Infirmary launches institute to focus on AMD, diabetic retinopathy

THE MASSACHUSETTS EYE AND EAR INFIRMARY IS NOW ONE STEP CLOSER TO PREVENTING AND CURING TWO OF THE LEADING CAUSES OF BLINDNESS.

On September 13, the Infirmary formally launched the Retina Research Institute for Macular Degeneration and Diabetic Retinopathy (RRI) and celebrated the opening of a new angiogenesis laboratory.

The RRI was made possible through the generosity of many, including the late Anthony Eannelli; the Ralph and Marian Falk Medical Research Trust; the Massachusetts Lions Eye Research Fund, the Lions Clubs International Foundation and Lions of Multiple District 33; the Paul and Phyllis Fireman Charitable Foundation; and Roberta W. Siegel, supporting the research of Anthony P. Adamis, M.D.

The Retina Research Institute will focus its efforts on macular degeneration and diabetic retinopathy by creating a long-term, comprehensive research program to develop new treatments and preventative measures for these two leading causes of adult-onset blindness. The Institute hopes to accelerate the pace of discovery by recruiting as many as nine new retina experts to work with the Infirmary's highly respected team of physician-investigators. In addition, the Institute hopes to build and equip a second new laboratory. All of these efforts will require an additional $4 million in fund-raising efforts.

"The Retina Research Institute for Macular Degeneration and Diabetic Retinopathy will strengthen and expand the collaborations underway among Infirmary physicians and scientists in our quest to prevent and cure diseases of the retina," said Frederick A. Jakobiec, M.D., Chief of Ophthalmology at the Infirmary.

Age-related macular degeneration (AMD) and Diabetic Retinopathy share the same pathological mechanism — angiogenesis, which is overgrowth of new blood vessels. RRI physicians and scientists will seek new ways to halt angiogenesis, which could preserve the vision of millions of people. AMD, a disorder that slowly robs people of their central vision, currently affects 13 million people in the United States alone and is the leading cause of blindness in people over age 55. Diabetic retinopathy is a blinding eye disease that affects patients suffering from diabetes. Over 3 million people suffer from diabetic retinopathy, making it the leading cause of vision loss in Americans aged 25-55.

Infirmary physicians seeking a cure for these diseases include Evangelos S. Gragoudas, M.D., Anthony P. Adamis, M.D., Joan W. Miller, M.D., Donald J. D'Amico, M.D., Johanna M. Seddon, M.D., Jorge Arroyo, M.D., Ephraim Friedman, M.D., and Thaddeus P. Dryja, M.D.

For more information, visit the Infirmary's web site at www.meei.harvard.edu. If you would like to make a gift to support the RRI, please call the Development Office at (617) 573-3345.

John MacGilvray, President of Mass. Lions (left) and Chuck Kostro, Past Mass. Lions International Liaison celebrate the launching of the Retina Research Institute.

Roberta W. Siegel (left), Anthony P. Adamis, M.D., (center), and Curt Smith (right) cut the ribbon signifying the opening of the new angiogenesis laboratory.

Massachusetts Eye and Ear Infirmary

Infirmary NEWS

Infirmary Ranks High in Best Hospitals Survey

For the tenth consecutive year, the Massachusetts Eye and Ear was named one of America's Best Hospitals by *U.S. News & World Report*. The Infirmary was ranked third in the category of Ear, Nose and Throat and fourth in Eyes.

Knights Templar Grant

The Knights Templar Eye Foundation, Inc., recently awarded a $30,000 grant to Zac Pujic, Ph.D., of the Massachusetts Eye and Ear Infirmary, to help in the advancement of eye research. The grant was presented by Knights, S.K. Sutterley, Right Eminent, Grand Commander of the Knights Templar of Massachusetts and Rhode Island, and S.K. Wolf, Eminent Grand Generalissimo of the Knights Templar of Massachusetts and Rhode Island. Dr. Pujic is currently researching the relationship between genetics and the development of eye disease.

Pictured from left to right: S.K. Sutterly, Right Eminent, Grand Commander of the Knights Templar of Massachusetts and Rhode Island, Frederick Jakobiec, M.D., Chief of Ophthalmology, Zac Pujic, Ph.D., of the Massachusetts Eye and Ear Infirmary, and S.K. Wolf, Eminent Grand Generalissimo of the Knights Templar of Massachusetts and Rhode Island.

Mother Grateful for Doctor's Cure —

When Sabrina Coombs took her daughter, Savannah, to the pediatrician for a fever, she thought the 9-month-old was suffering from a cold. Instead, her visit to the doctor's office was the start of a long journey that lead to the diagnosis of an eye tumor and surgery that saved Savannah's life.

Shizuo Mukai, M.D., Pediatric Ophthalmologist at the Massachusetts Eye and Ear Infirmary, diagnosed Savannah with Retinoblastoma, a rare cancer of the eye. Dr. Mukai discussed Savannah's options with her parents and together they decided the best course of treatment was to remove the eye. Anxious and frightened for her daughter, Mrs. Coombs wasn't sure she was making the right decision.

"Once Dr. Mukai explained what Savannah would have to go through, and this was the best chance at saving her life, we didn't hesitate," she said.

Savannah endured a lengthy surgery and recovery and was later fitted for a prosthetic eye. She continues her recovery with exercises to strengthen the muscles around the prosthesis. "Without the knowledge and quick thinking of Dr. Mukai, Savannah could have died," said Mrs. Coombs. "Savannah is doing exceptionally well, and I am extremely grateful."

Savannah's younger sister, Ava, is also a patient of Dr. Mukai and is continuously checked for occurrence of ocular tumors. Almost half the cases of Retinoblastoma are hereditary and usually appear in children under the age of 5. For information on Retinoblastoma, please visit our web site at http://www.meei.harvard.edu.

With the love and support of her family and the help of many doctors and nurses at the Massachusetts Eye and Ear Infirmary, Savannah Coombs, (center) will be able to enjoy a happy childhood. She is pictured with her father Roy (left), her sister Ava and mother Sabrina (right).

Annual Meeting Planned

The Annual Meeting of the Medical Staff and the Corporation of the Foundation of the Massachusetts Eye and Ear Infirmary, Inc., will be held on Wednesday, December 6, 2000 at 4:30 p.m., in the Meltzer Auditorium, 3rd floor. Anthony P. Adamis, M.D., Associate Surgeon, Cornea Service will discuss "Shedding Light on Diabetic Retinopathy." Also presenting is Saumil Merchant, M.D., Associate Surgeon, Otolaryngology. Dr. Merchant's presentation will focus on "New Approaches in Middle Ear Disease," followed by a patient's perspective. To reserve a space, please contact the President's Office at (617) 573-3006.

Howe Scientists Work to Uncover Molecular Basis of Eye Disease

TUCKED AWAY ON THE FIFTH FLOOR OF THE MASSACHUSETTS EYE AND EAR INFIRMARY IS A POWERHOUSE OF RESEARCH, A TEAM OF 40 SCIENTISTS AND STAFF WORKING TOWARD A COMMON GOAL — UNDERSTANDING THE MOLECULAR BASIS OF EYE DISEASE.

The Infirmary's Howe Laboratory has attracted talented researchers from all over the world — Russia, Italy, China, Japan, Australia, Israel, Bulgaria, and the United States — to carry on the groundbreaking vision research that has been the focus of this world-renowned laboratory for almost 75 years.

The Howe Laboratory was founded in 1926 by New York ophthalmologist Lucien Howe, M.D. It merged with the Infirmary's Department of Ophthalmology soon after and trained most of the nation's ophthalmic research scientists from the 1940s through the 1970s. Today the lab consists of several small labs concentrating primarily on retinal degenerations, such as retinitis pigmentosa and macular degeneration, and glaucoma, especially as it affects the retina and the optic nerve. The retina is the layer of nerve cells that line the back of the eye and detect light. The underlying goal of the lab, however, is to better understand the functions of the eye and the organization and interactions of the cells which make up its component parts.

The work at Howe is enriched by the multidisciplinary makeup of its researchers. Biochemists, geneticists, cell biologists, neurobiologists, and physiologists all benefit from exposure to each other's work in the lab and frequent collaboration.

Understanding genetic defects in eyes

Meredithe L. Applebury, Ph.D., brings a unique blend of biochemistry and molecular biology to the work of the lab. She is one of the world's leading researchers in the molecular biology of macular degeneration and is well known for her innovative research techniques. Dr. Applebury and others have identified the defective gene that causes retinal degeneration in mice. Studies are now addressing how these genetic defects lead to cell death. She hopes that her painstaking studies of the mechanisms of cell death in various retinal degenerations will eventually make it possible for the medical community to perform genetic repairs.

For more than 20 years, Dr. Applebury has been investigating the eye's visual cascade, the process in which the eye's components detect light, produce an electrical signal, and then transmit the signal to the brain. Her laboratory has recently turned its attention to defining the molecular mechanisms by which cones give a signal. Cones are the light-sensitive cells that absorb bright light and distinguish color. Rods are responsible for vision under low light conditions. In her laboratory, signaling components, cloned from mammalian cones, are expressed in vitro. "We seek to characterize the molecular properties that distinguish cone signaling and adaptation from that of rods," she explains.

Biochemist Vadim Y. Arshavsky, Ph.D., is widely published and recognized in the scientific community for his research into the molecular mechanisms of visual signaling. Arshavsky, who is studying the control mechanisms of photoreceptor proteins, hopes to answer some of the questions surrounding visual signaling mechanisms.

"Each photoreceptor solves three difficult problems," he explains. "It has to be sensitive to light and amplify an electrical signal to the brain. It has to make the signal short so that the next image can appear without interference from the former image. And it has to be able to shift its operating range from being extraordinarily sensitive enough to see stars at night to adjusting to sunlight without being blinded. We are trying to figure out how the protein molecules inside the photoreceptor cell are accomplishing these three tasks. Genetic diseases which cause retinal deterioration, such as retinitis pigmentosa, affect all three tasks.

"The molecular machinery that regulates the way a photoreceptor adapts to light is incredibly complex," he adds. "If we can determine how the visual cascade is regulated and how it adapts to light, we might one day be able to biochemically bypass a defect at one stage of the cascade and compensate for it at another —kind of 'fool' the cells through broadly-applied gene therapy."

The work of Dr. Arshavsky's lab could also have a much broader application, because the signaling system of the eye is very similar to many other signaling systems in the body, such as the regulation of the heartbeat, the response to hormones and drugs on the brain, and the regulation of blood pressure. According to Arshavsky, 40 percent of drugs on the market today act through receptor molecules, which are of the same family as the rhodopsin molecules which respond to light in the eye.

The very promising research of physiologist Clint L. Makino, Ph.D., involves "listening" to the photoreceptor cell's electrical signals. "By recording the electrical signal, I can assess a photoreceptor's function and may be able to determine what defects cause cell death," he explains. "This may lead to our ability to slow the progression of disease or to correct defects.

"We are studying the earliest events of vision, the transformation of light into an electrical signal by the photoreceptors in the retina. Absorption of a single photon

Massachusetts Eye and Ear Infirmary

sets off a controlled, biochemical explosion within the cell. Thus, rods are extremely sensitive. Rods are also capable of adjusting their response as a function of the ambient lighting conditions. This enables them to continue to provide visual information over a wide range of light intensities."

It is now known that genetic mutations in the proteins involved in the visual process cause retinal diseases. Using electrophysiological methods, Dr. Makino is probing the molecular mechanisms underlying photoreceptor function. He is also beginning to understand how disease-causing defects in certain proteins impair that function.

Dr. Makino is the first, and possibly the only person in the world, who has recorded the electrical signal produced by an individual mammalian photoreceptor whose protein composition has been altered to mimic retinal degeneration.

Learning from the fruit fly eye

The laboratory of Francesca Pignoni, Ph.D., is studying the genetic control of early eye development with the help of the fruit fly Drosophila. "Just in the last decade, a remarkable level of similarity has been discovered between the development of eyes as different as the fly and the human," she points out. "Genes involved in the establishment of 'eye precursor cells' and in the formation of photoreceptor neurons in the fruit fly have been shown to play related roles in vertebrate organisms, such as the frog, fish and mouse. Moreover, some of these genes have been implicated in a number of human eye diseases such as aniridia, a disease caused by mutations in a central regulator of eye development.

"The discovery of this striking similarity has resulted in a dramatic shift in how we think about the different types of eyes found across the animal kingdom. Eyes that show little similarity in structure and morphology, in fact, share much of their development at the level of molecules, giving us effective new tools with which to study early eye development.

"In my lab, we take advantage of powerful genetic techniques available in an invertebrate model system, the fruit fly, to further our understanding of eye development in vertebrates, such as the frog Xenopus. A better understanding of eye development will uncover the role of developmental processes in the causation of genetic eye diseases."

Other principal investigators in the Howe Lab include Cynthia Grosskreutz, M.D., Ph.D., who works on glaucoma, and Shizuo Mukai, M.D., on retinoblastoma and uveal melanomas; and Jarema Malicki, Ph.D., who studies neuronal pattern and identity in the Zebrafish retina. The underlying goal of all of these determined scientists is to better understand the functions of the eye and the organization and interactions of the cells which make up its component parts. "We basically work under the assumption that if we know how the eye and its different cell types work normally, we can understand what happens in the disease process and then we can develop some strategy for a cure," Dr. Arshavsky says.

PRIVATE FUNDING GROWING IN IMPORTANCE

The gap between private and government funding is narrowing for the Howe Laboratory. Howe scientists will receive almost $700,000 in research support from private sources this year and approximately $1.2 million from the National Eye Institute, a branch of the National Institutes of Health.

Private funding comes primarily from a number of foundations, led by Research to Prevent Blindness, which awarded more than $275,000 to lab researchers, and the Ruth & Milton Steinbach Fund, which gave $100,000. Others include the Massachusetts Lions Eye Research Fund, Inc., which has supported the lab for more than three decades, Ronald McDonald House Charities, The Whitehall Foundation, The March of Dimes Birth Defects Foundation, The Knights Templar Eye Foundation Inc., and The Glaucoma Foundation.

Clint Makino, Ph.D., Howe Laboratory Investigator, focuses on understanding the molecular bases of ocular diseases.

Focus on Patients Makes William Montgomery a Giant in his Field

EVERY CHANCE HE GETS, WILLIAM MONTGOMERY, M.D., RENOWNED HEAD AND NECK SURGEON AND INVENTOR, TAKES UP HIS CARVING KNIFE AND WHITTLES AWAY AT A PIECE OF BUTTERWOOD OR MAPLE.

This pastime, learned as a young boy in Vermont, does more than "keep him sane," as he puts it. It has also played a remarkable role in a distinguished career of almost 50 years and the many contributions Dr. Montgomery has made to the field of otolaryngology.

Drafted into the Korean War shortly after medical school, Dr. Montgomery left his hometown general practice and served as a combat doctor until he was wounded in 1952. "In Korea I had only one book, *Foundations of Otolaryngology* by Boise, and some bones to fool around with," he recalls. "I read it a few times, carved on those bones, and treated many wounds of the head and neck. I found it really interesting." When he started his residency at the Massachusetts Eye and Ear Infirmary two weeks after returning from the war, he was one of a few young men throughout the country training in the new field of otolaryngology.

Over almost half a century, "Monty," as he is affectionately known at the Infirmary, has been a powerful force in reshaping this field with improved procedures and his many inventions, some initially carved by him out of blocks of wood. He has treated kings and queens and the rich and famous. He has traveled the world to share his prodigious knowledge and has taught his specialty to more residents than anyone in the history of Harvard Medical School. Yet, what most pleases this unassuming genius is knowing, at the end of a 10-hour day, that he has helped ordinary people breathe easier, speak better, and enjoy a better quality of life.

Grateful patients include an 80-year-old former champion swimmer who regained his voice and breathing when Dr. Montgomery implanted in him the "T-tube" he had invented. This eliminated the need for the man's tracheotomy tube and allowed him to return to the pool. (See related story on this page.) Using a prosthesis he developed called a keel, he restored the speech and breathing of a 17-year-old accident victim whose airway had been reduced to the size of a pin. He used one of his newest inventions, a thyroplasty implant, to give a middle-aged man with a paralyzed vocal cord normal speech and swallowing for the first time in his adult life. For a more precise fit and better outcome, Dr. Montgomery designed the thyroplasty prosthesis in five sizes for men and five for women-each originally carved by him out of maple wood to provide a prototype for the manufacturer.

A simple man with solid "Yankee" values, Dr. Montgomery has spent his entire career looking for simpler, better ways to treat ear, nose and throat problems. He has been extraordinarily successful. He developed most of his devices and procedures, now standard practice in otolaryngology, in response to the needs of individual patients.

"From the beginning of his career, if he couldn't remedy a patient's situation with available technology," observes Mark Varvares, M.D., Infirmary head and neck surgeon, "he would design prostheses and surgeries to surmount the problem. I don't know many people in medicine with that ability."

Grateful Patient Created First Otolaryngology Chair for Montgomery

In 1992, Infirmary head and neck surgeon William Montgomery gave 80-year-old Philadelphia businessman and philanthropist John W. Merriam his voice back. A grateful Mr. Merriam responded with one of the final and most personal gifts of his life. He established the first fully funded professorship in otolaryngology at the Harvard Medical School with a gift of $2.2 million.

Income from the Merriam Professorship in Otolaryngology supports Dr. Montgomery in his work as the first Merriam Professor and will make possible the work of future generations of Infirmary otolaryngologists who succeed Dr. Montgomery to the chair. It is known as the Merriam-Montgomery Professorship.

Mr. Merriam's vocal cords, or larynx, had been paralyzed as a result of an emergency intubation following surgery in 1989. Laryngeal paralysis occurs in only about 1 percent of intubated patients. He lost his voice and airway and was dependent upon a tracheotomy tube to breathe. "His wife Betty was calling all around looking for help for him," Dr. Montgomery recalls. "I told her to bring him up to Boston and I'd take a crack at him. He went home with a voice and no trach tube."

Infirmary colleagues say it is very fitting that this new professorship will bear the names of doctor and patient in perpetuity. Both accomplished great things in an unobtrusive way.

Indeed, as a young surgeon barely out of training, Dr. Montgomery attacked the problem of chronic frontal sinus, a condition that was very difficult to treat. He perfected the osteoplastic front sinusotomy through laboratory experiments and popularized it throughout the United States. It was the only effective treatment for the next 30 years. In the early 1960s, he pioneered the use of fat following acoustic neuroma surgery to prevent the serious problem of spinal fluid leaks.

A major contributor to airway reconstruction, he invented a laryngeal stent and the Montgomery tracheal cannula for patients with sleep apnea (interrupted breathing), a simple but very effective replacement for the traditional tracheotomy tube. His salivary bypass tube is used to repair a damaged esophagus. According to colleagues, the operation he developed to restore a patient's voice after a total laryngectomy is so effective that patients have been known to sing, whistle, and even play the trumpet after the surgery.

Problem solving is never far from Dr. Montgomery's mind. He figured out how to design a valve for his tracheal cannula while driving to his vacation house in Vermont. He stopped at a machinist's shop on the way to ask him to make one for him.

Now working three days a week at the Infirmary and concentrating the rest of the week on research, Dr. Montgomery is currently developing a new device to restore speech after a laryngectomy and another for the treatment of chronic aspiration.

"Forty to fifty thousand people die in the United States every year from chronic aspiration due to the loss of motor and/or sensory use of the larynx from stroke," Dr. Montgomery explains. "They don't die easily, suffering repeated pneumonia, and it costs $3 billion to take care of them. To overcome this problem, we've tried closing the larynx and diverting the larynx. Now, I'm working with Dr. Varvares on a device to be implanted in the larynx that has a one-way valve system to allow speech. It could also be used for people with Multiple Sclerosis, ALS, or brain tumors. We always try to be the least invasive," he points out. "It's the best approach."

"Monty has been a mentor for doctors in training at the Infirmary spanning five decades," Dr. Varvares points out. "You go to meetings with him and people just flock to him. After all, he has trained five decades of otolaryngologists, many of whom are now chairmen at the top training institutions in the United States, including the Infirmary. He has been a major force in transforming our specialty from one that took out tonsils and packed noses to one that now does sophisticated head and neck surgery. And, besides being a talented inventor, surgeon and clinician, he is a great friend to his patients and colleagues. We're lucky to have him."

Dr. Montgomery sums it up in his usual simple way: "What's important is what you can accomplish in life and do for people."

William Montgomery, M.D., teaches a resident his technique for inserting a thyroplasty implant to restore speech and breathing to a patient.

William Montgomery, M.D., pictured right, is a man of many talents. One of these talents is wood-carving, which enabled him to design the thyroplasty prosthesis.

contact

is produced by the Office of Development and Public Affairs,
(617) 573-3340.
http://www.meei.harvard.edu

F. Curtis Smith, President
Bruce C. Jordan, Vice President for Development and Public Affairs

Mary E. Leach, Editor
Michele A. Prendergast, Mary Pat Prado, Contributing Writers
Eric Antonio, Public Affairs Staff, Photography
rhumba, Design

Pictured (left to right) are Chuck E. Kostro, Carl Munroe, Jesse Dowd, Nicolas Sabatello, Ed Ciampa and John MacGilvray.

LIONS ATTACK BLINDNESS THROUGH RESEARCH FUNDING

Carl and Cindy Munroe are a couple with a cause: they have spent the last 12 years, working 300 nights a year, raising money to cure blindness. The Munroes, along with thousands of Lions Clubs members from throughout the Commonwealth and around the world, raise money one pancake breakfast and penny drive at a time. The proceeds of these efforts — $1 million dollars in just one year, the largest in Mass. Lions history — enable the group to support research efforts at the Massachusetts Eye and Ear Infirmary.

"Every person can make a difference," said Carl Munroe, Mass. Lions Eye Research Fund Past President. "It may take a lot of fund-raisers, but we Lions are determined to do our part to help make blindness a disease of the past." The Massachusetts Lions Eye Research Fund, Inc., and the Lions Clubs International Foundation recently awarded grants totaling $310,000 to the Infirmary to support ophthalmology research (see related story page 2).

Members of the Massachusetts Lions Clubs who were responsible for championing the grants were Jesse R. Dowd, Charles E. Kostro, John MacGilvray (current Mass. Lions President), Mr. Munroe and Nicholas Sabatello. These grants bring the total of funds donated to the Infirmary by Lions Clubs through the years to more than $3.6 million.

"The Department of Ophthalmology and I are deeply grateful to the Lions for their partnership in raising awareness and funding to combat blinding disease," said Frederick A. Jakobiec, M.D., Infirmary Chief of Ophthalmology. "Their support has enabled us to 'seed' innovative approaches to research that will undoubtedly lead to new methods of prevention and treatment."

Founded in 1917, the Lions Clubs are active in 185 countries worldwide. In 1925, at the urging of Helen Keller, the Lions adopted the fight against blindness as a primary focus of their efforts.

Massachusetts Eye and Ear Infirmary

243 Charles Street
Boston, Massachusetts 02114-3096
www.meei.harvard.edu

Non profit Org.
U.S. Postage
P A I D
Boston MA
Permit No. 51711

inside…