John R. Oishei Foundation Support

In fall 2004, the University at Buffalo received a number of generous grants from the John R. Oishei Foundation. The following are descriptions of several of the clinical and biomedical research programs these grants support.

The John R. Oishei Foundation is committed to enhancing the quality of life for Buffalo-area residents by supporting education, health care, scientific research, and the cultural, social, civic and other charitable needs of the community. The foundation was established in 1940 by John R. Oishei, founder of Trico Products, one of the world's leading manufacturers of windshield wiper systems.

Nanomedicine and "Nanoclinics"

THE NANOMEDICINE PROGRAM of the University at Buffalo's Institute for Lasers, Photonics and Biophotonics has received a $925,000 grant from the John R. Oishei Foundation.

The funding will allow the institute to extend the impact of its discoveries and developments in nanomedicine and nanobiotechnology—fields concerned with developing new diagnostic devices and therapies on the scale of one-billionth of a meter—and to advance them to the clinical stage.

The Institute for Lasers, Photonics and Biophotonics has a broad, multidisciplinary emphasis, linking researchers in UB's College of Arts and Sciences, School of Medicine and Biomedical Sciences, and School of Engineering and Applied Sciences. "To our knowledge, ours is the only program in the world that connects academic units in the sciences, medicine and engineering to achieve the integration of materials, lasers, nanotechnology and biomedical research that nanomedical research requires," says Paras Prasad, PhD, executive director of the institute and SUNY Distinguished Professor in the Department of Chemistry in the UB College of Arts and Sciences.

Nanomedical advances developed by the institute include new, minimally invasive diagnostic methods, targeted delivery systems for drugs and genes, new methods of boosting photodynamic cancer therapy, new modes of medical imaging and ways to monitor drug effects in real-time.

A key focus for the institute lies in expanding testing and applications for its unique, patented nanoparticles, a multiple-use, silica nanoshell, dubbed the "nanoclinic," that can be constructed and used in different ways to treat human disease.

"While other groups are focusing on using nanoparticles to carry a payload inside," explains Prasad, "our group is exploring and exploiting all aspects of nanoparticles—not just their ability to carry drugs or genes, for example, but also attaching to their surfaces treatments or probes and developing porous nanoparticles, which allow for diffusion of substances in and out."

The institute has filed for, and in some instances received, patents for a broad range of applications, including:

- Porous nanoparticles that allow for more effective biodistribution of drugs that otherwise aggregate in body fluids to cause problems
- Bioadhesive nanoparticles that serve as ocular drug-delivery vehicles, overcoming the extensive drug loss that occurs with water-soluble ophthalmic medicines
- Magnetic nanoparticles that selectively rupture membranes of cancer cells when activated, potentially allowing cancer patients to receive treatments through ordinary magnetic resonance imaging procedures in their doctors' offices.

Also under development at the institute are nanoparticles that function as carriers for diagnostic-imaging agents that enhance MRI scans, X-rays and other diagnostic-imaging techniques and gene therapy vectors that carry none of the immunogenic problems of viral vectors.

The institute's researchers have formed strong collaborations with those at other institutions, including Roswell Park Cancer Institute and Kaleida Health System.

—Ellen Goldbaum

Medicinal Tarantula Venom

Frederick Sachs, PhD, and his colleagues in the UB Center for Single Molecule Biophysics have received a $900,000 grant from the John R. Oishei Foundation to further their research on a peptide they have isolated from tarantula venom that shows promise as a therapy for muscular dystrophy, cardiac arrhythmias and urinary incontinence.

The researchers discovered the peptide, purified it and changed its structure to its mirror image to prevent it from being destroyed by stomach enzymes or the immune system. Their most recent research results were published in July in the journal *Nature* (see the autumn 2004 issue of *Buffalo Physician* for a description of this study). Earlier findings were published in *Nature* and the *Journal of General Physiology*. With the aid of the Oishei grant they now will study ways to turn the peptide into treatments for specific disorders.

"These funds will help us identify the key components of the peptide's molecular structure and learn how it works to block mechanical transduction in cells," says Sachs, a professor of biophysics and lead researcher on the work. "We expect the results will accelerate the path leading to clinical applications."

Co-investigators Tom Suchyna, PhD, research associate, and Philip Gottlieb, PhD, associate professor of physiology and biophysics, play pivotal roles in the research.

Thomas E. Baker, president of the John R. Oishei Foundation, says Sachs' work advances the foundation's interest in supporting translational research for common illnesses.

"We believe the best role we can play is to move excellent, promising new approaches from the lab to the clinic," he says. "We also believe we can provide the boost of extra time that researchers like Dr. Sachs need to establish a case for new support from the federal level."

In addition to the Oishei Foundation, Sachs' laboratory has been funded by the National Institutes of Health, the United States Army Research Office and NPS Pharmaceuticals.

To learn more about Sach's work with tarantula venom, visit the UB News Services Web site at http://www.buffalo.edu/news/ and search "tarantula."

—Lois Baker

A Special Scientific Meeting

Elizabeth and Fred compare notes

Little Miss Muffett wouldn't set foot in Fred Sachs' laboratory. He keeps tarantulas there. Little Miss Elizabeth Mulé, however, finds the lab close to perfect. The 10-year-old from New Orleans raises tarantulas as a hobby—she currently has 60 of the rather large arachnids and has an avid interest in science. Sachs and colleagues at UB's Center for Single Cell Biophysics have discovered a peptide in the venom of the Chilian Rose tarantula that shows promise as a treatment for several chronic diseases (see article, above).

Sachs and Elizabeth struck up a long-distance friendship when the girl learned of his research while searching the Internet for treatments for her father's congestive heart failure, one of the conditions thought to respond to the peptide's action.

When Sachs received $900,000 from the Oishei Foundation to advance his findings from the lab to the clinic, he invited Elizabeth and her mother to come to Buffalo for the press conference announcing the grant and to learn more about the lab's research.

Elizabeth already is a media star. She has appeared with Oprah, Jay Leno and Ellen Degeneris. But meeting Sachs and his coinvestigators was different.

"Elizabeth can hold her own with Leno or Oprah any day," says Susan, her mother. "But she was nervous about coming to UB. These scientists are her heroes."

—Lois Baker

Photo: Jenny Luk

Ross Eye Institute

In support of improved eye care in Western New York, the John R. Oishei Foundation has made a $1.2 million gift to the University at Buffalo School of Medicine and Biomedical Sciences, helping it move closer to a challenge grant issued for the Ira G. Ross Eye Institute.

The institute is named in honor of the late husband of Elizabeth Pierce Olmsted Ross, a 1939 graduate of the UB medical school. Planned as a center for teaching and research, clinical care and community service, it will consist of a free-standing complex at 1176 Main Street, next to the Elizabeth Pierce Olmsted, M.D., Center for the Visually Impaired, and research facilities on the UB South (Main Street) Campus.

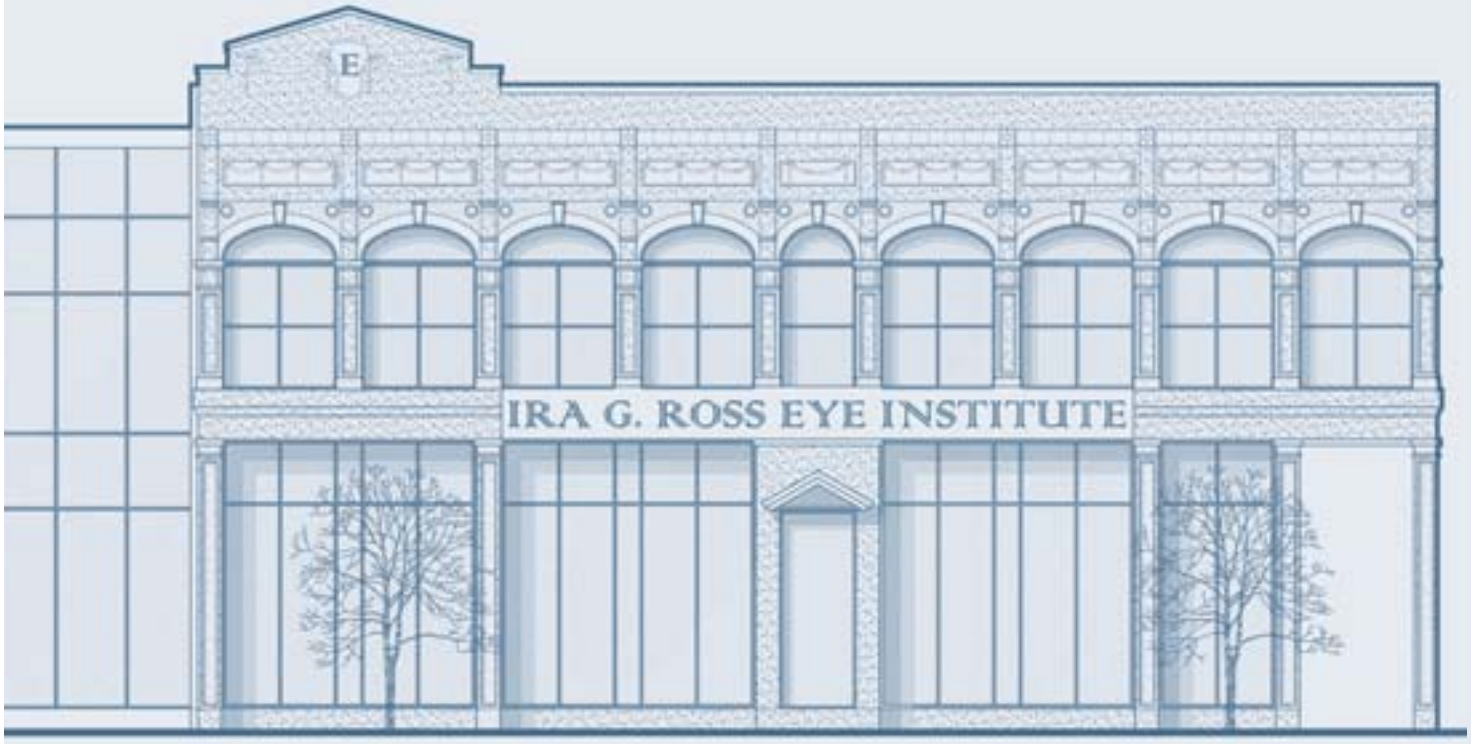
UB's Department of Ophthalmology has designed the institute as a collaborative enterprise with the Olmsted Center. Last November, Olmsted Ross issued a $3 million challenge grant to the institute.

The $1.2 million response from the Oishei Foundation helps make it possible to bring expert physician scientists to join the Ross Eye Institute staff. Two faculty members already on board are ocular pathologist Federico Gonzalez-Fernandez, MD PhD, and Jack Sullivan, MD, PhD, who specializes in retinal physiology and disease (see opposite page for more information on Dr. Sullivan).

The institute's site on Main Street, within the Buffalo Niagara Medical Campus, will be the primary teaching facility for the residency program in the Department of Ophthalmology, as well as for the school's medical students. Together with the Olmsted Center, the Main Street space will provide clinical care to area residents, as well as community education to patients, practicing physicians and other health-care professionals.

Faculty in the Department of Ophthalmology also will conduct research in UB medical school facilities on the UB South (Main Street) Campus and in research laboratories at the VA Medical Center.

—Mary Cochrane



Hereditary Retinal and Macular Degenerations

A research focus for Jack Sullivan, MD, PhD

Jack M. Sullivan, MD, PhD, has joined the UB faculty as associate professor of ophthalmology, pharmacology & toxicology and neuroscience, and as director of the Laboratory of Hereditary Retinal and Macular Degenerations in the Department of Ophthalmology. The laboratory is located in the Veteran Affairs (VA) Western New York Healthcare System, where Sullivan is a staff physician-scientist.

Sullivan also serves on the faculty of the emerging Ira G. Ross Eye Institute, an alliance between the UB Department of Ophthalmology and the Elizabeth Olmsted Ross M.D. Center for Visually Impaired (see related article on opposite page).

"This alliance is unique and offers a preexisting bridge between the realms of academic ophthalmology and training and job placement for those suffering from visual disability," says Sullivan.

"For a clinician-scientist dedicated to the field of retinal and macular degenerations it creates unexpected and unprecedented opportunities for translational ophthalmological medicine. On the one hand, in the Olmsted Center we have a rich community and national resource for those who are visually impaired from retinal and macular degeneration whom I see in my clinic, and, on the other hand, at UB we have an emerging group of clinicians and scientists who share a common interest in deciphering the mechanisms of retinal and macular degenerations and in developing therapies."

Sullivan earned a bachelor of arts degree in microbiology at Rutgers University in 1979 and completed dual training in medicine and biophysics & physiology to receive his MD, PhD degrees at the Mount Sinai School of Medicine in 1987. A component of his scientific training was in visual physiology, a strong interest that has shaped his career development. After a transitional internship in 1991, he entered residency training in ophthalmology at Washington University School of Medicine in St. Louis, during which he maintained the clinician-scientist career track, serving an additional year there in a clinical/research fellowship in ophthalmology and neurobiology.

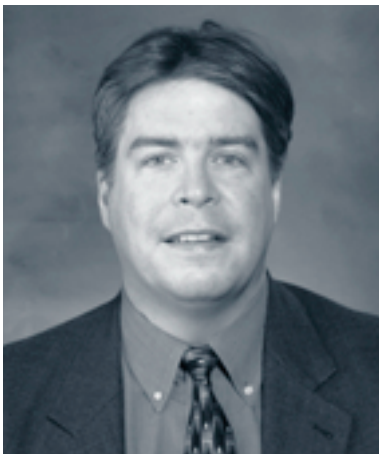
Sullivan was one of three physician scientists in the United States selected for a Research/Clinical Career Development Award by the Foundation Fighting Blindness, a private foundation whose core mission is the understanding and treatment of retinal and macular degenerations. In 1992 he matriculated under this award to the Department of Ophthalmology at the University of Michigan to train with Paul A. Sieving MD PhD, an expert in this discipline and now director of the National Eye Institute. Sullivan began the early development of his current research programs in mechanisms and therapies of retinal degenerations at the Kellogg Eye Center at the University of Michigan and completed his Hereditary Retinal and Macular Degeneration fellowship there in 1994.

Prior to coming to UB, Sullivan served as assistant professor of ophthalmology and neuroscience & physiology at SUNY Upstate Medical University in Syracuse, New York. At Upstate he focused on research program development, one of which has achieved international recognition, and on teaching and service.

At UB and the VA Western New York Medical Center Sullivan's laboratory focuses on understanding the molecular and biophysical mechanisms of hereditary and metabolic retinal and macular degenerations and on developing novel gene therapies for such diseases. He is currently funded by the National Eye Institute and by a recent Interdisciplinary Research and Creative Activities Fund (IRCAF) award from UB. He also has initiated a new Retinal Degeneration Service at the Buffalo VA and hopes to build this resource into a National Center of Excellence and the first of its kind in the VA system.

"Our plan is to build a first-rate clinical diagnostic and, eventually, therapeutic service in retinal and macular degenerations and to consolidate these resources for access by both veterans and non-veterans alike," says Sullivan.

"On the scientific side," he continues, "our long-term goal is to understand, measure and model retinal degenerative disease processes, to use this information to develop and test candidate therapeutics, and, ultimately, to translate therapies for human retinal disease back into the clinic for patients and their families who wait each day with hope."



Jack M. Sullivan, MD, PhD

Sullivan's current research includes working to understand the impact of mutations in human retinal and macular degeneration genes on the structure and function of the proteins that these genes specify.

"In the case of the rhodopsin protein there are over a hundred mutations in that gene alone that cause retinal degeneration," he explains, "and, in most cases, we do not yet fully understand the mechanism of disease at the cellular level."

Currently, Sullivan is collaborating with Thomas Furlani, associate director of the UB Center for Computational Research, to apply advanced computational tools to the study of the structure and function of rhodopsin and related proteins.

His group is also working to develop ribozyme and siRNA gene-based therapies for retinal and macular degenerations.

"Ribozymes and siRNA are advanced molecular tools that give us an opportunity to selectively downregulate the expression

"I see an unprecedented opportunity at this university not only to develop new technologies and therapies to aid the visually disabled, but also to translate them back to the patients."

of genes that are known or suspected to be involved in retinal and macular degenerations," he explains. "By selectively downregulating genes that play a role in retinal and macular degenerations we expect to slow or stop the degenerative process."

In a collaboration with Paras Prasad, PhD, executive director of the UB Center for Lasers, Photonics and Biophotonics and SUNY Distinguished Professor in the Departments of Chemistry and Physics in UB's College of Arts and Sciences, Sullivan's group is working to develop more refined tools in the diagnosis and treatment of pathological angiogenesis in the retina and choroid.

"Photodynamic therapy [PDT] has demonstrated promise for retinal angiogenic disease," notes Sullivan, "but there are several distinct limitations that impede highly efficacious and stable clinical outcomes. We are working to both understand the biophysical limitations of PDT and to circumvent them."

"At UB, there is a rich environment of ideas and technologies under development across a range of disciplines in both basic science and clinical departments," says Sullivan. "The challenge, I feel, is to be fully aware of these technologies and to discover how to bring to the table for collaboration all of those who can contribute to technological and medical developments in diagnosis and therapy.

"I see an unprecedented opportunity at this university not only to develop new technologies and therapies to aid the visually disabled, but also to translate them back to the patients. Remarkably, this can all be done in our own backyard; the resources are already in place."

—S. A. Unger