Dr. Michael G. Malkowski, Hauptman-Woodward senior research scientist, has received a $6.5 million grant from the National Institutes of Health in support of his work to establish the Membrane Protein Structural Biology Consortium (mpsbc.org) as one of nine centers in the United States responsible for determining membrane protein structures within a larger NIH biology-based initiative.

Why is this important?
The grant entitled Multi-Level Optimization of Membrane Proteins was awarded as part of the NIH National Institute of General Medical Sciences Protein Structure Initiative (PSI). The PSI now begins its third five-year phase, PSI:Biology.

Each cell in the human body is surrounded by a kind of ultrathin skin called a cell membrane, which isolates the inside of the cell from its surroundings. This membrane is punctuated by protein molecules, some of which mediate the passage of important molecules—such as nutrients or wastes—into and out of the cell, and others of which transmit signals of various kinds. Membrane proteins are key to many life processes.

The MPSBC combines the diverse expertise of three investigators: Malkowski, Dr. Mark Dumont, associate professor in the Department of Biochemistry and Biophysics at the University of Rochester School of Medicine and Dentistry in Rochester, New York, and Dr. Michael Wiener, associate professor in the Department of Molecular Physiology and Biological Physics at the University of Virginia in Charlottesville, Virginia.

Malkowski, who in addition to his HWI post is also an assistant professor at the University at Buffalo, said: “I am pleased and excited to be working with my colleagues in Rochester and Virginia to tackle the technical challenges associated with determining the structures of membrane proteins. We have assembled a strong team. Each of us brings unique experiences and expertise to the problem that together, will provide us with a strong knowledge base to meet these challenges head on.”

What will the Center do?
The Center will focus on central problems associated with membrane protein structural biology, with the emphasis on overcoming the technical barriers, using improved technologies to solve structures, and disseminating these improvements to the biological and structural biological communities. The involvement of the three different laboratories also brings together a range of pre-existing facilities and personnel, ongoing structural projects, ties to collaborators working on important targets, and existing infrastructures for interacting with the broader scientific community.

Membrane proteins play critical roles in the physiology of humans and other organisms. However, little is known about their three-dimensional molecular structures. This project is designed both to solve structures of medically important membrane proteins and to improve the available technologies for solving such structures. Knowledge of protein structure is crucial for understanding the functions of proteins and designing drugs that modify their functions.

Malkowski’s research is focused on solving those structures and improving the technologies to lead to an understanding of why and how these biological processes in the human body...
Artists’ Open Studios

Holiday Season A Success

Hauptman-Woodward hosted, for a third time, in December the 2010 Artists in Buffalo’s Holiday Open Studios. This year’s event, showcased more than 20 local artists who generously donated twenty percent of their sales to support the life-altering research being done at the Institute.

“We were so pleased to be involved in the event again this year, it’s always exciting to see the turnout and new faces at the Gallery Walk,” Event Chair Julia Duas-Skop said.

Some notable artists who participated were: Julia Duas-Skop: Antinomy Designs sculptural torch-worked glass jewelry; Temi Kucinski - T.E.K. Gemstones: handcrafted jewelry and Missy Crowell and Carolyn Clark - Roostertail2: hand-fabricated sterling silver and ceramic jewelry.

In addition to the artist’s exhibition, the weekend opened with a cocktail reception sponsored by Duncan Ross of Arrowhead Spring Vineyards and closed with a silent and basket auction organized by Beth Marks and Holly Tiflckick. All of the funds raised will support the ongoing research at Hauptman Woodward.

Crystal Leader Maximilian Riedel

Comes to Buffalo to Support HWI Research

Is it possible the shape of a glass can actually make wine taste better? A little more than a decade ago, that notion would have been scoffed at, even by winemakers and connoisseurs. Yet, Maximilian Riedel, CEO of Riedel Crystal of North America and 11th generation glassmaker, led more than 400 supporters of the Institute on November 5, 2010 at Salvatore’s Italian Gardens on a journey. This journey proved just that, exactly what a difference a glass can make.

Hauptman-Woodward was honored to have Jesse and Emily C. Doren and David and Hallie Schneeweiss co-chairs of the 2010 Riedel Wine Glass Tasting Experience. “We are so grateful to our chairs who worked very hard to make Riedel a success,” Tricia Furnari, development director, said. “We hope all of the attendees and sponsors who invested their time and resources had a wonderful experience and that they plan to attend and bring friends to our next Riedel event in May of 2012.”

If you missed Riedel, but would like to start or add to your Riedel glass collection or just need a great gift, you can purchase a pair of Riedel Vitis champagne flutes for $50 per pair (suggested retail of $85) by calling Jill Szczesek at 898-8597.

Proceeds from the glass sales help support HWI!
Kinex Pharmaceuticals is now leasing lab and office space at the Hauptman-Woodward Institute. Kinex will occupy the lab space at the New York State Center of Excellence in Bioinformatics and Life Sciences. The one-year lease at HWI began in January of this year.

Founded in 2004, Kinex has developed a pipeline of drug candidates using its proprietary platform technologies for drug discovery. Hemitoc™ and Opal™ are two drug candidates, KX01, is being evaluated in a Phase 2 clinical study for castration-resistant prostate cancer. Other Phase 2 studies will be launched in 2011 and will target acute myeloid leukemia (AML), ovarian cancer, and triple-negative breast cancer. Another drug candidate, KX02, targets brain tumors and is at the IND preparation stage. The pre-clinical pipeline is aimed at immunomodulatory therapies to treat diseases such as rheumatoid arthritis, inflammatory bowel disease, and multiple sclerosis.

Their business model is to develop compounds to Phase 2 proof of concept and then to partner with pharmaceutical companies for later stage trials and commercialization. More than $20 million in investment capital and $2 million in grant finding has been secured to date. Efforts to secure $25–30 million to fund clinical development of its lead compounds is underway.

Nobel Prizes are awarded annually in recognition of cultural and scientific advances with international magnitude. Prizes are awarded in the fields of Physics, Chemistry, Physiology/Medicine, Literature, and Peace. Twenty-five years ago, in 1985, Dr. Herbert A. Hauptman received jointly with Dr. Jerome Karle this prestigious prize in the field of Chemistry.

Dr. Hauptman and Karle were awarded the Prize for their achievements in the development of direct methods for the determination of crystal structure outputs from X-ray diffraction data. Even through today, the impact of Hauptman’s mathematical methods changed the field of chemistry and continues to open new areas of research.

Dr. Hauptman interestingly is one of 160 Jewish Nobel Laureates. Nobel laureates of Jewish heritage make up roughly twenty percent of all Nobel Prize winners since 1901. In honor of this distinction, there is a bouquet dedicated to Jewish Nobel Laureates in a town called Kiryat Hatanat Pras Nobel (Nobel Prize Laureates’ Town) outside of Tel Aviv, Israel. On this bouquet, a monument and plaque have been dedicated in Dr. Hauptman’s honor.

The red and blue rubbing of Dr. Hauptman’s plaque as displayed above, was done by his friend and colleague Harvey Breverman. Breverman, an artist and graduate of Carnegie Mellon University, has exhibited in cities all over the world including New York, London, and the Israel Museum, Jerusalem. Today, a print of this rubbing is displayed at the Institute.

Dr. Hauptman has a long and distinguished career as a mathematician and is author of more than 170 different publications. He received his bachelor’s degree from City College of New York in 1937, his master’s degree from Columbia University in 1939 and his doctoral degree from the University of Maryland, College Park in 1945. In 1970, he joined the crystallographic group of the Medical Foundation of Buffalo (since renamed the Hauptman-Woodward Medical Research Foundation) and in 1982, he became its Research Director. He has held academic positions at the State University of New York at Buffalo in the Computer Science and Engineering and the Structural Biology departments, as well as the position of President of Hauptman-Woodward.

Dr. Walter Pangborn, HWI Executive Vice President, feels that “the presence of Kinex at HWI presents a valuable opportunity for both organizations to work together. A major advantage of having Kinex at HWI is that it will allow the possibility for both organizations to collaborate on projects which can be applied to other critical areas of research.”

“We are very pleased to be sharing space with friends and colleagues at HWI. These are first-rate facilities with world-class researchers. We expect that the collaboration between HWI and Kinex will be synergistic because each organization has its unique knowledge base and experience”, said Dr. Lyn Dyster, co-founder and vice president of research operations for Kinex Pharmaceuticals.

Dr. Lyn Dyster, Executive Vice President, Kinex Pharmaceuticals

Dr. Walter Pangborn, Executive Vice President, Hauptman-Woodward Institute

The second annual Pioneers of Science event is scheduled for Thursday, October 27, 2011. The educational, daytime portion of the program allows local students to attend presentations by the awardees and will be held at the recently renovated school located on the Buffalo Zoo property. The evening program will be held at Salvatore’s Italian Gardens and will include a formal dinner and awards presentation. Larry and Margaret Whittier have kindly agreed to chair this event for the Institute. Further information about this event, or other upcoming educational programs can be obtained from Dr. Jane Griffin at (716) 898-8618.

Nobel Prize Laureate Boulevard
Rishan LeZion Small Town Outside of Tel Aviv

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ten Museum, the Whitney Museum, the Jewish Museum, the Library of Congress, Washington, D.C., the British Museum, London, and the Israel Museum, Jerusalem. Today, a print of this rubbing is displayed at the Institute.

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Dr. Wayne Schultz, Senior Research Scientist
Scouting, Woodworking and Camping Round out a Life in Science

Where are you from?
Schultz: I am originally from Painesville, Ohio.

Where did you receive your education?
Schultz: I received my undergraduate degree in Chemistry from the College of Wooster in 1990. I then went on to Cornell University for my Ph.D., followed by post-doctoral research at the University of Wisconsin-Madison.

How long have you been at HWI?
Schultz: I started at HWI in August of 1998.

What inspired you to pursue a career in chemistry?
Schultz: I can remember having an interest in science from an early age. When I was younger my friends and I would play around with mail order science kits. My high school chemistry teacher had an impact on my career path. She was a bright and exciting woman that seemed like she always knew everything. The way that she impressed me with her intelligence is something that I think guided me toward my profession as a scientist.

What would you say is the most challenging aspect of being a scientist in the United States?
Schultz: For scientists, it can often be challenging to obtain the appropriate funding for our research. There are different areas of research that scientists are interested in, but may not always be able to pursue due to lack of funding. Only through significant increases in government funding for science can we continue to be successful.

If you had the chance to go back and change anything about your career, would you?
Schultz: Early in my career I would have benefited from having a mentor. My only other regret would be that I did not pay better attention during math classes. I can honestly say there is not much else that I would change about my career. HWI is a great place to be and I could not ask for a better group of colleagues to work with. My career allows me to collaborate with talented individuals and provides me with the opportunity to pursue unique areas of research.

What are your interests outside of your professional work?
Schultz: When I am not working I enjoy spending personal time with my wife and three sons. My sons are all Boy Scouts so I help them with events and projects related to scouting whenever I can. I do enjoy golfing, although I think some additional practice would help. Camping and woodwork are a few other activities that I enjoy.

As the father of three boys, would you encourage any of your sons to pursue a career in science?
Schultz: To be a scientist, you have to be curious about the world and have the desire to ask questions. My sons are at the curious age where they ask a lot more questions and they all do well in math so a career in science is a possibility. I would definitely support the decision to pursue an education and a career in the field of science if that is what they decide to do.

What type of projects are you currently working on?
Schultz: I am currently working on a project involving the study of how viruses are transmitted from animals to humans. My research is focused on the non-structural proteins that combine to form a replication complex that is the central engine driving viral reproduction. Through the identification of common pathways that viruses use to infect humans, we are working to develop methods that will interrupt the same pathways used for infection. I am also working on a separate project that involves discovering new antibiotic targets in multidrug-resistant bacteria.

What are your plans for the future?
Schultz: Right now I love what I am doing and still have a strong passion for my work. The overall goal of our research is to develop a method to successfully identify and characterize protein interactions so that we can better treat infections. I hope our research will eventually progress toward applied research for new drug development.

Structures:
- Schultz:

Roopa Thapar, Ph.D., is not only one of HWI’s newest research scientists, but also an ambassador for the Institute and her science. Thapar who received her doctoral degree in Biochemistry from the University of Washington in Seattle, Washington, has focused her research on structure and dynamics of RNA-Protein Interactions that control gene expression. She has been sharing information about her lab’s work throughout the world.

In October 2010, Thapar traveled to Montreal, Canada, for the 4th annual RNA Stability Meeting to give an invited talk and her lab presented four posters. The meeting covered a wide range of topics related to RNA stability and translation and how it applies to basic areas of science. The conference drew many students and principal investigators from all over the world, including North America, Europe, and Asia. That same month, she attended the first Upstate New York RNA meeting, RNA-UNY Structure, Function, in the Hudson Valley where she gave a lecture and four members of her laboratory presented posters.

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Later that year, Thapar spoke at PacificChem, an international chemical congress of Pacific Rim countries, which was held in Honolulu, Hawaii. At the meeting, which is only held every five years, Thapar presented a lecture on, “Structure and dynamics of the phosphorylated Stem-Loop Binding Protein (SLBP)-Histone mRlNA complex.” A number of internationally leading NMR spectroscopists from around the globe were in attendance.

Most recently, she spoke at the University at Buffalo’s Organic Chemistry and Chemical Biology 2011 Seminar Series in March 2011. Her lecture was entitled, “Structural Insights into Histone Pre-mRNA Processing and Its Regulation by Phosphorylation.” She elaborated on the recent structural and functional work using NMR and other biophysical and biological techniques to understand the signaling pathways that control histone pre-mRNA processing.

Training Tomorrow's Scientists

The Hauptman-Woodward Institute's high school program is a unique learning experience that affords area high school students the opportunity to study evolution and bioinformatics in the laboratory of H. A. Hauptman Distinguished Scientist Dr. William L. Duax.

HWI's high school program originated from a program created at City Honors School of Buffalo to support talented young people who are interested in medical research. Although the first students were from City Honors, the popular program has been expanded to include students from other schools.

According to Dr. Duax, "The students' impressive ability to communicate the essence of their work to a broad audience including grade school students, college students, university professors and layman, will help the development of their education and professional careers.

This program is sponsored by the Roy Carver Foundation, Time Warner Foundation, Buffalo Renaissance Foundation and other generous donors. To help ensure the sustainability of HWI's high school program, please consider making a donation.

For more information, contact Tricia Furnari at tfurnari@hwibuffalo.edu or (716) 898-8609.
National Center to be Established at HWI

continued from page 1

happen – knowledge which is critical to the long-term future development of new or combined therapeutic approaches for the treatment of a wide range of diseases with fewer unwanted side effects. His research has the potential to have medical relevance for literally millions of people worldwide.

“There are very few membrane proteins that have been characterized in molecular detail. These proteins carry out many significant biological processes in our body,” Malkowski said. “As roughly 60 percent of the drugs prescribed today for different ailments target membrane proteins, any additional structural knowledge we can contribute has the potential to be targeted for the design of new and improved drugs.”

About Malkowski

Malkowski received his Ph.D. in Biochemistry from Wayne State University in Detroit, Michigan and his bachelor’s degree in Chemistry from the University of Detroit in Detroit, Michigan. He resides in Williamsville, New York with his wife Lisa and their children. In addition to the research discussed above, the Malkowski laboratory also conducts research to better understand the biological processes that occur as the human body reacts to anti-inflammatory medications, as well as work on the structural characterization and functional analysis of other enzymes involved in lipid metabolism. Malkowski served as the Project Manager and a co-PI for the Center for High-Throughput Structural Biology (CHTSB), housed at HWI, where he was involved in the development of tools for high-throughput characterization of membrane proteins. The CHTSB was one of six specialized research centers established nationally in the second phase of the Protein Structure Initiative within the National Institute of General Medical Sciences at the NIH. His work there laid the foundation for the establishment of the Center announced within this release.

Drs. Michael Malkowski, Michael Wiener and Mark Dumont