Congresswoman Slaughter Announces $3 Million for Hauptman-Woodward Medical Research Institute
HWI’s Drs. Timothy Umland and Wayne Schultz to conduct research on how viruses mutate and transfer from animals to humans

Local print, radio and television reporters joined Congresswoman Louise M. Slaughter, chairwoman of the House Rules Committee, Dr. George DeTitta, CEO of Hauptman-Woodward, Dr. Herbert A. Hauptman, president of HWI and Drs. Wayne Schultz and Timothy Umland, research scientists who will head the project, to announce $3 million in federal funds to conduct research on how viruses mutate and transfer between animals and humans.

Representative Slaughter secured the funding in the FY 2008 Department of Defense Appropriations Bill for a study on the mechanism of animal to human transfer of disease.

“The Buffalo-Niagara region is well known as a leader in cutting-edge scientific research, and with this funding, we will continue that distinction,” Representative Slaughter said. “This Hauptman-Woodward project not only has the potential to save hundreds, if not thousands of lives, but will attract world-class scientists to our community and bolster our local economy.”

“We are grateful to Congresswoman Slaughter for her support in securing this funding,”

Dr. George T. DeTitta

George learned early on that he is a true scientist. This meant that he could be fulfilled only to the extent that he could actively do his science.

George’s work is best described as basic biomedical research which means that it is done for no purpose other than the generation of new knowledge designed to improve our understanding of life processes.

It is a tribute to his sense of responsibility that he chose to sacrifice some nine years of his life to be an administrator, overseeing the daily activities of others in order to help them advance their careers at a critical period during his own career.

His colleagues at HWI are very grateful that he made this selfless choice and that he chose now to resume his career as a scientist; all of us will surely benefit from his decision.

Molecular Cell

First High-Res 3-D Structure of Critical AIDS, Sepsis, Cancer Target Solved

Dr. Dan Gewirth, Hauptman-Woodward senior research scientist, has solved the structure of the first mammalian GRP94 protein implicated in immune diseases such as sepsis, AIDS and certain cancers. His work recently was published in a cover article in a top scientific journal - Molecular Cell.

Gewirth’s study confirms his 2001 hypothesis that this protein – GRP94 – is from the same family as the better known HSP90 proteins. As
Boardroom Bits ...

The Board of Directors voted unanimously in March to welcome Dr. Eaton Edward Lattman to become HWI’s next Chief Executive Officer as of July 1, 2008. Lattman, joins us after a 37 year career at Johns Hopkins University (JHU). Most recently, Lattman served as the Dean of Research and Graduate Education in the School of Arts & Sciences. A full profile on Lattman will be published in the next issue of Structures. Dr. Walter A. Pangborn will serve as HWI’s interim CEO from April 1 - June 30, 2008.

Carol E. Heckman has been elected to the HWI’s Board of Directors. Heckman is a partner in the law firm of Harter Secrest & Emery. Prior to that she served as a Magistrate Judge in the Western District of New York for eight years. She has served as a trial attorney for the U.S. Department of Justice, was an Assistant U.S. Attorney in Buffalo and has worked as a litigation partner in private practice. Heckman has been admitted to the Bar Associations in both New York and Colorado. She currently serves on the board of the Burchfield-Penney Art Center, as an editor for the Cornell Law Review, and as first editor-in-chief for the Federal Courts Law Review. Heckman has served as a board member for Women and Children’s Hospital, Chardon Beach and the American Lung Association. She has been a member of the Advisory Group of Magistrate Judges, and also a member of the executive committee in the Federal and Commercial Litigation Section. She was a member of the Judicial Council’s Education Committee for Magistrate Judges. She formerly served as an officer in the Federal Magistrate Judges Association. Heckman has published more than 340 judicial opinions and is the author of many articles in the New York Law Journal. Heckman received her bachelor’s degree from Lawrence University in 1974. She received her juris doctorate from Cornell Law School in 1977. Heckman resides in Orchard Park, New York with her husband.

Stuart H. Angert has been elected to the Foundation Board of HWI. Angert is co-founder and former chair executive officer of Remarking Services of America, Inc. He currently serves on the boards of trustees at Nichols School, Paul Smith’s College, Medaille College, Leadership Buffalo and the Adirondack Park Institute, the advisory boards for the University at Buffalo (UB) Center for Entrepreneurial Leadership (CEL), KeyBank, ECIDA Niagara Region Community Development Corporation; the board of directors of Meszaros International Center for Entrepreneurship, and as Commissioner of the NYS Office of Parks, Recreation and Historic Preservation for the Saratoga-Capital District. He also serves as coach/mentor for both Canisius Women’s Business Center and for the UB Advanced CEL Program. Angert holds a bachelor’s degree from Colgate University and a master’s in Business Administration from the University of Pennsylvania, Wharton School of Business. Angert and his wife, Joyce, reside in Amherst, New York.

Mary Engler Roche, a partner in the Lipps Mathias Friedman LLP Law Firm, has been elected to the Foundation Board of HWI. Roche concentrates in estate planning and estate administration, working with business owners and individuals on estate planning and tax matters, related corporate, insurance matters and retirement planning. She also serves as a referral attorney for several eldercare associations and community agencies. Roche is a member of the New York State Bar Association and the Erie County Bar Association, the Women’s Bar Association of Western New York and the Women’s Lawyers Association; serves on the Practice and Procedure in Surrogate’s Court Committee and the Erie County Surrogate Court Liaison Subcommittee, participates on the Coalition of Western New York Medicaid Advocates and as part of the Financial Planning Counselors of Western New York. Roche received both her juris doctorate and her bachelor’s degree from the State University of New York at Buffalo. She resides in Buffalo, New York with her family.

Dr. Herbert A. Hauptman Celebrates His 91st Birthday

Valentine’s Day is always extra special at Hauptman-Woodward because we celebrate our President Dr. Herbert A. Hauptman’s birthday. This year in addition to the many friends and colleagues who gathered to celebrate, a close friend and professional violinist Walter Greizerstein performed a special piece to honor Dr. Hauptman.
What’s Happening at Hauptman-Woodward

Two HWI Investigators attended the Recent Advances in Macromolecular Crystallization (RAMC) meeting held September 23-26, 2007 in San Diego, CA. Dr. Edward Snell won an award for his poster presentation, The Efficient Use of a 1536 High-Throughput Crystallization Screen to Guide Subsequent Optimization. Joseph Luft presented an invited lecture, Decostruction of Drop Volume Ratio/Temperature Optimization Experiments, and a poster, Technology Development at the Center for High Throughput Structural Biology. Edward Snell and Joseph Luft attended the Keystone symposium, Structural Genomics and its Applications to Chemistry, Biology and Medicine, held in Steamboat Springs, CO January 6-11, 2008. Snell presented a poster and an invited lecture, Order from chaos - The design and interpretation of high-throughput crystallization screens to guide optimization. Luft presented a poster, Cloning through diffraction: Goals and technologies at the Center for High-Throughput Structural Biology.

Dr Vivian Cody, HWI Principal Research Scientist is a member of the ADDT – AIDS Discovery and Development of Therapeutics Study Section in the National Institutes of Health. She has served since 2004 and concludes her term this year. This study section encompasses discovery, design, identification, isolation and synthesis of novel agents, structural characterization of target proteins in the HIV life cycle and other AIDS-related protein targets. She also participates in the Centers for Biomedical Research Excellence (COBRE) reviews. This is a program to increase competitiveness of investigators from institutions located in states with limited access to competitive research funding. It helps strengthen their infrastructure by designing center programs that bring a critical number of successful investigators together. She also reviews the NIH Postdoctoral Fellowship applications and various program project and center grants and does ad hoc reviews on several other study sections as well.

Dr Michael Malkowski, along with graduate students Danielle Simmons and Alex Vecchio traveled to the Keystone Symposia on Eicosanoids and Other Lipid Mediators of Chronic Inflammation, held January 7-12, 2008 in Big Sky, Montana. The Malkowski laboratory presented their recent research results dealing with aspirin-acetylation and cyclooxygenase-2. Simmons was the recipient of the University at Buffalo School of Medicine and Biomedical Sciences Virginia Barnes Endowment Travel Award and presented a poster at the meeting titled The Molecular Basis for Aspirin-Trigged Lipoxin Formation by Cyclooxygenase-2.

Malkowski and Vecchio traveled to the 10th Winter Eicosanoid Conference held March 9-12, 2008 in Baltimore, Maryland. The poster abstract submitted by Vecchio, titled Structural Insights Into Endocannabinoid Metabolism by Cyclooxygenase-2 was meritoriously selected for a $500 Conference Travel Award.

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What’s Happening at Hauptman-Woodward

HWI Hosts WNY State Delegation Meeting

On February 29, 2008, Hauptman-Woodward hosted the Western New York state delegation meeting. New York State Senators and Assembly Members and their staff members participated in a presentation given by BNMC Board Chair Bill Joyce. BNMC Institution leaders, including HWI CEO and Executive Director Dr. George DeRita, all spoke in support of the collaborative nature of the campus and the benefits to the WNY community and economy.

Assemblyman Robin Schimminger’s Annual Upstate Economy Report Held at HWI

New York State Assemblyman Robin Schimminger held his annual state of the upstate economy roundtable at Hauptman-Woodward on March 7, 2008. Nearly 75 local economic development experts, local business owners, civic leaders and community members attended and discussed the state budget. There was a lively question and answer period during which participants shared suggestions and opinions related to state policies and funding procedures.
In March of 1973 Adele and I were contemplating a future in Sweden. I was poised to accept a post-doctoral research fellowship in the labs of Sixten Abrahamsson, at the University of Gothenburg. We had gone so far as to listen to Swedish language LP’s in preparation for our move from Pittsburgh. There was, however, the matter of an American Crystallographic Association meeting in Los Alamos, New Mexico where I had plans to present work that came out of my doctoral studies at the University of Pittsburgh with Professor Bryan Craven. At the ACA, I made the acquaintance of Herb Hauptman, Bill Duax, and Jane Griffin. They attended my talk. There must have been something in that talk that made them believe I would be a good fit for the Medical Foundation of Buffalo, as we were known before our days as HWI. The opportunity to work with the Buffalo group, then (as now) considered one of the most energetic crystallographic groups in the country, was too much to pass up; I sent my regrets to Sixten and by June 1973, Adele and I had made the move to Western New York.

I arrived as a scientist in training, and worked for Dr. James Edmonds who was doing very exciting things with the newly discovered class of biological compounds known as the prostaglandins. When Jim departed for a position in industry I took over the prostaglandin project, and shortly thereafter I started a structural project on the vitamin bombin. For the first twenty-six years of my HWI career I was a bench scientist. In 1999, I moved into an executive role here. It’s been nearly nine years since I stopped being a full time scientist.

One of the most pleasant parts of my job has been the opportunity to meet with you, the friends and supporters of HWI. I’ve learned a lot about what we do within the various research groups here by having to explain those projects to you, in a language that wasn’t littered with technical terms. In the doing I’ve come to appreciate that what we do is of great importance to your health and the health of those you love. One of our newest board members, Stuart Angert, took me to task for describing what we do as “basic biomedical research.” Stuart accepted the description as factually accurate but much too limiting; he suggested we describe what we do as life-altering research. My first reaction was that this sounded much too grandiose, but on second thought I came to agree with Stuart that without the kinds of discoveries we (and other basic biomedical researchers) make, the entire effort to improve the general health of our fellow citizens falls completely flat.

The opportunity to work with, and to serve, the talented scientists, technicians and support personnel at HWI has been rewarding. Not everyone can claim to be a scientist but nearly everyone has experienced the thrill of discovery. That’s what we scientists do on a daily basis: think about how things happen and then devise scientific hypotheses to test in the lab. There’s really nothing like it in the world: that thrill when you find out something new and important. It’s time for me to get back to the lab, to experience that feeling again on a daily basis.

~ Dr. George T. DeTitta

A Fond Farewell to a Favorite CEO as He Returns to His Lab

people I have to thank for this opportunity to serve the lab. Such lists are dangerous things; you inevitably forget to thank someone who was important. To all who helped me, let me say a sincere thank you. I especially thank my wife Adele for her patience and always good advice, and her enduring support and love.

I leave the lab in good hands. As many of you know, and as reported elsewhere in this issue of Structures, Ed Lattman, Dean of Graduate Education and Research at Johns Hopkins University, has accepted our offer to become the next chief executive officer of HWI. Ed will undoubtedly take us in new, exciting directions. You will find him accessible, friendly and smart. Give him a couple of months to get on his feet; then come to meet him and let him know of your interest in HWI.

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"George became CEO at about the time that I became a director and I have had the pleasure of seeing him mature into a very effective manager with style that is open, collaborative, and decisive. Under his leadership, HWI has replaced its outdated physical plant with a new facility that is both beautiful and functional, recruited new scientific to Buffalo, established the UB Department of Structural Biology, and won its largest federal research grant (with George as the Principal Investigator). With George taking his scientific and management talents back to the lab fulltime, I am confident that we will see both more grants awarded and knowledge gained for the benefit of humanity."

Donald A. Hess, Chairman of HWI Board

"George stepped into the CEO job at HWI at a time that was to become a time of major change for HWI. A beautiful new building and a major expansion were both in the cards. I don’t think George had a clue what he was signing up for. He, who preferred to stay in his isolated lab, accepted the challenge with grace and soon developed admirable diplomatic abilities. We are all appreciative of the time and effort that George has put into the growth and well-being of HWI."

Connie Constantine, Emeritus Director and Former Chairman of HWI Board

"George is a Renaissance man - a very talented scientist and teacher who loves performing arts, wine, and cooking, among other things. Much to the benefit of HWI, he also developed strong and deep interests and talents in building design, construction, negotiation, finance, and human resource management. Besides all this, George is a pleasure to work with, which has made his years at the helm good ones for HWI."

Shelly Heffernan, HWI Board Member and Partner with Jaeckle, Fleischman and Mugel
Congresswoman Louise Slaughter Announces $3 million in Federal Funding

Congresswoman Louise Slaughter and Dr. Herbert A. Hauptman

Gewirth and his lab have been using the technique of X-ray diffraction to solve the first high-resolution structure of this protein from mammalian sources. The structure and activity patterns of this protein prove conclusively that this is indeed a member of the same family.

“Our work opens the door to a more intensive evaluation of this protein both from a mechanistic as well as a therapeutic point of view. In addition to aiding our understanding of the fundamental biology of chaperone-mediated protein folding, this work lays the foundation for the design of drugs that specifically target individual members of the HSP90 family,” Gewirth said.

Why Is This Important?

This is groundbreaking work for a number of reasons. It is the first high-resolution picture of any member of the HSP90 family. High resolution is needed for an intensive evaluation of this protein both from a mechanistic as well as a therapeutic point of view. In addition to aiding our understanding of the fundamental biology of chaperone-mediated protein folding, this work lays the foundation for the design of drugs that specifically target individual members of the HSP90 family,” Gewirth said.

Scientific Understanding – The mammalian member of this protein family is different from those previously studied which were solved from either bacteria or yeast. Human energy production and consumption rates are more similar to those found in the GRP94 proteins than to the more widely studied HSP90 proteins. This means that the insights gained by a greater scientific understanding of how GRP94 works will have more direct applications to human diseases.

Medical Implications and Drug Development – Inhibitors currently are being designed for HSP90 in an attempt to treat the diseases in which HSP90 plays a role. However, these are broad-spectrum inhibitors of all HSP90s which means that unwanted side effects may occur. The Gewirth lab’s work clarifies GRP94’s place in this family and has already stimulated interest in this chaperone as a drug target. This understanding would allow for the long-term development of a family of drugs that could be narrowly targeted for individual proteins, for example specifically treating sepsis only.

Economic Impact – Just as companies have been founded to develop HSP90 inhibitors, the same potential exists here. This will spur a new line of inquiry into GRP94. While this work is

Broad-spectrum anti-virals to deal with pandemic threats which affect vulnerable populations such as those found in military settings and densely populated communities.

About Gewirth

In addition to his position as an HWI senior research scientist, Gewirth is an associate professor of Structural Biology at the University at Buffalo. Prior to joining HWI in 2005, Gewirth was an assistant professor in the Department of Biochemistry at Duke University. He completed post-doctoral research at both Yale and Harvard, received his Ph.D. from Yale University in 1988 and his bachelor’s degree from the University of Chicago in 1982. Gewirth’s research is focused primarily on structural studies of HSP90 chaperones, drug design, protein folding, nuclear hormone receptors; and basal transcription factors. Gewirth and his wife live in Buffalo.

Congressman Dave Camp and Dr. Daniel T. Gewirth

Ligand-regulated chaperones – proteins that help other cellular proteins achieve their active shapes – the HSP90s are key players in cellular regulation and recognition. The HSP90 proteins have been the subject of increasing international interest as scientists have discovered that they can be targeted therapeutically with drugs that lead to either stimulation or inhibition. For example, inhibitors of HSP90s are being developed as therapies for diseases ranging from cancer to sepsis, and drugs that stimulate HSP90 action may be appropriate therapies for diseases involving protein folding, such as cystic fibrosis, prion diseases, and Alzheimer’s Disease.

Since 2001, Gewirth and his lab have been using the technique of X-ray diffraction to solve the first high-resolution structure of this protein from mammalian origins, to understand its function and to determine if it is indeed a member of the HSP90 family of proteins. The structure and activity patterns of this protein prove conclusively that this is indeed a member of the same family.

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THE STEPS TO A CURE BEGIN WITH BASIC RESEARCH

The health of friends and family is important to everyone.

Here are just a few of the companies in our community that match employee charitable donations.

Ask your employer today if they match donations, or make in-kind donations of equipment.

Does your organization coordinate an annual fundraiser? Many companies organize golf tournaments, auctions or events where the funds benefit various community organizations. Implementing a fundraiser is a great way to develop company spirit, camaraderie and to give back to our home community.

Hauptman-Woodward would be honored to be the recipient of your next fundraiser.

For more information on partnering with us on an event, please call Laurie Elliott Krajna at 898-8597

1. DONOR MATCHING

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Bristol-Myers Squibb  •  Fannie Mae Foundation  •  Hewlett Packard  •  HSBC

KeyBank  •  Merrill Lynch  •  National Fuel  •  UBS

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What was your inspiration to become a scientist?

I attended a high school that was 20 miles from my home and had to wait two hours after school for my ride home. I asked if I could work in the chemistry lab while I waited. I made things explode, scattering iodine crystals around the room, it was great. I had the naïve curiosity of a cook – which I love to do. In college, I thought about being an actor or writer, but wanted a family and thought those might be unstable careers. In graduate school, my professor Norman Baenziger convinced me that crystallography was the career for me. There is nothing like being the first person to see the structure of a molecule that has been around since the beginning of time. It is a beautiful, rich field – and I still get to act and write...

Where were you born and how many siblings do you have?

I was born in Chicago and have two brothers and one sister. There were 400 people in my hometown and it was important to my mom that I attend college so she sent me to St. Patrick’s, a Catholic school in nearby Kankakee.

Tell us a little about your family – wife and children and grandchildren?

My wife Caroline is a pianist, social worker, photographer, upholsterer, seamstress and gardener and we have four children and seven grandchildren including gymnasts, cooks, a dancer, an artist, a composer, a fledgling actress, a young scientist, an IT specialist and world authority on Thomas the Tank Engine.

What has been your proudest scientific achievement?

There are several – the first direct methods structure I solved with Herb Hauptman and Chuck Weeks that led me to believe that I could make a career in science; starting the International Union of Crystallography (IUCr) newsletter; and nurturing third world science, working with the City Honors high school students who are currently helping me to pursue what is probably the most important problem I’ve ever worked on, which is tracing the origin and evolution of the genetic code; promoting the advancement of women in the field of crystallography...