal of Pain and Symptom Management
<http://www.elsevier.nl/inca/publications/store/5/0/5/7/7/5/>
- Pain
<http://www.elsevier.nl/locate/inca/506083>
- World Health Organization Cancer Pain Release
<http://www.whocancerpain.wisc.edu/>

Medical

- American College of Physicians Home Care Guide
http://www.acponline.org/public/h_care/contents.htm
- Association for Death Education and Counseling
<http://www.adec.org/>
- Growth House, Inc.
<http://www.growthhouse.org/>
- M. D. Anderson Cancer Center Pain Management
<http://www.mdanderson.org/topics/paincontrol/>
- National Pain Foundation
<http://www.painconnection.org/>

Other Programs

- American Academy of Hospice and Palliative Medicine
<http://www.aahpm.org/>
- Hospice Care Association
<http://www.hca.org.sg/>
- Hospice Foundation of America
<http://www.hospicefoundation.org/>
- Last Acts
<http://www.lastacts.org/>

UPDATE:

Study of Tamoxifen and Raloxifene (STAR) Nearing Completion

Recruitment Efforts Focus on Women in Minority, Medically Underserved Populations

by Gayle Nesom

In October 1998, the first major Breast Cancer Prevention Trial (BCPT) ended dramatically and prematurely when tamoxifen was found to decrease by 49% the incidence of invasive breast cancer in women at increased risk. One year later, the National Surgical Adjuvant Breast and Bowel Project opened a second trial, this one to compare the effects and long-term safety of tamoxifen with those of raloxifene, an osteoporosis prevention drug that may also reduce the risk of breast cancer.

Nationwide, more than 16,000 women have enrolled in the Study of Tamoxifen and Raloxifene (STAR), according to Therese Bevers, M.D., an assistant professor in the Department of Clinical Cancer Prevention and medical director of the Cancer Prevention Center at The University of Texas M. D. Anderson Cancer Center. The total enrollment goal of STAR is 19,000 participants, down from an initial 22,000.

"Fewer women are needed than originally planned because the women who have volunteered have been at higher risk than anticipated," Dr. Bevers said. As a result, the study will be able to accrue the defined number of events (breast cancer diagnoses) required for a valid analysis more quickly. Data from the study should be available by early 2007.

The trial is open to postmenopausal women older than 35 years who meet either of the study's two criteria: they must be at increased risk of breast cancer, as defined by the Gail risk-assessment model, which was used in the first BCPT, or they must have been diagnosed with lobular carcinoma in situ (LCIS), a condition that is sometimes a precursor of invasive breast cancer. The trial is limited to postmenopausal women because raloxifene's long-term safety has not been adequately tested in premenopausal women.

Recruitment at M. D. Anderson and its satellite trial sites has been successful, according to Dr. Bevers, and several recruitment initiatives are in place. "We recognize that potential participants may not be able to travel to Houston," said Dr. Bevers, "so getting the trial out to other communities, particularly those with large minority populations, is a big focus. We are just about to open our seventh and eighth satellite sites, which will make participating through M. D. Anderson possible in Houston, El Paso, Laredo, Beaumont, Lufkin, and Tyler, Texas,

as well as Shreveport, Louisiana, and Orlando, Florida."

In Houston, M. D. Anderson has established a collaborative relationship, called Houston STAR, with the Texas Cancer Institute/St. Luke's Episcopal Hospital and the Baylor College of Medicine and Methodist Hospital Breast Care Center.

As part of this collaboration, a community outreach coordinator was hired to recruit minority and medically underserved women. "African-American women are at higher risk of dying of breast cancer than women in other racial groups, and we would like to reach as many women in this population as possible," Dr. Bevers said.

M. D. Anderson has a professional outreach coordinator who talks with health-care professionals about the trial and about their patients' opportunities for participating. The coordinator also gives physicians feedback about their patients' participation in the study.

Dr. Bevers and her colleagues also are exploring an opportunity that would enable them to distribute breast cancer risk assessment and prevention information to a large group of women in Texas. "Besides recruitment, a major goal is to make requesting a cancer risk assessment as common as requesting a mammogram. Women who learn that they are at increased risk need to know their options for decreasing the risk," she said.

Recruitment for STAR will continue through 2004. Physicians who want more information are encouraged to call Diane Birkner, professional outreach coordinator, at (713) 745-8361. Women who would like information about participating in the trial should call M. D. Anderson's STAR line at (713) 792-8064 or toll free at (866) 699-4400. Additional information is available at M. D. Anderson's Web site at <http://www.mdanderson.org>, the National Surgical Adjuvant Breast and Bowel Project Web site at <http://www.nsabp.pitt.edu>, and the National Cancer Institute's clinical trials Web site at <http://www.cancer.gov/clinicaltrials> or from the Cancer Information Service at (800) 4-CANCER (422-6237). ●



Diane Kasek Birkner (right), a professional outreach coordinator in the Department of Physician Relations, speaks with **Dr. Judi Shaw-Rice**, a physician in private practice, about the STAR trial.



Getting the Best Treatment

If you or someone you love has cancer, you've probably felt a loss of control, a sense of helplessness in the face of a powerful disease. It's true that you can never go back to the time before you heard the words, "You have cancer," but there are things that you can do, such as taking steps to ensure that you receive the best possible treatment.

The following are suggestions to help you get the highest-quality cancer care available:

■ Pick the right doctor.

Choosing the right doctor is one of the most important decisions you'll make. Your primary care physician may refer you to an oncologist, a doctor specializing in cancer. You can find information on the Internet about physicians, their specialty areas, their medical training, and where they practice. Two sites to try are the American Medical Association's online service "AMA Physician Select" (<http://www.ama-assn.org/aps/amahg.htm>) and the American Society of Clinical Oncologists' online list of cancer specialists (http://www.asco.org/ac/1,1003,_12-002215,00.asp).

You might want to meet with several doctors before choosing one. Find out if the physicians are board certified and how much experience they have with your type of cancer. Also, it's important to find a doctor who listens to you, explains things clearly, and welcomes questions.

■ Consider getting a second opinion.

After your doctor offers a diagnosis and a treatment plan, you might want to get another physician's advice before

you start treatment. This is common, and your doctor should not be offended. A second specialist's assessment of your case can make you aware of all the available options for treatment, confirm your proposed treatment plan, or suggest some modifications to it. It also can reassure you that you've taken the right path.

■ Choose the best hospital.

If you've already picked your physician, you may automatically be admitted to the hospital where your doctor practices. Sometimes, though, you have some choices.

According to the American Cancer Society, the best cancer hospitals have round-the-clock physician staffing, pathology and diagnostic laboratories, a blood bank, social services, advanced diagnostic and therapeutic equipment, respiratory and physical therapy, rehabilitation services, and an intensive care unit.

You can check out the hospital you're considering by accessing the Quality Check service on the Web site of the Joint Commission on Accreditation of Healthcare Organizations, a nonprofit organization that evaluates health-care facilities (<http://www.jcaho.org/qualitycheck/directry/directry.asp>).

■ Learn everything you can about your condition.

Being well informed about your cancer can only benefit you. But be sure that the health information you rely on is accurate. Two reliable sources of health information are the Cancer Information Service (1-800-4-CANCER) and the National Cancer Institute's Web site (<http://cancer.gov>), which offers the latest cancer information from its database.



Consider getting a second opinion.

Don't be misled by information on the Internet that touts questionable treatments or miracle cures. The Federal Trade Commission, which investigates false or misleading health claims posted on the Internet, has an Operation Cure-

All Web page (<http://www.ftc.gov/bcp/online/edcams/cureall/>) that can help you evaluate claims about health products.

■ Help yourself during cancer treatment.

You can be an active participant in your own care. Keep your doctor or nurse informed about your health. Tell them, for instance, about any side effects you're experiencing or other medications you take.

Try to eat healthy foods, drink plenty of liquids, and get enough rest. Discuss your feelings of sadness, anger, or fear with your friends, family, or a counselor. It helps to talk about your feelings.

By picking the right physician and hospital, learning all you can about your illness, communicating with your doctor, and taking care of your health, you can make sure that you receive the best possible treatment. ●

For more information, contact your physician or contact the M. D. Anderson Information Line:

 (800) 392-1611 within the United States, or

 (713) 792-6161 in Houston and outside the United States.

July/August 2003

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Staff Publications

Below is a partial list of staff publications appearing in July.

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