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The Beat



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OCTOBER 1996

FIGHTING THE BIGGEST SERIAL KILLERS OF MANKIND

Research in the laboratory of Dr. Sailen Barik of the Department of Biochemistry and Molecular Biology focuses on the molecular basis of gene expression and pathogenesis of Respiratory Syncytial Virus (RSV virus or RSV), a deadly respiratory pathogen of the Paramyxovirus family that kills as many people as does AIDS and malaria combined. Nearly 4 million children die worldwide every year from RSV infection, and unlike AIDS, one can catch it by merely shaking hands.

In an average year on this planet, 50 million people die from all sorts of conditions. Of them, 19 million are killed by infectious agents. It may come as a surprise to many that RSV remains the single largest killer of mankind, claiming about 4 million human lives annually (compared to 2.5 million by HIV, the AIDS virus). Virtually every human being gets infected with RSV (not to be confused with Rous Sarcoma Virus, a cancer-causing virus) multiple times in the first 2 years of life. A typical RSV infection in a child is known as "croup", a flu-like disease with severe dry cough ("barking" sound), bronchospasm, and troubled breathing that persist for 3-5 days. There are no drugs effective against RSV. Natural immunity is short lived, and reinfections are particularly common in crowded environments, such as in the day care centers, and in the winter. Often times, a childhood RSV infection will lead to asthma later in life.

The problems that confront scientists in their fight against RSV are many. Perhaps the most difficult one stems from the RNA nature of the 15,000 nucleotide long viral genome, which mutates so rapidly that the antigenic make-up of the virus constantly changes, thus guaranteeing the failure of any vaccine. Moreover, standard vaccines formulated from heat-killed or formalin-inactivated RSV lead to, for reasons not understood, a more severe respiratory disease, including death. It is even believed that some cases of SIDS (Sudden Infant Death Syndrome) may have a RSV connection.

In 1982, when Dr. Sailen Barik received his Ph. D. from Bose Institute in Calcutta, India, he was trained primarily as a microbiologist studying *E. coli* and bacteriophage lambda, the two common laboratory organisms that have historically served as tools in teaching and learning molecular biology. During his post-doctoral work at the University of Connecticut Health Center, his findings laid the groundwork for a mechanism that is fundamental in all living cells: control of transcription termination and anti-termination. The basic mechanism proposed in those studies was later confirmed in studies on the regulation of HIV genes and cancer genes such as c-myc. Following a faculty appointment in the newly founded Department of Molecular Biology in the Cleveland Clinic in 1989, Dr. Barik

applied his transcriptional expertise to RNA viruses of eukaryotic nature, and began unraveling the transcriptional control mechanisms of vesicular stomatitis virus (VSV, a prototype RNA virus that infects cattle) and RSV. Two postdoctoral fellows, Dr. Barsanjit Mazumder and Dr. Gautam Adhikary, joined his laboratory and initiated RSV research. In 1994, he opted to move to an academic environment and to a warmer climate, and accepted the position of Assistant Professor at the University of South Alabama College of Medicine.

In the last few years, Dr. Barik and his colleagues have made significant contributions in RNA viral gene regulation, many of which stand as pioneering achievements in the field. In an early study, he deduced the complex cap structure of the RSV messenger RNAs single handedly. Subsequently, his laboratory became successful in dissecting and then reconstituting the transcription complex of RSV in the test tube, a difficult biochemical feat that was regarded as the "Holy Grail" in RSV research. This technique in turn opened up new avenues to study the structure and function of the various viral proteins. Studies in Dr. Barik's laboratory, initiated primarily by Dr. Mazumder and continued by Lesley Dupuy, a graduate student, and Tammy McLean, an aspiring medical student, resulted in a detailed analysis of the role of cellular casein kinase 2 in phosphorylating and thereby activating the RSV phosphoprotein, an essential component of viral RNA-dependent RNA polymerase machinery. The sites of phosphorylation were also mapped with precision. Exploiting this observation, members of his group have isolated a "dominant negative" mutant of the phosphoprotein in which the sites of phosphorylation have been destroyed by site-directed mutagenesis. As expected, this mutant protein is non-functional, but additionally, it also inhibits the function of the normal protein, and thus abrogates RSV transcription. In a parallel study, Dupuy used antisense technology to inhibit two unique non-structural RSV proteins of unknown function, a discovery that is being patented for its obvious clinical implications. His studies and those of another student, Ms. Emily Burke, indicated that these proteins may have an essential role in viral morphogenesis, the mechanism of which is under intense scrutiny by Emily. Studies initiated by Andrew Velazquez, a sophomore medical student carrying out summer research in Dr. Barik's laboratory last year, provided unequivocal evidence that infection of RSV leads to augmented synthesis of a variety of cytokines by the infected cells. Dr. Vira Bitko, a postdoctoral associate from Ukraine, has continued these studies and has

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Class of 2000
New Faculty

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already demonstrated that RSV infection activates NF- κ B (nuclear factor "kappa-*bee*"), an important transcription factor essential for transcription of many genes of immunological importance, including cytokines. RSV-cytokine interaction, with its far-reaching implications in RSV immunopathology, is being studied in detail.

Once protein phosphorylation became a major theme in Dr. Barik's research, it led to the logical study of the loss of such phosphates, a reaction catalyzed by enzymes called protein phosphatases. His search for a phosphatase for RNA viral transcription factors led to his discovery of the first bacteriophage protein phosphatase, encoded by phage lambda. Dr. Toshihiro Ansai, a visiting scientist from Japan, aided by Mr. Dupuy, carried out fundamental mutational analyses of the lambda enzyme. In a tryst of these two lines of research, the effect of this phosphatase on RSV transcription is being pursued. Very recently, Russell Taylor, a graduate student, and Dr. Ansai, in collaboration with Dr. Debopam Chakrabarti of the University of Central Florida have identified and characterized protein kinases and phosphatases in another human pathogen, the malarial parasite, *Plasmodium falciparum*. The role of such enzymes in signal transduction in the *Plasmodium* is being studied.

In spite of the high mutability of RSV, the active domains of its most fundamental gene products, such as transcription factors, have remained amazingly unchanged during evolution. The simplest explanation is that these domains are essential for RSV growth, and viruses with a crippling mutation in these domains simply did not survive. Dr. Barik and his associates believe that drugs targeted against these molecular domains will, therefore, become our magic bullets against the killer pathogens. The effectiveness of antisense oligos designed against such domains and the success of the dominant negative mutations have sustained their conviction. It may not happen tomorrow, but a time will perhaps come when four million children will no longer stay up in the middle of the night, coughing, gasping for air, and become statistics in the morning.

ORTHOPAEDIC SURGERY CHAIR NAMED



Arthur Manoli, II, M.D., has been appointed Professor and Chair of Orthopaedic Surgery. Dr. Manoli received a B.S. degree in pre-medicine and the M.D. degree from the University of Michigan. He completed his internship at St. Joseph Mercy Hospital, and a residency in general surgery/orthopaedic surgery at Oakwood Hospital and Wayne State University.

In July 1975, Dr. Manoli joined the U.S. Army at Fort Polk, Louisiana as an orthopaedic surgeon. In September 1977, he was appointed as Assistant Professor in the Department of Orthopaedic Surgery at Wayne State University. Dr. Manoli was primarily an orthopaedic traumatologist at Detroit Receiving Hospital, where he was Chief of Orthopaedic Surgery for seven years. In 1989, he received a one-year fellowship award from the American Orthopaedic Foot and Ankle Society. Upon completion of his fellowship, he joined the University of Pittsburgh as Associate Professor in the Department of Orthopaedic Surgery, but returned to the Detroit area in 1992, to accept a position as Professor of Orthopaedic Surgery at Wayne State.

Dr. Manoli is a member of fifteen different international, professional and scientific societies. Currently, Dr. Manoli is Chair of the Trauma Committee of the American Orthopaedic Foot and Ankle Society (AOFAS). He is also Associate Editor of Foot and Ankle International and a consultant reviewer for two other peer-reviewed journals.

Dr. Manoli's research interests include the etiology and treatment of adult acquired flatfoot, screw fixation in traumatic and adult reconstructive surgery, and compartment syndromes of the lower extremities. As a clinician, his interests involve complex reconstruction of the foot and ankle, rheumatoid and diabetic foot care, and amputation surgery and rehabilitation. He has recently finished the development of a Foot and Ankle Severity Score (FASS) which is a rating scale of injury severity and long-term impairment of the various traumatic foot and ankle injuries. With increased use of seat belts and airbags, trauma centers are now seeing an increased incidence of severe injuries of the lower extremities. FAAS is intended to be used by basic and crash researchers as a tool for measuring the severity of this major public health problem. It is hoped that this tool will also be useful in the development of injury prevention programs.

Dr. Manoli's family include his wife of thirteen years, Carole Anne, and two children, Arthur, III age 9 and Christian age 6. The Manoli family has interests in gardening, fishing, water sports and travel. Dr. and Mrs. Manoli's hobby is growing prize-winning orchids and they are members of the American and Michigan Orchid Society. In the last year they have won two trophies and ten ribbons for their orchid exhibits. Dr. Manoli says they are looking forward to the challenge of growing warm weather orchids. We expect that the Department of Orthopaedics will also benefit from the green thumb of its new chair.

NEW VIDEO SERIES ON RESEARCH INTEGRITY AVAILABLE

The American Association for the Advancement of Science (AAAS) has produced a series of ten minute videos. Five different videos portray hypothetical situations in research that raise ethical issues, but leave them unresolved in order to stimulate discussion. The video series were developed by AAAS for use in educational programs and to assist scientists in meeting their responsibility for maintaining the quality and integrity of their research. A discussion and resource guide accompanies the series. It includes discussion questions and a bibliography of related subject matter.

These videos are available in the Office of the Senior Associate Dean, CSAB 180, and can be checked out free of charge for a maximum of five days. For additional information call 460-6041.

NEW GRADUATES OF THE BASIC MEDICAL SCIENCES DOCTORAL PROGRAM

Congratulations to the following individuals on this significant achievement:

Li Liu, sponsored by Dr. Gopal Nair in the Department of Biochemistry and Molecular Biology. Her dissertation was entitled "Folate Based Antimicrobial Agents."

Timothy Moore, sponsored by Dr. Aubrey Taylor in the Department of Physiology. His dissertation was entitled "Adhesion Molecules and Nitric Oxide in Ischemia and Reperfusion Injury of Isolated Rat Lungs."

AWARDS

Gopal Nair, Ph.D., Professor of Biochemistry and Molecular Biology, has received a four-year research award totaling \$200,000 from the American Cancer Society. The award was based on the recommendations of the American Cancer Society Peer Review Advisory Committee, the Council for Research and Clinical Investigation Awards and the Research and Clinical Investigation Committee of the Board of Directors. This grant will support Dr. Nair's research studies on "Metabolism Blocked Antifolates and Novel GARFT Inhibitors."



The National Institutes of Health has awarded a \$165,462 grant to **Steven J. Pittler, Ph.D.**, Associate Professor of Biochemistry and Director of the Center for Eye Research. Dr. Pittler's research has led to the identification of a DNA sequence in the gene that appears critical for expressions of the gene in the photoreceptors. Dr. Pittler will continue to study the function of this gene using several experimental paradigms.



Ronald S. Kaplan, Ph.D., Professor of Pharmacology, has received a four-year grant award totaling \$805,361 from the National Institutes of Health. Dr. Kaplan's research project is entitled "Structure and Function of Mitochondrial Citrate Carrier", and his objective is to determine how citrate, an important metabolite found in all cells, crosses the mitochondrial inner membrane via the citrate transport protein at the chemical and atomic levels. If successful, the proposed studies will provide the foundation for obtaining the first high-resolution information for this class of membrane protein, and thus will represent a major scientific advancement.



Michell Ardell, Ph.D., a postdoctoral fellow in the laboratory of Dr. Steven Pittler in the Department of Biochemistry and Molecular Biology, was awarded a \$20,000 grant by the Knights Templar Eye Foundation Inc. for her research on the disorder Bardet-Biedl syndrome, a form of retinitis pigmentosa.

The Knights Templar Eye Foundation Inc., founded in 1956, is a non-profit Masonic charity that provides support for surgical treatment, vision research, and hospitalization for people suffering from eye injury or eye disease.

CONGRATULATIONS

William Gardner, M.D., Chair and Louise Lenior Locke Professor of Pathology, has been awarded a Fulbright Fellowship. During a three

month sabbatical period, Dr. Gardner will lecture at Comenius University in Bratislava and Safarik University in Kosice, Slovakia. His lecture topics will include: the evolving American medical school curriculum; the administration and management of hospitals; and the pathophysiology of prostatic disease.



Jonathan Scammell, Ph.D., Professor of Pharmacology, has accepted an invitation to serve as a member of the NIH Biochemical Endocrinology Study Section, Division of Research Grants. Members are selected on the basis of their demonstrated competence and achievement in their scientific discipline as indicated by the quality of research accomplishments, publications in scientific journals, and other scientific activities, achievements and awards.



Amy DeVasher, a first year medical student, was named one of 10 finalists for the 1996 NCAA Women of the Year Award. The award recognizes advancements in athletics, academics and community leadership. The former University of Alabama swimmer also received Postgraduate scholarships from the NCAA and Southeastern Conference.



Jorge L. Herrera, M.D., associate professor of medicine in the Division of Gastroenterology was a guest speaker at the XVII Gastroenterology Congress in Caracas, Venezuela and at the XIV International Congress of Hepatology in Buenos Aires, Argentina. He addressed various topics related to liver disease including viral hepatitis, medication-related liver disease, liver tumors and complications of cirrhosis.

Dr. Herrera was also selected to participate in an expert panel to develop a consensus statement on the evaluation and management of viral hepatitis in Latin America.

SURGERY RESEARCH/ TEACHING SUITE DEVELOPED IN COMPARATIVE MEDICINE

The Surgery Research/Teaching Suite is located in the Department of Comparative Medicine and is designed for a variety of animal surgery applications. The suite includes approximately 800 square-feet of operating room space and 900 square-feet of support space. Technologists and Technicians, certified by the American Association for Laboratory Animal Science, are available to assist with procedures.

The surgery suite includes operating rooms, surgeon's prep area, surgical prep/instrument prep and a recovery room. The operating room facility includes one aseptic surgery room and one large nonsterile surgery room. Support facilities include a fully equipped animal diagnostic laboratory, pre and post operative housing for animals, and animal procurement.

For further information, please contact Dr. Alan Brady or Mr. Jon Garcia at 460-6239.

NEW FACULTY MEMBERS

Welcome to the University of South Alabama



Cox



Mitchell



Quillen



Fan



Shakoor



Stevens



Kemp



Soni



Shibo



Graves



Clark



Nelson



Estrada



Stevens



Corboz



Khimenko



Pence



Sebelik



Shartava



Wang

EMERGENCY MEDICINE

Robert J. Cox, M.D., Assistant Professor, received a B.S. in biology and a M.D. from the University of Missouri. Dr. Cox completed his internship and residency in emergency medicine at Emory University.

Barbara Mitchell, M.D., Assistant Professor, received a B.A. in English and a M.D. from the University of South Alabama. She completed her internship and residency in medicine at USAMC.

FAMILY PRACTICE

David M. Quillen, M.D., Assistant Professor, received a B.A. in chemistry from Colby College and a M.D. from the University of North Carolina. He completed his internship and residency in family and community medicine at Duke University. He also completed a Faculty Development and Predoctoral Education Fellowship at Duke.

MEDICINE

T. Michael Fan, M.D., Ph.D., Assistant Professor, received a M.S. and Ph.D. in pharmacology from the University of Rochester and a M.D. from State University of New York. Dr. Fan completed his internship and residency in internal medicine at Strong Memorial Hospital, Rochester, NY and a fellowship in cardiology at the University of Rochester Medical Center.

Ahtisham Shakoor, M.D., Assistant Professor, received a M.B.B.S. in medicine and surgery from Rawalpindi Medical College, Pakistan. He completed his residency in internal medicine at USAMC.

Thomas E. Stevens, Jr., M.D., Assistant Professor, received a B.S. in physics from Rhodes College and a M.D. from the University of Mississippi. He completed his internship and residency in internal medicine at the University of Mississippi and a geriatric medicine fellowship at Johns Hopkins University in Baltimore.

Stephen E. Kemp, M.D., Assistant Professor, received a B.A. in history from Duke University, a B.S. in biology from Virginia Commonwealth, and a M.D. from the Medical College of Virginia. Dr. Kemp completed his residency in internal medicine at the University of Tennessee and subspecialty fellowship training in allergy and immunology and clinical laboratory immunology at the University of South Florida.

Bhavik P. Soni, M.D., Assistant Professor, received a B.M.E. in mechanical engineering from Georgia Institute of Technology and a M.D. from the Medical College of Georgia. He completed his

internship in internal medicine at the University of North Carolina and residency in dermatology at the Bowman Gray School of Medicine, Winston-Salem, North Carolina.

MEDICAL GENETICS

Shibo Li, M.D., Assistant Professor, received a M.D. from Norman Bethune University, P.R. China. He completed a postdoctoral fellowship in laboratory medicine and genetics at Yale University and in medical genetics at the University of South Alabama.

NEUROLOGY

George C. Graves, M.D., Assistant Professor, received a A.B. in biology from Rollins College and a M.D. from the University of South Alabama. He completed an internship in internal medicine and a residency in neurology at USAMC.

ORTHOPAEDICS

Carey A. Clark III, M.D., Assistant Professor, received a B.A. in chemistry from the University of North Carolina and a M.D. from the University of Tennessee. Dr. Clark completed his internship and residency in orthopaedics at Indiana University Medical Center and an orthopaedic traumatology fellowship at the University of Washington Harborview Medical Center in Seattle.

PATHOLOGY

Beverly P. Nelson, M.D., Assistant Professor, received a B.S. in microbiology from Pennsylvania State University and a M.D. from Temple University. Dr. Nelson completed her pathology residency at Temple University Hospital and the Medical College of Pennsylvania and a hemato-pathology fellowship at the University of Pittsburgh Medical Center.

PEDIATRICS

Benjamin Estrada, M.D., Assistant Professor, received a B.S. in medical sciences and a M.D. from Universidad Francisco Marroquin (Guatemala). He completed his pediatric internship and residency at USAMC. He also completed a pediatric infectious disease fellowship at Tulane University.

PHARMACOLOGY

Troy Stevens, Ph.D., *Assistant Professor*, received a B.S. in health education from Chadron State College and M.S. and Ph.D. degrees in physiology from Colorado State University. He completed postdoctoral training in cell physiology at the University Colorado Health Sciences Center in Denver.

PHYSIOLOGY

Michel R. Corboz, Ph.D., *Instructor*, received his Ph.D. with highest honors in biology from the University Joseph Fourier Grenoble (France). Dr. Corboz completed postdoctoral training in physiology at the University of South Alabama.

Pavel Khimenko, M.D., Ph.D., *Instructor*, received a Ph.D. in medical sciences from Kharkov Branch of N.D. Strazhesko Research and a M.D. from Kharkov Medical Institute in Ukraine. Dr. Khimenko completed a postdoctoral fellowship in physiology at the University of South Alabama.

RADIOLOGY

Angela M. Pence, M.D., *Assistant Professor*, received a B.S. in biology from Springhill College and a M.D. from the University of South Alabama. She completed her internship in internal medicine and residency in diagnostic radiology at USAMC.

SURGERY

Merry E. Sebelik, M.D., *Assistant Professor*, received a B.S. in biology from the University of Wisconsin and a M.D. from the Medical College of Wisconsin. She completed her residency in otolaryngology at the Medical College of Wisconsin and a head and neck surgical oncology fellowship at the University of Texas Systems Cancer Center in Houston.

STRUCTURAL AND CELLULAR BIOLOGY

Archil Shartava, Ph.D., *Assistant Professor*, received a M.S. in physics from the University of Tbilisi, USSR and a Ph.D. from the Institute of Biophysics, Puschino, USSR. He completed a postdoctoral fellowship in structural and cellular biology at the University of South Alabama.

Gan Wang, Ph.D., *Assistant Professor*, received a B.S. in microbiology from the University of Shandong and a Ph.D. in molecular genetics from the Shanghai Institute of Plant Physiology. Dr. Wang completed postdoctoral training in microbial genetics at the University of Connecticut and in molecular biology and gene therapy at Yale University.

Research:

*The process of going up
alleys to see if they're blind.*

Anonymous

23RD ANNUAL MEDICAL STUDENT RESEARCH DAY

Medical Student Research Day took place on Friday, August 16, 1996. A total of seventeen first and second year medical students participated in summer research projects with members of the basic science and clinical faculty. The culmination of the student's summer research occurred at the Annual Medical Student Research Day with presentations in either oral or poster format.

This year's keynote speaker was Dr. Michael Artman, Professor of Pediatrics, Physiology and Biophysics and Director of the Division of Pediatric Cardiology at New York University. Dr. Artman has received many awards for teaching of basic medical sciences and clinical medicine. His research has focused on biochemical and physiological mechanisms regulating cardiac development using experimental techniques that range from the molecular level to whole organ physiology. His lecture was entitled "The Vanishing Physician Scientist."

In special recognition of their summer research, the Clyde G. Huggins Medical Student Research Awards were presented to **Phillip Fortenberry** (best poster presentation), sponsored by Dr. Blaine Moore, Department of Pediatrics and **Steven Werdehoff** (best oral presentation), sponsored by Dr. Anne Hackman, Department of Pediatrics.

The summer research program is attended to help medical students acquire a better appreciation for biomedical research, and the scientific method.



Dr. Daniel Beals, (right) observes the research findings of Mr. Chris Cave (upper left), freshman medical student.

SOUTHmed SYSTEM IMPLEMENTED

The Biomedical Library has implemented the SOUTHmed electronic system and is available from terminals on Campus and the USAMC Biomedical Library, as well as any workstation connected to the Internet or the USA network. SOUTHmed network is a managed information system developed to assist health care professionals in accessing needed medical information.

The following are some benefits that SOUTHmed has to offer: full resources of the largest Biomedical Library in south Alabama, southern

Mississippi and northwest Florida; full MEDLINE and CINAHL databases online, as well as full text of fifteen medical journals (ie., Annals of Internal Medicine, JAMA, New England Journal of Medicine and more).

For further information on the SOUTHmed Network system or to obtain your own personal network account, contact the Biomedical Library, 460-6892.

CHERNOBYL'S GENETIC LEGACY

An accidental explosion of a nuclear reactor occurred 10 years ago along the easternmost reaches of Europe. That disaster in Chernobyl, raised grave concerns and questions which have persisted over the years and provided motivation for a recent workshop. "Chernobyl: Implications of a Decade" was held in Rio de Janeiro, August 24, 1996, in conjunction with the 9th International Congress of Human Genetics. The workshop was co-organized by **Wladimir Wertelecki, M.D.**, Chair of the Department of Medical Genetics, and **Carlos Salinas, M.D.**, Medical University of South Carolina, Charleston, SC.

This meeting brought together scientists involved in investigations of the effects of radiation and its relationship to birth defects and genetic mutations. Dr. J. Neel (University of Michigan Medical School), a world renown radiation geneticist who pioneered many studies of the Hiroshima-Nagasaki bomb survivors and their children, pointed out that "if we had to do such studies over again, the most obvious change in the research design would be to include studies at the DNA level from the outset". The workshop discussion culminated with a proposal by representatives from Lithuania, Belarus and Ukraine to circulate a position paper calling for greater participation by independent scientists interested in enhancing the teratologic and genetic understanding of the Chernobyl tragedy. A draft of the position paper will be finalized by Dr. Wertelecki for consideration by international experts. The draft proposes strategies to broaden collaborative approaches to ensure that the Chernobyl tragedy will translate into a greater understanding of its consequences as well as the prevention of future disasters of this type.

If you would like to submit an article for publication, please forward it to:

Karrye E. Jackson
College of Medicine
CSAB 170

or
FAX (334) 460-6073

The Class of **2000**

The class of 2000 began medical school on August 26th. To select the class, a total of 238 applicants were interviewed by the Admissions Committee, of which 232 were residents of Alabama. Of the candidates interviewed, 112 acceptances were advanced to fill a class of sixty-four. Nine students in this year's class enrolled through the Early Acceptance Program. The average GPA of matriculants was 3.63, the highest since the first class which matriculated in January 1973. Also, the average combined MCAT score was 29. The average age of this year's matriculating class is twenty-three, with 79% of students falling between the ages of 20-24. The class consists of 40 men and 24 women; 10 students are residents of rural counties and 7 are graduates of the BEAR program.

The Class of 2000 are graduates of 25 colleges and universities. The traditional disciplines of biology, chemistry and biomedical sciences account for 60% of the undergraduate majors of these students.

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