

STRUCTURES

A PUBLICATION OF THE HAUPTMAN-WOODWARD INSTITUTE

WINTER 2018

Celebrating Women in Science



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- Powerful new imaging methods
- At the heart of the BNMC



“Science is a wonderful field. You can collaborate with people all over the world and really make a difference.”

— Jane F. Griffin, PhD

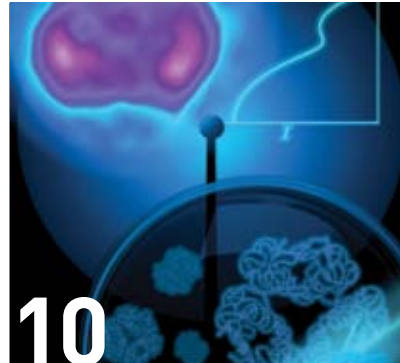


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From the CEO

WELCOME! To use the phrase of the American Crystallographic Association housed in the Hauptman-Woodward Institute: “Structure matters.”

This issue focuses on all that makes structural knowledge happen – the cures for the future and the people who shape that future. It describes the scientists, methods, and the collaborations initiated by the Institute, and the supporters that make this possible. Dr. Elizabeth Wood was one of the founders of the American Crystallographic Association (ACA) and became its president in 1957. We showcase women in the structural biology field in this issue with some well-known Buffalo stars and some of the stars-to-be. Today, our own Dr. Lisa Keefe is the president

of the ACA, elected by the community of crystallographers in the United States and Canada.

We are also delighted to introduce new faces at the Institute, such as Dr. Aviz Paz, who has declared war on cancer and joins our efforts in this area. We have a strong board with John Horn as the new chair and are excited to introduce Michelle Heffernan and William Constantine as new board members. There is too much in this issue to describe in detail so I suggest you sit back, glance through, and discover how friends like you make all of this happen!

– *Edward Snell, PhD*

Edward Snell named Director of NSF BioXFEL



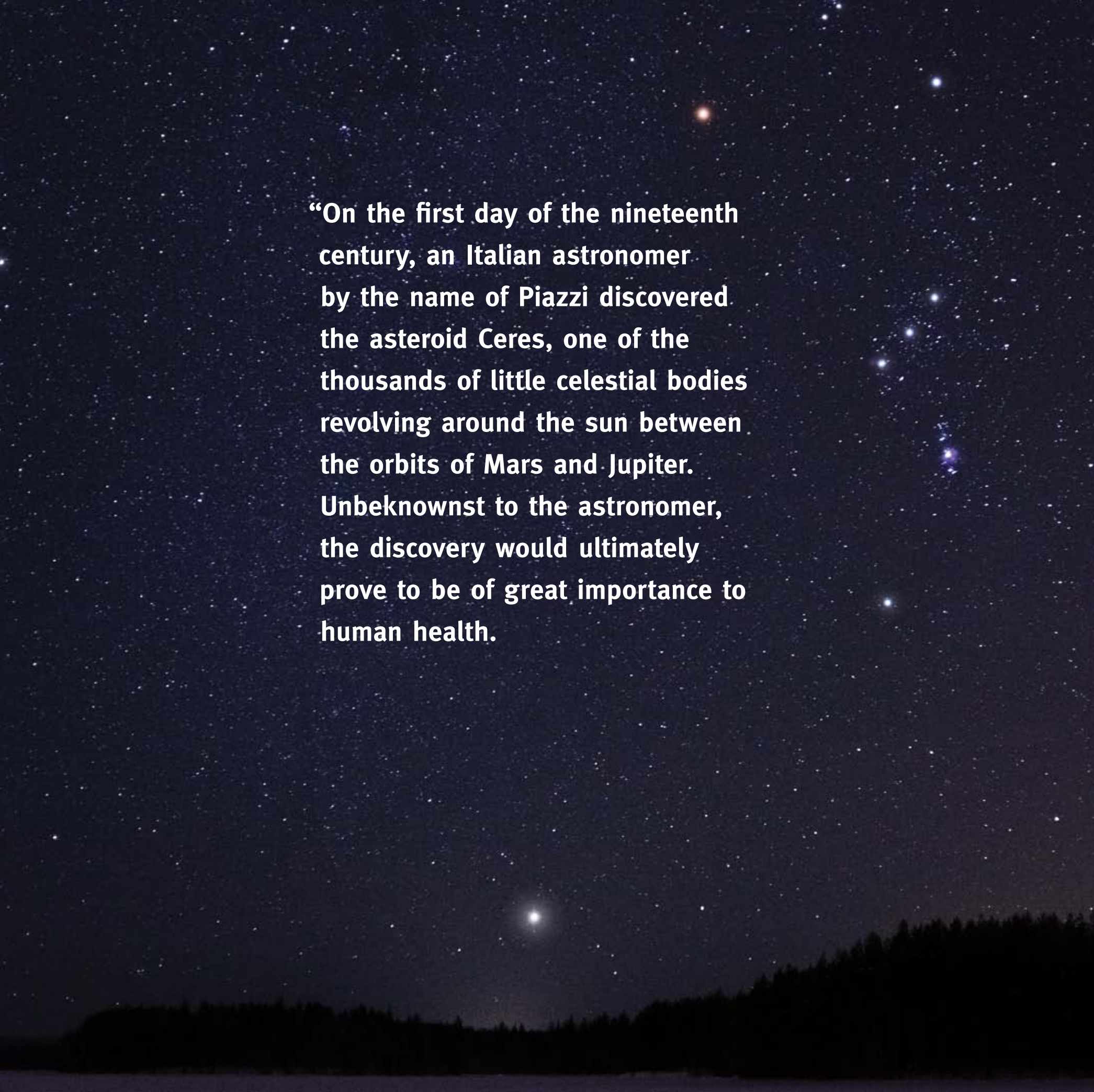
“Scientific efforts in Buffalo are having an impact not only nationally, but internationally in this field.”

SINCE 2013, the National Science Foundation-supported BioXFEL Science & Technology Center has been developing the use of a new scientific tool called an X-ray Free Electron Laser for applications in structural biology. In October of 2017, Edward Snell, PhD, was named Director of the Center, replacing Dr. Ed Lattman, who served at the organization’s helm since its inception. Dr. Snell shared his thoughts about the importance of BioXFEL’s work and his new role with the organization:

“A good analogy for a drug and its target is a baseball and a baseball glove. The baseball is the drug, and the glove its disease target in the body. Instead of designing a glove to catch the ball, we look at the shape and movement of the glove and build a ball (a drug) that will fit snugly into the glove when caught. Until recently we viewed the glove and ball largely as static – a snapshot so to speak. Now through the NSF-supported

BioXFEL project, we aim to see the whole game and the intricate biological motions that happen as fast as a billionth of a second that can be crucial to designing effective drugs.

By understanding how the biology inside all of us works on this time scale, we can understand what happens in our bodies and thus create a much wider array of new drugs to treat disease. The NSF BioXFEL Center is headed by the University of Buffalo and eight collaborating institutes. To date, those collaborators have produced over 500 new scientific results and detailed almost 400 potential drug targets. In May 2018, the Center was awarded another five years of support to continue this research. Scientific efforts in Buffalo are having an impact not only nationally, but internationally in this field. We are opening the door to others and hope that generations of new scientists will be able build on this transformative research.”



“On the first day of the nineteenth century, an Italian astronomer by the name of Piazzi discovered the asteroid Ceres, one of the thousands of little celestial bodies revolving around the sun between the orbits of Mars and Jupiter. Unbeknownst to the astronomer, the discovery would ultimately prove to be of great importance to human health.

That’s because Piazzi’s discovery, made during his pursuit of knowledge within both his own specialty and the general realm of science, would be the start of a series of such pursuits and discoveries that would coalesce one day into the mathematical tools we are using now to unlock biomedical secrets on the Buffalo Niagara Medical Campus and elsewhere throughout the world. **And that process – the search for answers to questions in a wide range of fields, and the eventual coalescing of those answers in sometimes surprising ways – offers powerful support for the value of scientific research.”**

Excerpt from “The case for science from asteroids to X-rays to human health, it’s all interconnected,” by Dr. Herbert Hauptman, Special to the News, in the December 10, 2006 edition of The Buffalo News. To read the full article, visit bwi.buffalo.edu/latestnews.

The Duax High School Research Program: Cultivating the next generation of scientists

Forty-five students participate in the program from seven local high schools, which include public and private schools in Buffalo and its suburbs.



Students interested in a career in science or medicine have the ability to immerse themselves as early as their freshman year of high school in real-world research thanks to an innovative program devised by William Duax, PhD, at the Hauptman-Woodward Medical Research Institute (HWI).

“These young people are getting training, exposure, and experience well beyond what can be achieved in a classroom.”

— Todd Richards, Science Teacher and Research Program Coordinator for City Honors High School



“THIS is a serious program,” says William Duax, PhD, the emeritus research scientist who began an innovative program that equips young scientists with world-class tools and training at HWI. “Students have the opportunity to conduct actual research with their mentor scientists and are expected to make contributions, give presentations, and formally report their findings.”

In this innovative program, Western New York high school students examine the structure and fabric of life on earth using state-of-the-art computer programs to analyze the sequence of bacteria and eukaryotes. The training, which is computer intensive, employs high-level web programs for biological analysis and a suite of unique programs developed in the HWI laboratory for protein and gene analysis. The students mine the data in the gene and protein banks of the world.

“These students are conducting cutting-edge experiments that have never been done before,” says Dr. Duax. “They are challenging basic tenets of structural biology and,

along the way, learning the demands of research, such as flexibility, adaptability, creativity and, most of all, patience.”

Since its inception, the program has grown to include 45 students from Buffalo City Honors, Nardin Academy, Amherst High School, Orchard Park High School, Elmwood Franklin, Nichols School, and the Park School. Todd Richards, a science teacher and Science Research Program Coordinator at City Honors, wholeheartedly believes in the benefits of the curriculum for his students.

“These young people are getting training, exposure, and experience well beyond what can be achieved in a classroom,” says Richards. “It helps them understand what they want – and don’t want – out of a research or science career. It gives them a real leg up by the time they get to college, and saves them a lot of time and aggravation.” Richards says he’s extremely impressed with the program and how in-depth it is. “Usually by the second year, the students are talking about

information and data well above my professional training,” he says. “Bill Duax is an incredible teacher and has great rapport with the students, and it shows in their enthusiasm and their accomplishments.”

Dr. Duax credits the students for the program’s success. “These students are inspiring,” says Duax. “I truly enjoy watching them and I learn from them! I constantly give them problems that are in process and, often, they come up with better ways to find answers. It’s very encouraging to see this kind of enthusiasm in our youth right in Buffalo. Their potential to embark on successful scientific careers is what HWI is all about and all we’ve seen with the innovations on the Buffalo Niagara Medical Campus. We are all working together to build a better tomorrow for Buffalo and human health.”

In addition to the school-year program, Dr. Duax also runs a summer workshop on molecular bioinformatics for high school students. More details can be found at www.hwi.buffalo.edu/education.

NEW VIEWS

A novel imaging method allows greater visualization of biological molecules

A powerful new imaging method developed by Thomas D. Grant, PhD, reveals in great detail how particles move in solution. According to his recent paper published in *Nature Methods*, this new imaging of a biomolecule reveals its intricate internal structure. Until now, scientists have only been able to see an outline. Such information could be a major boost to the study of viruses.

THIS method is an entirely new approach to a decades-old problem and is bound to revolutionize the field of solution scattering and have a significant impact in other imaging fields, too,” says Dr. Grant.

Rather than visualizing only the outline of a molecule, such as a virus, Dr. Grant’s new method will allow scientists to see inside the molecule to better understand how genetic information is arranged, potentially giving insight into how the virus injects this information into its host.

Grant’s method has solved the phase problem for a particular molecular determination technique called “solution scattering.” The phase problem is akin to having a camera that accurately records all the intensities of each pixel, but scrambles where those pixels are, based on a complex mathematical equation. What remains is a useless, scrambled image.

“Scientists,” Grant says, “have typically worked to decode that mathematical equation by changing the image bit by bit to make sure it looks approximately as they would expect. For example, in a landscape photograph, the blue pixels depicting the sky should naturally be at the top. Solving the phase problem is like being able to place all the pixels where they are meant to be.”

Most protein structures today are solved using X-ray crystallography, a

technique that HWI has spearheaded for decades, where crystallized proteins scatter X-rays in patterns on a surface. These patterns, consisting of hundreds of thousands of unique pieces of information, are captured, ultimately revealing the structure at high resolution.

The drawback to this method is that more than 75 percent of proteins do not readily form the ordered crystals needed. That means many key elements of our bodies are difficult to visualize in three dimensions. Additionally, such proteins can exhibit motion, giving us clues as to how they function. Yet these motions are absent when structures crystallize. A workaround for this obstacle is solution scattering in which X-rays bounce off molecules floating in a fluid, rather than traditionally used crystals.

Grant developed a new algorithm enabling reconstruction of a three-dimensional image of a molecule, similar to a 3-D rendering of the brain produced by a CT scan. It’s analogous to the recognition possible when all of a person’s facial features are visible as opposed to just their silhouette. His method builds on similar principles developed by HWI’s own Dr. Herbert Hauptman. These principles, called direct methods, solved the phase problem for crystallography and subsequently won Hauptman the Nobel Prize in Chemistry in 1985.

“Grant’s method for recovering a 3-D map of randomly-oriented molecules in solution without modeling is a big advance on earlier methods,” notes John Spence, PhD, Director of Science for NSF BioXFEL, Richard Snell Professor of Physics at Arizona State University, and one of the world’s foremost experts on using X-ray lasers for structure determination. “We can now potentially determine structures for proteins that cannot be crystallized under natural conditions. This should have wide impact.”

“Grant’s method for recovering a 3-D map of randomly-oriented molecules in solution without modeling is a big advancement on earlier methods.”

— John Spence, PhD
Director of Science for NSF BioXFEL,
Richard Snell Professor of Physics
at Arizona State University

A new ally joins THE FIGHT AGAINST CANCER



“When I saw an opening at HWI, I was very excited. I knew from my own experience that it is a superb center for structural biology that focuses on cutting-edge crystallography as a means to study the foundation of disease.”

This summer, Aviv Paz, PhD, joined the ranks at HWI to lead a new research group studying proteins that are essential to understanding how cancer works – and how better to fight it.

What drew you to HWI?

I heard of HWI in 2013 while I was working on a difficult research problem that was yielding poor results with the resources available in the lab I was in. To increase our chances of success, we reached out to HWI’s High-Throughput Crystallization Screening Center, which had the tools and the expertise to improve our potential outcome. A huge obstacle researchers in my field have to overcome is getting a protein – the machines in our bodies – to form a crystal. We aim to form crystals because they allow us to study proteins in detail and determine their shape with the use of X-rays and mathematical formulas (Herb Hauptman was the genius behind the math). HWI is one of a few places in the world that can take a protein and experiment with it in 1,536 different solutions to see what is effective in forming a crystal. In the case I mentioned, the screening facility at HWI allowed us to identify a

condition that achieved a fine crystal, then solve the protein’s structure and publish the study.

When I saw an opening at HWI, I was very excited. I knew from my own experience that it is a superb center for structural biology that focuses on cutting-edge techniques and technology as a means to study the foundation of disease. In my PhD and ever since I have focused my studies on medically critical targets using biochemistry and structural biology. The overlap between HWI’s mission and my own vision motivated me to seek a position here.

Can you explain to the layperson the value of the research you are pursuing?

Cells of animals, plants, yeast, and bacteria are separated from each other and from the environment by lipid membranes. These membranes act as a barrier that is impermeable by many materials such as nutrients and drugs. Within these membranes are highways

of sorts – we call them channels – that transport things in and out. When we can visualize these highways, we can better understand how they function and design drugs to treat numerous conditions like depression, diabetes, and obesity. My work is centered in this area, primarily on cancer.

In my new lab at HWI, I am focusing on transporters that shuttle a wide variety of molecules in and out of our cells. These transporters are involved in myriad cellular processes in both healthy cells and cancerous ones. Revealing the structures of these transporters and how they function will greatly

facilitate our understanding of how they work well, and how they fail us – leading to a disease state. Our work will open up many new opportunities for drug development and for the treatment of cancer.

How does a self-directed research program suit your style compared to a more structured environment?

I enjoy a high level of autonomy to plan and execute my research projects, as it allows me to be creative in problem solving. An independent institution offers me the freedom to self-direct my research and not be burdened by layers of bureaucracy.

I am happy to have found an organization in which I can be driven by my own unique questions, but still have the benefits of collegiality amongst our research teams.

What are your career goals?

In the short term I would like to accumulate enough structural and functional data on transporters that would provide me with a clear picture of how they work. In turn, this knowledge would serve as the basis for one of my longer-term goals: the development of drugs or targeting of drugs for the treatment of cancer. This could be done by stopping unwanted cancer-related transport processes or

by designing novel, effective drugs. Additionally, working with human membrane proteins is extremely challenging due to their inherent instability. I believe that there is room for developing new genetic and biochemical tools that would push the field forward. I am in a place where I have the tools to do just that.

Dr. Paz’s wife Neomi joined him in the move to Buffalo along with their 11-year-old daughter Shir and 6-year-old son Eilon. Buffalo and Western New York are very different from all of the places he has lived so far, but he is looking forward to experiencing the local cuisine, hiking trails, ski slopes, and the changing seasons.

Fifth Annual NSF BioXFEL International Conference grows into premier event

Top researchers, students, and postdocs from around the world gathered in New Orleans in mid-February to share results and form collaborations with significant scientific potential.

“OUR goal is to be considered the premier X-ray Free Electron Laser (XFEL) conference, and I think we are accomplishing that,” says Erin Uppington, NSF BioXFEL’s Associate Director of Administration. “We aimed to have the latest, most exciting results from top international researchers, and have achieved that. Keynote speakers tackle issues of diversity in STEM fields guiding students and investigators through potential obstacles in their careers. Professional development seminars expose students to career choices in science and enhance technical skills such as grant writing. Networking is a significant focus of the event and we’ve seen new global collaborations born as a result. As new facilities in our field come online around the world, relationships forged at this meeting are critical to novel advancements.”

Session topics included Exploiting the Time Resolution of Serial Femtosecond Crystallography (SFX), Using XFELs on Non-crystalline Targets, Getting Sample to the Beam, New Applications in SFX and New Measurement and Analysis Strategies.



The 2018 event gathered 155 participants from 19 countries including Australia, China, Germany, Hungary, Japan, Korea, New Zealand, Puerto Rico, Switzerland, and the United Kingdom in New Orleans, Louisiana.



BioXFEL exhibit reaches tomorrow’s scientists

Last spring, Hauptman-Woodward Institute unveiled a new permanent display at the Buffalo Museum of Science that gives young visitors a chance to discover proteins through play. The interactive BioXFEL (Biology with X-ray Free Electron Laser) exhibit connects HWI science with concepts kids are learning in school.

“The installation is designed to teach students about the science that we do, including the basic principles of how we collect data, what we do with it, and why,” says William Bauer, PhD, a research scientist at HWI. “There are a few components to the display, including posters that explain how we use X-rays instead of microscopes to look at molecules, because they’re too small. There’s also a touch screen that offers a quiz based on information found within the display, or it can be switched over to our game mode.”

The museum exhibit also features a hands-on simulation using a “protein crystal” (actually a diffraction grating) that is hit with “X-rays” (a green laser). The X-rays bounce off the crystal and make a diffraction pattern. So far, the hands-on elements have been especially popular with students in middle school and up who have a few years of STEM under their belt.





ON THE COVER

Celebrating Women in Science

Facing the challenges, making a difference

For centuries, women have made significant contributions to science despite facing many barriers, both personally and professionally, along the way. In the late nineteenth century, as the opportunity for women to attend college and advance their education increased, more jobs for women scientists became available. Marie Curie advanced not only science, but also women's place in the scientific community, becoming the first woman to be awarded a Nobel Prize, the first person to be awarded two of them, and the first of only two people to win a Nobel Prize in two different fields (Physics, 1903 and Chemistry, 1911).

In 1956, Dr. George Koepf had a vision of opening an institute that would specialize in basic research which he believed vital to improving human health. One of his patients, philanthropist Helen Woodward Rivas, shared his vision. With her donation of \$3 million (equivalent to \$28 million today) Dr. Koepf was able to found the Medical Foundation of Buffalo. Now known as the Hauptman-Woodward Medical Institute, this organization is well regarded in the national and international science community for cutting-edge medical research. Through the years, women scientists have contributed greatly to the success of the Institute. We are proud to highlight several of them. ▶

Noteworthy women in science and HWI researchers, pictured above from left to right:

Marie Curie, Sarah Bowman (HWI), Kristin Sutton (HarkerBIO), Dorothy Hodgkin, Josiris D. Rodriguez Perez (NSF BioXFEL Science & Technology Center), Linda B. Buck, Nanette Que (HWI), Vivian Cody (HWI), Barbara McClintock, Rosalyn Sussman Yalow, Dorita Norton (HWI) Ada Yonath, Gertrude B. Elion, Jane Griffin (HWI), Gerty Cori.



Sarah E.J. Bowman, PhD

HWI Associate Research Scientist

Sarah Bowman's first college degree was in English literature and women's studies. After a few years working at a bookstore in Denver, CO, she enrolled in a chemistry class that ended up changing her life.

"I didn't like science in high school," says Dr. Bowman. "Then, after I already had a degree, just for curiosity, I took this general chemistry class that completely opened my eyes to the wonder of atoms and molecules. It's like a whole world opened up to me, and I haven't looked back since." She went back to college and earned a second Bachelor's Degree in Chemistry from Metropolitan State College of Denver, followed by a PhD in Chemistry from the University of Rochester, where she worked in Professor Kara Bren's laboratory. Dr. Bowman then went to Massachusetts Institute of Technology, where she started working in protein crystallography with Professors Catherine Drennan and Collin Stultz as a NIH-NRSA Ruth L. Kirschstein Postdoctoral Fellow. She joined HWI to direct the High-Throughput Crystallization Screening Center, which works with scientists from around the world to find new ways to make protein crystals. Her research focuses on investigating the role of metals in biology using protein crystallography and spectroscopy.

"Working at the Institute has been a great experience for me," says Dr. Bowman. "I am surrounded by so many gifted scientists doing great work, and there's so much flexibility here to explore and grow."

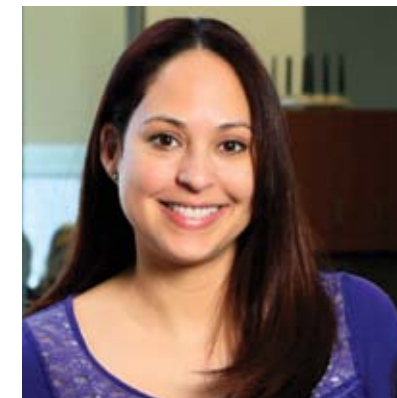
Her background makes Dr. Bowman very aware of the continued challenges that women face in the sciences, including both outward and subtle discrimination and harassment. She has been blessed to have been mentored and advised by many strong, successful women in science throughout her career, and that has fueled a passion to make science and STEM disciplines more accessible to women and underrepresented minorities.

"Teaching science by memorization of facts versus exploring the beauty and wonder of everything from a scientific perspective is a disservice to students," says Dr. Bowman. "I try to interact with the students I mentor, giving them hands-on experience that engages their curiosity and interest. And I think it is important to let them know that they can change their path to do something they have discovered that they love."



"I try to interact with the students I mentor, giving them hands-on experience that engages their curiosity and interest."

"You can see the trend that more women are getting the training and skills they need to pursue a career in STEM, and it's great that it's changing."



Josiris D. Rodriguez Perez

NSF BioXFEL Scholar

A native of Puerto Rico, "Josie" Rodriguez Perez always liked science. A professor at the University of Puerto Rico, where she obtained her chemistry degree, told her she was very observant and should do research, words of encouragement that sparked her career path. Her parents were supportive, but hesitant at first, worried that she might not achieve her career goals and that she was studying too much. Eventually they saw how happy she was and quickly turned around.

Rodriguez Perez, who is in the early stages of her career, says she has definitely observed a field still largely dominated by men, and would like to see more women scientists in roles as speakers, mentors, and researchers.

"I would like to see more women in science, particularly more Latin women," says Rodriguez Perez, who credits her confidence and success to female professors who supported and mentored her. "You can see the trend that more women are getting the training and skills they need to pursue a career in STEM, and it's great that it's changing."

Josie completed a graduate internship at the University at Buffalo's NSF BioXFEL Science & Technology Center that she said was "life changing," working on a project related to her doctoral thesis (she is currently working toward her PhD through the University of Puerto Rico). She wants to continue working in crystallography, incorporating the XFEL research. She credits HWI with supporting her studies and says the opportunity to work with scientists at the Institute has greatly improved her research.

"I have so much opportunity at HWI in terms of funding, access to equipment and technology, talented, experienced colleagues, and the flexibility I need to complete my studies while raising my family and dividing my time between Buffalo and Puerto Rico," she says. "I am hoping to finish my PhD this year, and am looking forward to the opportunity to continue working with the Institute. My husband and I love Buffalo."

Vivian Cody, PhD

HWI Principal Research Scientist Emeritus

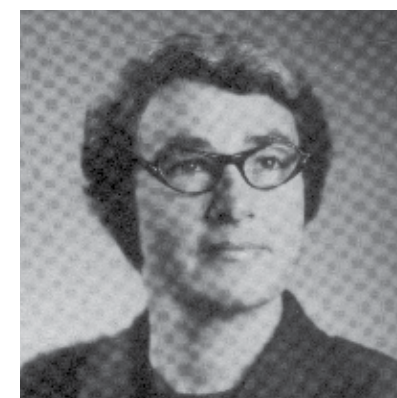
When Vivian Cody was working toward her PhD in Chemistry from the University of Cincinnati, she encountered professors who were quite proud she was the only female in the class – and professors who would point at her and tell her they didn't need her to be there. She was asked questions such as, "Why aren't you home baking cookies?" and "Why are you trying to take a man's job?" She was told many times, "Go home, you're not good at this!"

"These were the typical ups and downs women dealt with in those days, but it gave me an accurate glimpse of what it would be like pursuing a career as a woman scientist," says Dr. Cody. "It just made me dig in my heels and work all that harder." She's glad she did.

During her 46 years at the Institute, her major specialty was crystallography and endocrinology. "My first endocrine focus was on the thyroid and thyroid hormones, which I knew nothing about," says Dr. Cody. "I had to immerse myself to write a grant, which we eventually got." She found everyone, particularly Dr. Hauptman, to be very supportive. "All the doors were open to me. I was welcomed at meetings, asked to present papers at conferences, and included in some very interesting projects."

She thinks part of the reason so many opportunities exist for women in crystallography is that it involves attention to detail, and a lot of number crunching – two things at which women typically excel. "Today, women are more accepted in the field of science, but there are still challenges. I tell young women they can absolutely achieve their career goals in this field if they work hard enough and are up to the challenge."

She was asked such questions as "Why aren't you home baking cookies?" and "Why are you trying to take a man's job?"



Dorita Norton, PhD

Crystallographic Research Director, Medical Foundation of Buffalo

Dorita Norton received her Bachelor of Science degree from Columbia University and her PhD from Bryn Mawr in the late 1950s. While at Roswell Park Comprehensive Cancer Center, she worked on steroid hormones and authored or co-authored more than 50 scientific papers. Dr. Norton was also a professor in the Biophysical Sciences at the University at Buffalo, and directed summer programs in X-ray crystallography for gifted high school students.

In the late 1960s, Dr. Norton and her staff transferred to the Medical Foundation of Buffalo (now the Hauptman-Woodward Medical Research Institute). She was inspired to come to the Foundation because it was founded through a large donation from a woman with a thyroid problem, Helen Woodward Rivas.

During the last three years of her life, Dr. Norton established a center for molecular endocrinology. By 1968 she began a collaboration with Dr. Herbert Hauptman on the application of direct methods to steroids and the structures of steroid hormones, specifically a hormone that may be involved in the spread of some breast cancers.

"Dorita brought crystallography to the Foundation, and her work in crystallography was groundbreaking," says William Duax, PhD, HWI Principal Research Scientist Emeritus, whom Dr. Norton hired at the Foundation. "She faced the challenges of women of her time – and women today – who pursued science careers, but she persevered and became a valued role model for the women who came after her," says Dr. Duax.

"Dorita brought crystallography to the Foundation, and her work in crystallography was groundbreaking."

Jane F. Griffin, PhD

HWI Principal Research Scientist Emeritus

Jane Griffin believes that women are attracted to X-ray crystallography partly because of the beauty and symmetry of the science, but also because many of the scientists making major contributions to the field from the beginning in 1912 were women who served as role models for those who followed. Griffin's first role models were her two older sisters, who both had studied chemistry in college and graduate school.



Dr. Griffin began her graduate degree in chemistry at the University at Buffalo after being out of school for 10 years raising a family. In her first year, she heard a lecture by Professor Philip Coppens, who later became her research advisor, where he showed pictures of the electron cloud that forms the bonds between atoms from his experiments in X-ray crystallography. She was hooked. Following her degree, she joined the Medical Foundation of Buffalo, now HWI, and has retired after 42 years at the Institute. Dr. Griffin credits Dorita Norton with bringing crystallography to the Institute and with hiring women scientists.

"Dr. Norton was a visionary," says Dr. Griffin. "She wanted to get a 3-D picture of important endocrine hormones in the body to help explain how they worked. Some of the hormones had only recently been discovered. At the time even a small hormone was a difficult problem to be solved, but she realized that in time even proteins would be visualized, and she was right."

As a Buffalo native, Dr. Griffin finds it amazing that she had a career working with Dr. Hauptman, a Nobel Laureate; Dr. Coppens, a leader in the field; and Dr. David Harker, an early giant in the field –

without ever moving from her hometown. That is extremely rare for a scientist. Although she is now retired, Dr. Griffin's work is still being cited, which she finds very gratifying.

In contrast, when she was in graduate school in the late 1960s and early 1970s, there were no women faculty in the University at Buffalo chemistry department and some professors refused to mentor women. This is one reason why she took an active role in the Institute's college and university internship program.

"I encourage young women to become scientists if they have a passion for figuring out how nature works, especially the workings of the human body," says Dr. Griffin. She also recommends internships for all students as a reality check on what is actually involved. "Science is a wonderful field. You can collaborate with people all over the world and really make a difference."

"Science is a wonderful field. You can collaborate with people all over the world and really make a difference."

One woman's vision



HWI has always relied on the intelligence and vision of women scientists whose work in foundational research has advanced medicine around the globe. This work wouldn't be possible without Helen Woodward Rivas, who understood the value of this groundbreaking research and supported it generously. Her gift of \$3 million in 1956 – an amount equivalent to \$28 million today – helped launch the institute that now bears her name.



Partnership in a TIME OF NEED

When Hurricane Maria ripped through Puerto Rico last September, the category 5 storm did more than damage the U.S. territory's homes, businesses, and infrastructure. For graduate students at the University of Puerto Rico, the hurricane also wiped out their research and the opportunity to continue their studies.

HAUPTMAN-WOODWARD Institute heard the news and wanted to help, and secured a grant from the National Science Foundation to bring several doctoral students to scientific institutions on the mainland to continue research while their community rebuilt. HWI, in partnership with the University at Buffalo, leads the NSF Science & Technology Center BioXFEL consortium that includes Arizona State University, University of Wisconsin-Milwaukee, Cornell University, and Stanford University, among others.

"After seeing the devastation caused by Hurricane Maria, we knew we had to act quickly to help our colleagues and friends. We moved fast to shift initiatives to focus on relief efforts and provide necessities," says Edward Snell, PhD, Principal Investigator of NSF BioXFEL and Chief Executive Officer at HWI.

In addition to loss of essentials like access to water and being displaced from their homes, the students also lost months of research as power loss impacted the labs where their research was housed.

"We knew we had to act quickly to help our colleagues and friends."

"There was so much devastation, we first and foremost wanted to focus on peoples' safety and wellbeing," says Dr. Snell. "At the same time, we had a portion of our team thinking about their research and how we could get people off the island to resume their important work."

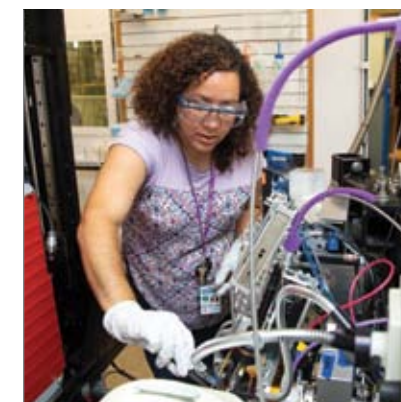
Four student researchers traveled to Buffalo with their families, while five others went to Stanford University. The accommodation of students at these institutions allowed them to spend four months continuing groundbreaking work largely focused on studying protein structures and looking at the role of proteins in diseases such as breast cancer.

"All of the students were able to collect data and advance their thesis projects while they were here," says Bill Bauer, PhD, Associate Education and Diversity Director at NSF BioXFEL. "Most of the students were near the end of their graduate



careers and some have since defended their theses at the University of Puerto Rico. For a few of the students, we extended their stay because it was still difficult for them to do their research in Puerto Rico. The science buildings still haven't fully recovered; a lot of their equipment was damaged because the air conditioning couldn't function and mold took over."

While the National Science Foundation grant and the generosity of the Buffalo community allowed the researchers to come to HWI immediately, the relationship between the institutions has been ongoing for years. HWI also partners with the University of Puerto Rico to offer students a graduate internship program, fellowship program, summer internship for undergrads, customized science workshops, and travel scholarships to attend conferences.



Top: HWI invited four University of Puerto Rico graduate students to continue their research here.

Above: Five other University of Puerto Rico students continued their research at Stanford University in California.

Facing page: While research buildings remained intact, weeks without electricity destroyed refrigerated samples and rendered equipment useless.



A place of honor for the late Robert J.A. Irwin III



When Robert J.A. Irwin, beloved emeritus board chairman of the Hauptman-Woodward Medical Research Institute, passed away on January 9, 2017, it didn't take long before the question was posed: How can we appropriately honor a man who was so deeply connected and committed to HWI and the organization's mission?

A WELL-KNOWN businessman and philanthropist who also served as Director and Treasurer of the James H. Cummings Foundation for many years, it's impossible to look around the Institute without noticing Mr. Irwin's presence.

"He truly understood the need for both not-for-profit research and philanthropy in our community," notes HWI Emeritus Chair Christopher Greene, Esq.

After consultation with leadership at the James H. Cummings Foundation, the decision was made to memorialize Mr. Irwin with a physical space at HWI that would remain in perpetuity and honor his legacy. The

generosity of the Foundation created a space that is now known as the Robert J.A. Irwin III Conference Center. The new center is located directly across from HWI President and CEO Dr. Edward Snell's office and was designed by Maddy McCauley of Madelena Lee Design, LLC in Orchard Park, NY.

Unlike traditional board and meeting rooms that can be somewhat stuffy and intimidating, the Irwin Conference Center has an inviting, comfortable atmosphere. Incorporating books that once belonged to Dr. Herbert Hauptman, multiple awards bearing his name, and some of Dr. Hauptman's own

stained glass sculptures, it is space that invites visitors to roll up their sleeves and get to work. State-of-the-art technology features make the space cutting-edge, and it has become essential in connecting HWI in a sophisticated way with its numerous global partners.

"The National Science Foundation BioXFEL Science & Technology Center is a primary user," says Jill Szczesek, HWI Chief Operating Officer. "We coordinate and deliver regular webinars for a group of PhD students and postdoctoral scholars from across the globe. Our CEO Ed Snell uses it when he collects data on his experiments on the International Space Station. The technology in the room allows people to present to each other with ease and the interactive monitor allows them to really interface. Science is global and we reach our international partners and build collaborations with these tools."

The James H. Cummings Foundation has been a loyal and generous supporter of the Institute's mission for decades and this new space is yet another example of that. HWI recognized the Foundation's longstanding friendship and philanthropy with an award at HWI's 60th anniversary gala in 2016.

"The James H. Cummings Foundation was established to support the philanthropic vision of its namesake," says Mary Jo Hunt, the Foundation's Executive Director and Secretary. "Our relationship with Hauptman-Woodward Institute began with the first grant in 1968 for an ultraviolet spectrophotometer. Over the last 50 years, the James H. Cummings Foundation has contributed almost \$3 million to support the groundbreaking work of HWI researchers in crystallography and

structural biology. Robert J.A. Irwin III joined the James H. Cummings Board in 1978. At that time he was also a member of the HWI Board of Directors. The Cummings Board wanted to honor the memory of Bob and recognize his decades of service to the Foundation. Doing something with HWI seemed a logical fit."

It's the kind of room that makes you want to roll up your sleeves and get to work.

"The educational videoconferencing center was the perfect fit with the Cummings' focus on medical research, science, and education," adds Charles Kreiner, President of the James H. Cummings Board. "We are thrilled that researchers, students, and staff will be able to exchange knowledge with others through the use of this room."

When not booked internally, the Irwin Conference Center can also be utilized by outside organizations.



Maddy McCauley found Dr. Hauptman's books to be an inspiration as she designed this wired and inspiring space.

HWI welcomes new board members



Michelle Heffernan

Retired from Bond, Schoeneck & King, PLLC, Heffernan’s career focused primarily on retirement plans, executive compensation, and employee benefits in acquisitions and divestitures.

Her introduction to HWI

Heffernan worked with HWI during her entire career as a lawyer; one of her first assignments fresh out of law school in 1975 was a project for HWI. The law firm she joined had represented HWI since the research institution was founded. When the attorney who served as counsel to HWI retired from the position about 12 years ago, Heffernan served as Institute counsel until her own retirement.

What she finds most compelling about the organization

“I have always thought HWI is a very valuable organization in the role it plays in basic scientific research. It is an exciting place to be because of the work people do. It provides a lot to the

city by virtue of its reputation, being able to attract talented scientists, and what it gives back through the research it does. After I retired, I thought it would be great to continue working with HWI in a different capacity as a board member.”

The part of her board service she is most looking forward to

“I am interested in the governance aspect; I am very familiar with the organization’s structure, and that is a role in which I would have something to offer. I am of course happy to do other things as well.”

Her perception of the public’s understanding of HWI’s work

“There are certain aspects of the population that are familiar with

“I have always thought HWI is a very valuable organization in the role it plays in basic scientific research. It is an exciting place to be because of the work people do.”

what we do, but we could better tell our story through the medical campus because it does attract so much publicity. Being part of the bigger picture would be a great way to let people know this basic research is being done right here in town, and what that means for applied research – you cannot create drugs without the basics first.”

William Constantine works at 19/19 Investment Counsel, Inc. as Managing Director, where he oversees portfolio construction and ongoing monitoring for individuals, families, foundations, endowments, and institutional clients.

His introduction to HWI

William’s sister-in-law and HWI Emeritus Chair Constance Stafford Constantine invited him to become involved with the organization 20 years ago as an annual donor. Recently his niece and goddaughter, HWI Board Member Emily Constantine Doren, encouraged him to join her on the board of directors.

What draws him to the science

“I am a trustee of NYU Medical Center and the Bellevue Association. To me, there’s a tie between those organizations and HWI; all center around health and investment in the sciences. When I joined an auxiliary of Bellevue Hospital in 1978, the experience introduced me to the importance of public health and the role of a big public health system. A few years ago, I was in a meeting where they talked about the one Zika patient who was being treated in New York. As big as Bellevue is, we had to draw from 12 area hospitals to provide 24-hour care for one patient. Had there been a national outbreak, there wouldn’t be enough doctors and nurses to follow that protocol. Ultimately it came down to keeping the patient hydrated and outlasting the virus; we can do that in the U.S., but not in other countries. It underscored the fact that the important drugs are the ones that can reach millions of people.



William Constantine

True healthcare is about science, huge expenditures to devote to that science, and teaching so we have doctors and nurses who grow in knowledge. In a sense HWI is at the tip of that sword – they can develop something that’s useful and reach the public.”

His view of the Medical Campus role in Buffalo’s transformation

“It’s important to Buffalo to have a unique high-tech institute with international renown like HWI. I think the growth in Buffalo is spectacular. I had a job at the blast furnace at Bethlehem Steel in college; that was the height of the blue color jobs in 1965. In the last 10 years or so there have been hints of the value of Buffalo, its location on the border, the support of the Rich family, the Jacobs family, and the Pegula family – it means a lot for pride and branding in Buffalo. Families are supporting their city. Now everything is moving back

downtown – it’s interesting, and there are attractive new buildings. The Buffalo Niagara Medical Campus’s location is important; lots of extremely well-educated doctors and scientists are gathered together in one location.”

“True healthcare is about science, huge expenditures to devote to that science, and teaching so we have doctors and nurses who grow in knowledge. In a sense HWI is at the tip of that sword...”

FORM & FUNCTION



On Friday, October 12, dear friends and new faces gathered at Buffalo RiverWorks for the 9th Annual Riedel Tasting Experience to benefit the Hauptman-Woodward Medical Research Institute. The event raised over \$150,000, an incredible sum that exponentially supports HWI's essential work.

THE generosity of attendees and sponsors at events like this is the catalyst for HWI scientists to initiate new research projects. It gives them the seed funding needed to gather preliminary data and then move to securing federal funding for their important work," says HWI Advancement Officer Tod A. Kniazuk.

The theme of "Form & Function" is drawn from the notion that just as the structure of a protein defines its interactions with drugs, the shape of a glass influences the taste of its contents.

To illustrate this intriguing concept, David Christensen, Vice President of Riedel Retail Sales, led 350 guests through a series of tastings featuring two sparkling and two still wines. Each libation was served in a specific selection of Riedel glassware designed to highlight the flavor nuances of that particular beverage. Guests went home with a set of the four Riedel glasses featured during the event.

HarkerBIO Chief Scientific Officer Dr. Timothy Craig chaired the event along with his wife

Dr. Yangyang Zhao. He spoke eloquently about how important HWI's research is to the larger scientific community, and how integral this organization is to the Buffalo Niagara Medical Campus.

Ashley Rowe and Jeff Russo, news anchors from WKBW-TV, kept guests engaged and informed as emcees for the evening's program, while auctioneer Kelly Schultz took the helm for the live auction. Schultz stepped in last year for the iconic Cash Cunningham, who had served as HWI auctioneer for several years



and passed away in November of 2016. While Cunningham's shoes were certainly hard to fill, Schultz brought great enthusiasm and success to the event, and raised a significant portion of the evening's total proceeds.

This evening was made possible by presenting sponsor M&T Bank, who has shown generous support of this event since the beginning as part of their commitment to engaging with the community in meaningful ways.

Thank you to the generosity of our sponsors: Moog, Inc., Mr. and Mrs. David Pietrowski, Ferguson Electric, Lace & Day, Abino Mills Glassworks, Arthurs Malof Group at USB Financial Services, Bank of America Merrill Lynch, Buffalo Niagara Medical Campus, Delaware North, Georgetown Square Wine & Liquor, Grover Cleveland Press, Harter Secrest & Emery LLP, Imagine Staffing Technology Inc., KeyBank, Lace & Day, Life Storage Inc., Phillips Lytle LLP, and Roswell Park Comprehensive Cancer Center.

Clockwise from top:

The 2018 Riedel Tasting Experience featured sparkling wines and took place at a new venue – Buffalo RiverWorks.

Holly Constantine Ortman and Emily Constantine Doren, owners of Lace & Day with John G. Horn, HWI board chair and partner at Harter Secrest & Emery, LLP.

Hosts Jeff Russo & Ashley Rowe, WKBW-TV news anchors.

HWI researchers, Nanette Que, PhD and Daniel Gewirth, PhD.

At the heart of the “City of Good Neighbors”

As the first new construction on the Buffalo Niagara Medical Campus, Hauptman-Woodward has made being a good neighbor part of its mission.

DESIGNED by internationally awarded architect Mehrdad Yazdani, the Hauptman-Woodward Institute’s 73,000 square foot state-of-the-art research facility opened in 2005 and was the first new construction on the Buffalo Niagara Medical Campus (BNMC). The \$24 million structure was a remarkable achievement for the Institute, an effort championed by Constance Constantine, George DeTitta, Finley Greene, Jane Griffin, and numerous donors who worked as a team to bring it to life. From the start, the spirit of collaboration was instilled and the Institute has never strayed far from that original vision.

More than 10 years after its dedication, HWI continues to leverage the space as a way of engaging with the region – especially the businesses and organizations on the BNMC. The HWI community regularly hosts numerous organizations in its Flickinger Lecture Suite, Constance Stafford Constantine Atrium, and Donald and Victoria Hess Boardroom, to name a few. These on-site events have ranged from seminars with academic content to formal dinners, such as the inaugural dinner for the BNMC Rotary, and even casual, lively gatherings like the

BNMC’s Beakers and Beer series, which encourages conversation and collaboration amongst campus partners. “On campus alone we have approximately 10 different groups that utilize HWI’s space on a regular basis,” says HWI Chief Operating Officer Jill Szczesek. “As the Campus has grown in leaps and bounds, making our space available for organizations to interact, grow, train, and educate is important to us. We are committed to being a good neighbor and helping the Campus continue to attract the tremendous talent and collaboration we see expanding daily.”

The Institute is also home to Roswell Park Comprehensive Cancer Center’s spin-off OmniSeq, HWI’s own spin-off HarkerBIO and the American Crystallographic Association. Each of these groups add value to the intellectual interactions within the space and embody the entrepreneurial advances on the Campus.

For a list of upcoming activities at HWI visit hwi.buffalo.edu/events.

HWI’s central location on the Buffalo Niagara Medical Campus makes it an ideal gathering spot for scientific collaboration and events focused on both fact-finding and fun.



Since opening its doors in 2005, HWI has exemplified its commitment to entrepreneurship on the Buffalo Niagara Medical Campus by acting as a home base to Athenex; Roswell Park spin-off OmniSeq; and its own start-up venture HarkerBIO, which is growing by leaps and bounds.



Lewis and Harriett McCauley

HAUPTMAN SOCIETY MEMBERS



Lewis and Harriett McCauley at the McGard factory in Orchard Park, NY.

THE Medical Foundation of Buffalo was established with a generous gift of \$3 million from Helen Woodward Rivas in 1956 (the equivalent of \$28 million in today's economy). Her philanthropy set the foundation for what today is the Hauptman-Woodward Medical Research Institute as we know it – an institute committed to science and transformative research through education, discovery, and innovation.

As was true in 1956, HWI today relies on the generosity of contributors to support scientists and their research teams in finding the cures for tomorrow. Gifts to HWI are primarily utilized to initiate new research projects that begin with an intellectual Cure•osity and need more data to allow a scientific research team to secure federal funding for further investigation. HWI frequently cites that it is an enlightened philanthropist who not only recognizes this process, but understands the impacts support of this fundamental research will have for generations to come. Lewis and Harriet McCauley have been dear friends of the Institute in countless ways, with their support of these seed-funded programs being just one example.

"I'll always look back at my years on the HWI Board as rewarding in many ways. It was an honor to work with top local businesspersons and endless others who gave so much of their energy and treasure. My mixed contributions pale in comparison to those too numerous to list here."

– Lewis McCauley, Emeritus HWI Director

Married for 63 years, the McCauleys founded McGard LLC, a manufacturer of high-quality security products, wheel locks, and chrome-plated lug nuts, in 1959. What began as a small business on Niagara Street in Buffalo employing five people evolved through work ethic and family commitment into a multimillion-dollar corporation headquartered in Orchard Park, NY. The company now employs approximately 600 individuals in Western New York and a total of 800 worldwide with operations in Germany, Japan, and Malaysia.

Lew McCauley recalls how he first became aware of HWI more than a quarter century ago when he was approached by now fellow Emeritus Director Albert Wright III. "Bert came to me and said he'd like me to join the board at HWI," Mr. McCauley recollects. "I said OK, but I was not sure if I had even heard of

HWI at that point. It was an amazing chapter as I reflect on it. I was there for 16 years and I really did enjoy that time and I grew to appreciate the impact the work being done has on advances in medicine."

Harriett has grown to respect the research being done at HWI as much as her husband and made it a point to attend as many open house events and other functions as possible. She was and is always ready and willing to assist, and would even come in to write personal notes on annual appeal letters.

When asked why they chose to recognize HWI in their philanthropic efforts, Lew jokingly stated, "Number one, because they can use it!" Then with seriousness, "The organization is efficient in its operations, was home to Buffalo's only Nobel Laureate and their work is noble simultaneously."

The McCauleys are very pleased with the advances being made at HWI, on the Buffalo Niagara Medical Campus, and throughout the City of Buffalo. "I think the progress is wonderful and I believe it will last," Mrs. McCauley says. "You can see so much building going on, and Buffalo really needs it. The city has a lot to offer, not just the cultural attractions downtown but sports, music, art galleries, and more. I think any scientists thinking about moving here will find that Buffalo has a lot to enjoy, and their personal and research funds stretch further." Lewis and Harriet's support of the Institute and the community in which they grew their business is impressive. Their support of basic research at Hauptman-Woodward through the time they've invested, the advocacy they've engaged in, and their philanthropy are evidence of what is tremendous about our community.

Workshop shares

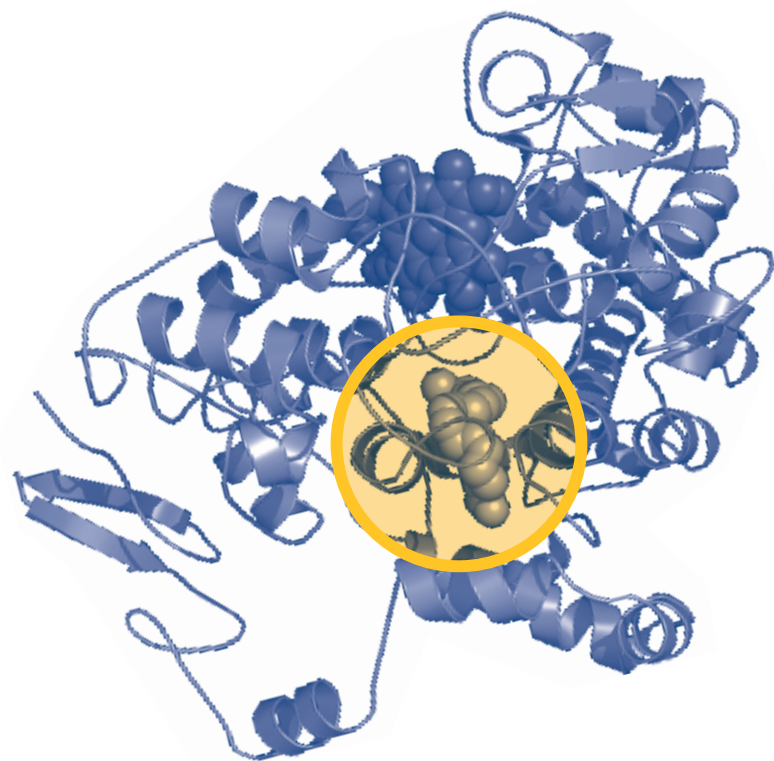
DISCOVERY & INNOVATION

with the next generation of scientists



Left: The goal of workshop activities was to supplement basic undergraduate education and inspire interest in this type of work.

Below: Students from area universities gathered for a three-day workshop, which included presentations by BNMC scientists.



Above: An example of how structural biology lays the foundation for the development of new and more effective drugs. Cyclooxygenase, an enzyme studied at HWI, is associated with the causes and symptoms of diseases, including inflammation, cardiovascular disease, and cancer. It is the target of medications like aspirin and ibuprofen. This 3D image shows how ibuprofen fits in the enzyme to stop a pain signal.

AN INNOVATIVE three-day structural biology workshop returned to HWI for the second time in August, growing in size from its inaugural year and welcoming a mix of interns and college students from Buffalo State, Canisius College, SUNY Fredonia, and the University of Puerto Rico.

“Over the three-day event we gave the students a primary in structural biology,” says facilitator William Bauer, PhD. “Most undergraduate institutions don’t offer a course in structural biology, yet it’s a big part of science and everyone wants to get a picture of what they’re working with – not just through X-ray crystallography, which is our primary technique, but other techniques as well. We introduced these students to the theoretical foundations of the field and even dove into more hands-on experiences with graphics software programs that we use daily to visualize proteins.”

Over the course of the workshop students were active participants in lab demonstrations setting up crystallization studies and growing crystals. They had the opportunity to implement different experimental variables affecting the crystal growth process and examine their results the following day. They were each able to grow a crystal and present the results to their peers. While the first two days taught valuable fundamentals for future research, day three gave student participants a broader look at the scientific activities happening right here in Buffalo.

“On the third day we had scientists from around the Buffalo Niagara Medical Campus (BNMC) come in and highlight some of the companies that are present here,” Dr. Bauer adds. “One of the things I realized after working here is that there’s not a lot of exposure to other research taking place on campus. So, we thought we should start at the

student level and make sure they’re educated about the opportunities that exist here in Buffalo. Everyone can see that the campus is expanding. That’s pretty obvious, but nobody knows what that means – does it mean that there are more jobs and that people are moving in to fill those jobs? We tried to give them a sense of what these companies do.”

Following the presentation by regional scientists, participants spent the afternoon touring several campus facilities. This activity sparked a second, standalone event held in May 2018 called BNMC Research Discovery Day designed for an audience of CEOs and directors from companies on Campus. Held at the new University at Buffalo Jacobs School of Medicine and Biomedical Sciences, the full-day event featured scientists talking with attendees about the research they do, plus a poster session that highlighted all of the services each company

provides in the hope of creating new collaborations between companies on the BNMC.

“A lot of people don’t know that Roswell Park offers over 50 core services to researchers in the area,” Dr. Bauer explains. “Before the poster session, I don’t know if I could have named five of them.”

Science increasingly becomes collaborative, the more accessible we make introductions, the more productive and successful we will be.

John Horn succeeds Judy Feldman as HWI Board Chair



Attorney John Horn served on the HWI Board of Directors for four years before being named chairman.

As **JUDY** Feldman completed her three full terms on the HWI Board, she passed the torch to current board member John G. Horn, Esq. to serve as Board Chair, adding to the four years of service and leadership Horn has shown to date.

During her tenure, Feldman was instrumental in reinvigorating the organization's strategic planning. She views the launch of the Fund for Cureosity as a way to bring exciting technology and new researchers to Western New York, was proud to see HWI's community relationships grow over the years as a founding member of the Buffalo Niagara Medical Campus, and is looking forward to seeing the organization's future impacts. Feldman was introduced to HWI quite accidentally, and formed a lasting relationship with the organization that she expects to continue long after her board departure.

"I met Herb Hauptman while I was swimming at the Jewish Center years ago – and I had no idea at the time that he was a Nobel Prize winner. He was so sweet. Later my son interned with HWI as a freshman in high school and interviewed with Herb Hauptman. I've always been a closet science junky so I asked to join the board, then got more involved over the years. I just love that this institution is in Buffalo. It's such a noble cause – very few places can say there is foundational research being done here. HWI's work impacts generations, and those who support this organization truly understand the science and what it means for the future."

John Horn's passion for the organization is rooted in similar sentiments. "Basic research is at the very foundation of creating cures for diseases that exist today and that we hope to eradicate in the future. Without this work being done at the molecular level, the cures that ultimately take shape through pharma companies will never happen. That's what I tell people is happening in that neat-looking building on the BNMC."

Horn, a business litigator at Harter, Secrest & Emery, LLP, was introduced to HWI in 2013 by Emeritus Director Joseph Voelkl. He mentioned to Horn that the board could use him, and once he met everyone and saw the work there, Voelkl did not need to do much convincing.

"Basic research is at the very foundation of creating cures for diseases."

– John G. Horn, Esq., HWI Board Chair

"We have an unbelievable group of talented and dedicated individuals all around – the scientists, leadership, board, and volunteers. We figure out how people want to serve, and then mobilize that energy and commitment. It's all about getting to know everyone's talent, sitting back to listen and understand where their concerns are, what gives them joy, and what is gratifying to them. There are too many boards where people want it on their resume, but they've underestimated the time and commitment. Here, that is not the case at all; we're as close to firing on all cylinders as you can get."

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Griffin and Feldman named emeritus members



Jane Griffin, PhD, an Emeritus Principal Research Scientist at HWI and Judy Feldman, Executive Vice President and Chief Information Officer of ValueCentric, have been named emeritus members of the HWI Board of Directors. Both gave generously of their time and energy on the Board for several terms, and will remain active with the Institute in the future. HWI is grateful for their service to the organization.



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