The Cures Begin Here

The Hauptman-Woodward Medical Research Institute (HWI) creates novel strategies and technologies to promote the understanding, prevention and treatment of many human diseases. Examples of current projects involve finding cures for AIDS, arthritis, cancer, cardiovascular disease, cystic fibrosis, and the transmission of emergent diseases from animals to humans.
The Hauptman-Woodward Medical Research Institute (HWI) is an independent, not-for-profit, biomedical research facility located in the heart of downtown on the Buffalo Niagara Medical Campus. We are a founding member of the BNMC together with our neighbors Roswell Park Cancer Institute, Kaleida, University at Buffalo, and the Buffalo Medical Group. For more than half a century, HWI scientists have been committed to conducting life-altering research to understand the causes and potential cures of many diseases.

Working under the leadership of our Chief Executive Officer and Executive Director Dr. Eaton E. Lattman, HWI scientists are studying a wide range of diseases which include AIDS, arthritis, breast cancer, cardiovascular disease, cystic fibrosis, prostate cancer and many others. In addition, researchers at HWI seek to improve the methods of crystallization and data analysis used by scientists worldwide which are critical elements in drug design.
On behalf of Hauptman Woodward’s researchers, staff and Board of Directors, I would like to thank each of you for your support of HWI. Your contributions make it possible for scientific endeavors at HWI to continue to advance and flourish. This past year alone HWI researchers expanded collaborations with other institutions, contributed to numerous scientific publications to share their research with others; and have played significant roles in the advancement of Structural Biology research through the education of students. Your support has facilitated these numerous achievements, and for that we thank you.

Since its inception in 1956, HWI has been a model scientific organization committed to outstanding science made possible by the support of a philanthropic community. Just this past year alone, HWI was fortunate to receive two large gifts from donors totaling over $300,000. I mention this, not to emphasize the amount, but to acknowledge how gifts impact the Institute. Seed funding like this allows HWI researchers to incubate new ideas, develop data needed to prove their concepts, and then gain outside funding from sources like NIH and the NSF. Your support initiates these projects and ultimately translates into research dollars in our community and excellent science.

For all of your support as a donor, a board member or a volunteer, I thank you for your commitment to HWI’s mission. Without you we could not achieve our goals.

The CEO’s column in the 2010 Annual Report drew an optimistic picture of the future of HWI, both in terms of research impact and financial stability. Much has happened since then, and it seems a good moment to revisit these topics.

In that report I mentioned sober projections about the future of academic research institutions: hard times and contractions are in the offing for many. One has to admit that, since 2010, the overall picture has gotten worse, at least for biomedical research. As an example, NIH, which provides much of the support for HWI research, has announced the following measures for the 2013 fiscal year.

- The NIH budget overall is cut by 5.5 percent to $29.1 billion in FY 2013, from $30.7 billion in FY 2012.
- Funding for Research Project Grants - these are the kinds we rely on most frequently - declined by 6.1 percent, with noncompeting awards (continuation) down 4.9 percent and competing (new) awards down 8.6 percent.
- The overall number of Research Project Grants will decrease by 1,282 in FY 2013; noncompeting awards will fall by 579, competing awards by 703.
- The inflation rate for research-associated expenses is between 3 and 4 percent, which only magnifies the cuts described above.

How is there a rational basis for optimism in the face of a stream of news like the above?

There are two major trends that justify a positive outlook. The first is that the University at Buffalo has developed a compelling interest in strengthening and expanding the Department of Structural Biology, for
which Hauptman-Woodward scientists comprise the entire faculty. As the Department is strengthened, HWI will be strengthened in parallel. The discipline of structural biology is critical to the new UB mission of translational research, and this new mission will in turn provide new arenas and outlets for HWI research. The exact details of how this support will be provided are not yet set, but strength will beget strength.

The other trend involves new emphasis on HWI research in less traditional formats, such as fee-for-service and paid collaborations. During the last year HWI scientists, members of the Board, and others have been working diligently to create a business plan for marketing to biotech firms and others services in the areas of biomolecular crystallization, structural biology, and related disciplines, where we have great existing strength and resources, and where we have many academic clients. In the very near future we will be hiring a full-time person to help bring our nascent business to fruition.

Please see the following web page for details of the structural biology services being offered and a downloadable marketing brochure that we have created to publicize our services, www.hwi.buffalo.edu/HT_Services/protein_structure/protein_structures.html

Much of the most important research at HWI has been in the area of technology development. Dr. Hauptman’s Nobel Prize was given for the solution of a recalcitrant mathematics problem that had enormous practical implications. The High-throughput Crystallization Laboratory has served thousands of clients, but keeps at the forefront because it carries out basic research on the process of crystallization, as well as providing crystallization services. These are the kind of achievements that can bring revenues as well as academic visibility and success. It will be a hallmark of the HWI marketing profile we are creating that it will be supported by, and intimately related, to our parallel and complementary research efforts. This evolution will only strengthen the HWI tradition of high-impact research.

Eaton E. Lattman, PhD
Chief Executive Officer and Executive Director

Our consolidated accrual basis net loss for the year ended October 31, 2012 was $1M and was driven by depreciation expense on our research facility as well as a continued reduction of our federal revenue support. Cash flow remained flush with the prior year positively impacted primarily by payments on outstanding pledges. Controllable expenses were maintained within budget. Non operating gains of $381k include realized and unrealized investment performance as well as the fair value of the derivative arrangement on our outstanding debt. We recently received word that Drs. Schultz and Umland are the recipients of a competitive DOD award. This award started in December 2012. We continue to respond to numerous solicitations for competitive funding and currently have nine outstanding applications pending, any one of which if funded, could have a significant positive impact on operations.

On the balance sheet, our total assets are just over $20M. This includes $7.1M in investments of which our permanent endowment represents $2.3M. We have set aside another $100k in a Reserve for Replacement as required by our covenants with our lender. This effectively brings our replacement reserve up to $800k. Lastly, we once again received a favorable “unqualified” report from our auditors. There were no deficiencies noted in accounting controls or major research programs.

Respectfully submitted,

Anne M. Kent
Controller

<table>
<thead>
<tr>
<th>Significant Financial Statement Elements</th>
<th>10/31/2012</th>
<th>10/31/2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Assets</td>
<td>$ 26,573,715</td>
<td>$ 28,131,916</td>
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<tr>
<td>Total Liabilities</td>
<td>$ 6,535,776</td>
<td>$ 7,103,189</td>
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<tr>
<td>Total Net Assets</td>
<td>$ 20,037,939</td>
<td>$ 21,028,727</td>
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<tr>
<td>Total Revenues &amp; Other Support</td>
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<td>$ 8,624,833</td>
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<tr>
<td>Total Operating Expenses</td>
<td>$ 9,269,827</td>
<td>$ 10,366,725</td>
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<td>Net Operating Loss</td>
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<td>$(1,741,892)</td>
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<tr>
<td>Non Operating Gains/(Losses)</td>
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<tr>
<td>Net Loss</td>
<td>$(990,786)</td>
<td>$(1,580,332)</td>
</tr>
</tbody>
</table>

1Source: The consolidated financial statements of the Hauptman-Woodward Medical Research Institute, Inc.
Proteins can be thought of as molecular machines that carry out a wide variety of functions in the body. Many of these machines speed up chemical reactions, for example breaking down the food we eat or building the important biological molecules that we need. Proteins that perform, or catalyze, these chemical reactions are known as enzymes. The Gulick Lab at HWI is using multiple biochemical techniques to study a number of different enzymes that play important biological roles. In particular, they are using X-ray crystallography to determine the molecular structure of these enzymes. These studies allow us to understand the fascinating biochemistry of a living cell.

The National Science Foundation has recognized the Gulick Lab’s advances in this avenue of research and has awarded them a four year grant that establishes a collaboration between Dr. Gulick and Dr. Peter Tipton, Professor of Biochemistry at the University of Missouri. The grant will support biochemical research and the training of graduate and undergraduate students at both institutions. The research project builds on both labs’ interests and expertise in the study of the enzymes involved in natural product synthesis.

Many bacteria produce small chemicals that they secrete into their environment. Bacteria use novel chemistry to produce many molecules that impact the interactions of bacteria with other bacteria and with other organisms. Some bacteria produce antibiotics and other pharmaceutically active compounds. Other bacteria produce virulence factors that enable them to establish an infection. Blocking the production of a virulence factor may lead to the development of a new antibiotic. This research project will examine the ability of several pathogenic bacteria to produce chemicals called isonitriles. The primary goal of the research is to understand how these proteins make these compounds. The work will involve structure determination of these proteins, a process for which HWI is internationally known, as well as a chemical investigation of how these proteins perform these difficult chemical transformations. Ultimately, this may lead to a better understanding of the chemical interactions between hosts and bacterial pathogens.

Awards from the National Science Foundation are contingent not only on the investigation of important scientific questions but also emphasize the broader impacts of the research experience for students. The project will support the research of two graduate students. Additionally, undergraduates in both labs will be provided an interdisciplinary training opportunity in the areas of biochemistry and molecular structural biology. In particular, Drs. Gulick and Tipton will identify research opportunities for first and second year undergraduates to try to increase the retention of excellent undergraduate students in the biological and chemical sciences.

This project is jointly supported by the Biomolecular Dynamics, Structure and Function Cluster in the Division of Molecular and Cellular Biosciences and the Chemistry of Life Processes program in the Chemistry Division of the National Science Foundation.

How the structure was solved:

In Structural Biology, a researcher considers a structure ‘solved’ when they have been able to determine what it looks like at the molecular level. The basis for the Gulick Lab’s solution of this protein is:

1. The researchers work to get the protein to crystallize. This crystal must be as perfect as possible.

2. The researcher, once successful at crystallizing a material can then irradiate it with an X-ray beam. As this X-ray passes through the crystal the electrons within the protein disperse the X-rays into a pattern. Each pattern is as unique to a protein as a fingerprint is to an individual.

3. The diffraction pattern from the X-ray experiment then is analyzed mathematically and through computer modeling to arrive at the ‘solved’ structure which you see to the right.

Once they have solved a protein structure, they share this information with the international scientific community to advance the research of all.
2012 RESEARCH HIGHLIGHTS

Understanding How Diseases Spread Between Species

The Umland and Schultz labs have received a grant from the Department of Defense to study the transmission of emergent diseases from animals to humans.

Zoonoses are infectious diseases that are transmitted between species. Typically, zoonotic pathogens are viruses, and they spread from other vertebrate species to humans either by direct contact with the animal, or its excretions, or via an arthropod (e.g. insect) vector. The appearance of a pathogen in a new host species is called “disease emergence”.

Zoonotic viruses are responsible for many of the most serious infectious diseases confronting modern medicine. Examples include avian influenza (H5N1), West Nile virus, several forms of encephalitis, SARS (severe acute respiratory syndrome), Ebola and AIDS, to name a few. The influenza virus alone accounted for several severe pandemics in the 20th century including the “Spanish flu” of 1918, the “Asian flu” of 1957, and the “Hong Kong flu” of 1968.

In animals and humans, the innate immune system provides the main defense against novel viral attack. Host cells release proteins called interferons in response to the presence of viruses or other pathogens. “Interferons” (named after their ability to “interfere” with viral replication within host cells) facilitate communication between cells, triggering the immune system to eradicate the microbial invaders.

In retaliation, viruses have evolved mechanisms for evading the innate immune responses of their established (donor) host species. Successful expansion to a new (recipient) host species would require the ability to control the immune response in that species as well.

It is known that certain viral proteins impair the interferon activation response through molecular interactions with specific host proteins, thereby disrupting the intracellular signaling pathways of the host species. Presumably, the ability of viral proteins to form similar interactions with proteins in a potential recipient species would lower the barrier to species jumping. However, little is known about the actual conservation of virus-host protein interactions in donor and recipient species or the extent of adaptation necessary for viruses to form comparable complexes with similar proteins in new hosts.

HWI Research Scientists Tim Umland and Wayne Schultz have been awarded a 3-year $1.1M grant from the Department of Defense to study the relationship between conserved protein-protein interactions and successful host-range expansion.

Drs. Umland and Schultz will identify instances of conserved, cross-species, virus-host protein interactions involving viruses with histories of host jumps, especially to humans. In particular, they will examine host proteins involved in the interferon response pathway for such interactions.

The HWI scientists will define and characterize the virus-host, protein-protein interfaces by using small-angle x-ray scattering (SAXS) to create structural models. The amino acid residues involved in forming the protein interfaces can then be identified. Mutagenesis studies will be used to verify critical residues that must be conserved for range expansion to occur.

The public is at risk from emerging infectious diseases. This danger is particularly high for diseases that infect animals of economic importance, or common wildlife where human contact and consumption create avenues of exposure. This HWI-based investigation will provide knowledge of the relative ease with which a given virus might adapt to a new species, particularly humans. It will also provide specific molecular details about common viral-host protein interactions that will be useful in the design of potential broad-spectrum antiviral therapeutic agents.
Our greatest assets are our people. Hauptman-Woodward is fortunate to be home to some of the most creative minds in science today and has the distinction of offering an investigator-initiated approach that allows our scientists to translate their passion for their work into their everyday experiences. The scientific team is supported daily by talented individuals who serve on our boards and a staff which includes individuals with a wide range of talents and experiences. Each employee at Hauptman-Woodward plays a role in ensuring the organization’s current and future successes.

BOARD OF DIRECTORS AND OFFICERS

The People of the Hauptman-Woodward Medical Research Institute

Our greatest assets are our people. Hauptman-Woodward is fortunate to be home to some of the most creative minds in science today and has the distinction of offering an investigator-initiated approach that allows our scientists to translate their passion for their work into their everyday experiences. The scientific team is supported daily by talented individuals who serve on our boards and a staff which includes individuals with a wide range of talents and experiences. Each employee at Hauptman-Woodward plays a role in ensuring the organization’s current and future successes.

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*HWI’s staff at IMCA-CAT

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The fifth annual Hauptman Society gathering took place on April 17th 2013. The Hauptman Society was created in 2008 to honor Corporate or Individual donors who contribute leadership unrestricted gifts of $1,000 or more annually. These gifts support HWI’s mission and the pursuit of life-altering research.

“Hauptman-Woodward is honored to receive these important donations which allow HWI scientists to contribute to cures to the diseases that plague our friends and families,” Dr. Vivian Cody said.
2012 PUBLICATIONS


