THE current

RESEARCH AND HAPPENINGS FROM RHODE ISLAND NSF EPSCoR | SPRING 2010

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RI NSF EPSCoR

THE current

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On the Cover:

An electron density map of an *E. coli* antitoxin protein studied by RI NSF EPSCoR graduate student Breann Brown (see page 11). Electron density maps are made with mathematical computer programs using X-ray diffraction patterns from a crystallized protein. They provide information about chemical bonding and other behaviors to form a protein's full 3-D structure, which provides critical insights into the protein's interaction and function.

Greetings From The Directors

Welcome to the Spring 2010 edition of *The Current*, the seasonal news magazine from Rhode Island NSF EPSCoR. This edition highlights our work in proteomics, the focus of one of our three Centers of Excellence (the other centers focus on genomics and marine life sciences).

Proteomics is becoming increasingly important in life sciences research and has a broad array of economically valuable applications. The RI NSF EPSCoR Proteomics Center is located in the area of Providence set to become the Knowledge District, a planned research-based hub for academia and industry, with the ultimate goal of advancing the state's economic development.

The Knowledge District is of keen interest to and is receiving strong support from Rhode Islanders and local and national leaders. For example, Congressman Jim Langevin and Providence Mayor David N. Cicilline recently toured the Knowledge District, including our Proteomics Center. Mayor Cicilline also visited our marine life sciences center and the genomics center located respectively at the URI Narragansett Bay and Kingston campuses. In November, Congressman Patrick Kennedy hosted the Chairman of the House Appropriations Committee, Congressman David Obey, for a day-long meeting on the Knowledge District. It is clear that the Knowledge District holds tremendous economic potential for our state, and that RI NSF EPSCoR will provide significant support for this initiative as it bears on the life sciences.

RI NSF EPSCoR has been busy during the first portion of our supplemental funding year. In January, we responded to NSF's clarification questions for our pending five-year proposal "Advancing Life Sciences in the Ocean State" and are looking forward to a positive response from reviewers in early June.

About NSF

NSF

In 1978, the National Science Foundation founded the Experimental Program to Stimulate Competitive Research (EPSCoR). EPSCoR stimulates sustainable improvements in academic science and technology infrastructure in states that receive low levels of NSF research funds. These investments create a foundation for economic growth based on science and technology. Several other agencies have also developed EPSCoR or EPSCoR-like programs.

welcome

SINCE OUR LAST ISSUE:

- Over 250 scientists, students, and administrators attended the 2009 RI Research Symposium. RI NSF EPSCoR researcher Dr. Bethany Jenkins of the University of Rhode Island gave a presentation and several EPSCoR affiliates and students presented posters.
- The Entrepreneurial Fellowship Program is underway with the Slater Technology Fund for the spring semester. We are looking forward to a more integrated program in this second year of training the knowledge entrepreneurs who will further develop the state's economy. We congratulate this year's fellows: Anup Mohanty and Steve Surrette of the University of Rhode Island, and Arjun Bansal, Naside Durmus, Vince Siu, and James Vecchione of Brown University.
- RI NSF EPSCoR can now be found on Facebook. Students, researchers, and others can become a fan of "Growing STEM in the Ocean State" to stay up to date with EPSCoR-related activities, events, and opportunities. Fans can also participate in discussions about topics such as scientific writing and the use of art in the visualization of science.

We hope you enjoy another issue of *The Current*.

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New Project Leadership

RI NSF EPSCoR welcomes Dr. Jennifer Specker, Professor of Oceanography at the URI Graduate School of Oceanography, as the Interim Associate Project Director through June 30th. Dr. Specker has served as the Director for the RI NSF EPSCoR Marine Life Science Center and has had a major role in our activities.

We would also like to welcome Dr. David Bogen, Associate Provost for Academic Affairs at the Rhode Island School of Design, and Tim Pelletier, EPSCoR Biotechnology Outreach Coordinator at the Community College of Rhode Island, to our Project Leadership Team. Their addition will further strengthen our relationships with both institutions.

In other news, we would also like to thank Dr. Kenneth Payne and Daniel Carrigg for their instrumental work with the RI NSF EPSCoR program. Both have taken positions at the State Department of Administration's Office of Energy Resources and we look forward to building partnerships in the critical arena of alternative energy in the Ocean State.

About RI NSF EPSCoR

RI NSF EPSCoR's mission is to create lasting improvement in Rhode Island's research infrastructure by advancing statewide innovation through strengthening Rhode Island's basic science and engineering research capacity and addressing Rhode Island's workforce needs using enhancement of science and engineering training and education for students.

THE RI NSF EPSCoR ACADEMY

The RI NSF EPSCoR Academy fosters the integration of research, education, innovation and communication statewide. It works to (1) Develop the human capital necessary to support and sustain the growth of competitive research capacity in the life sciences (2) Broaden the participation of women and underrepresented ethnic and racial minorities in the STEM workforce and (3) Develop and maintain sustainable communication mechanisms to build and enhance a strong statewide network of the state's and region's scientists, institutions of higher education, and private and public sectors.

RI NSF EPSCoR

Researching Cancer's Root Causes: Bongsup Cho

By: Sam Costello

Dr. Bongsup Cho, University of Rhode Island

Researchers whose breakthroughs lead to blockbuster drugs tend to get the most attention from the general public, but there's a second, less visible group of researchers that the first group depends on every day.

This second group focuses on understanding the basic mechanisms of how our environment and bodies work. Their discoveries are the foundations upon which other researchers base their breakthroughs.

Bongsup Cho, professor of medicinal chemistry at the University of Rhode Island, is proud to count himself among the second group.

"You really have to understand how things work in order to come up with some kind of prevention plan," he says.

The understanding that Cho seeks relates to one of the most serious and wide-ranging health issues of our time: cancer.

DNA DAMAGE AND THE CANCER LINK

Cho is investigating one of the fundamental causes of cancer: DNA damage. His research concerns naturally occurring or man-made chemicals including toxins and drugs that can damage human DNA.

"Once DNA is damaged, the cells have a defensive mechanism. If they see defective DNA, repair proteins come along and chop them off and synthesize new DNA," Cho says. "But the defensive system is not perfect. If the damaged DNA somehow escapes the repair process, then it can be used for replication … if that happens, then the mutation is copied over again and again."

These mutations are unpredictable – one type of DNA damage does not result exclusively in one type of mutation – and can lead to cancer.

Cho and his colleagues are studying small-molecule, DNA/protein, and protein/protein interactions at both biochemical and cellular levels to understand the connection between DNA damage and cancer.

"You have to understand how the carcinogens work to be able to come up with strategies for chemo prevention and novel drug discovery," he says. "You have to understand mechanisms to come up with ways to prevent certain processes."

To further this understanding, Cho uses two of the state's RI NSF EPSCoR core research facilities: the URI Genomics and Sequencing Center and the Proteomics Center located at Brown University in Providence (see Core Strength, page 6).

EQUIPPED FOR DISCOVERY

These facilities offer instruments key to Cho's research that aren't affordable for most researchers without initiatives like RI NSF EPSCoR.

"These things are not cheap," he points out, noting that some instruments used in his research carry price tags over $100,000.

"An individual grant would not allow me to purchase a machine like that," he says, adding that it could only be obtained through a core-facility initiative.

The availability of these instruments will help him advance his research.

"It's just very recently that those machines have become so sensitive that they can be used in biomedical sciences. It's kind of revolutionary," he says.

The facilities and instruments aren't the only things Cho appreciates about what RI NSF EPSCoR has helped bring to Rhode Island: He also praises the growing spirit of statewide collaboration.

"You have to understand how the carcinogens work to be able to come up with strategies for chemo prevention and novel drug discovery."

Though he's been at URI since 1991 (after conducting postdoctoral training at the University of Chicago and the Food & Drug Administration and a Ph.D. at the University of Illinois Medical Center in Chicago), only since the creation of the RI INBRE (Rhode Island IDeA Network of Biomedical Research Excellence; Cho is its program coordinator) and RI NSF EPSCoR core facilities has he seen connections with other universities deepening.

"Before (the core facilities), our connection to Brown and other universities was almost nil. It was mostly individual," he says.

Spreading the facilities across the state and among different higher ed institutions has been effective at promoting collaboration. RI NSF EPSCoR and the Rhode Island Science and Technology Advisory Council (STAC) have made major efforts in advancing statewide collaborative initiatives in research.

"People in Rhode Island get to know each other through these facilities. I think it's wonderful," he says.

HOPE FOR THE FUTURE

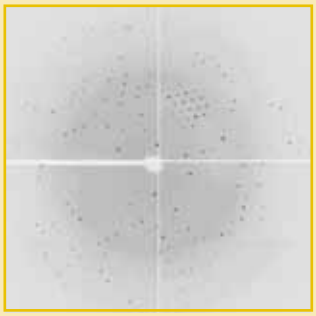
The local availability of these instruments has benefits not just for research, but also for education.

Cho appreciates that undergraduate and graduate students can get hands-on research experience on these machines. The machines' location also delivers test results more quickly; no more sending samples out of state and then waiting.

Among the benefits to education, collaboration, and research, Cho sums up the core facilities this way: "that facility has been a blessing for us."

As the facilities and Rhode Island's increasingly robust research community continue to develop, Cho's research could lead to greater understanding of the mechanisms of cancer formation and help point the way to an even greater blessing: a cure.

explainer



Proteomic experiments performed in the center allow investigators to identify specific protein molecules from complex mixtures.

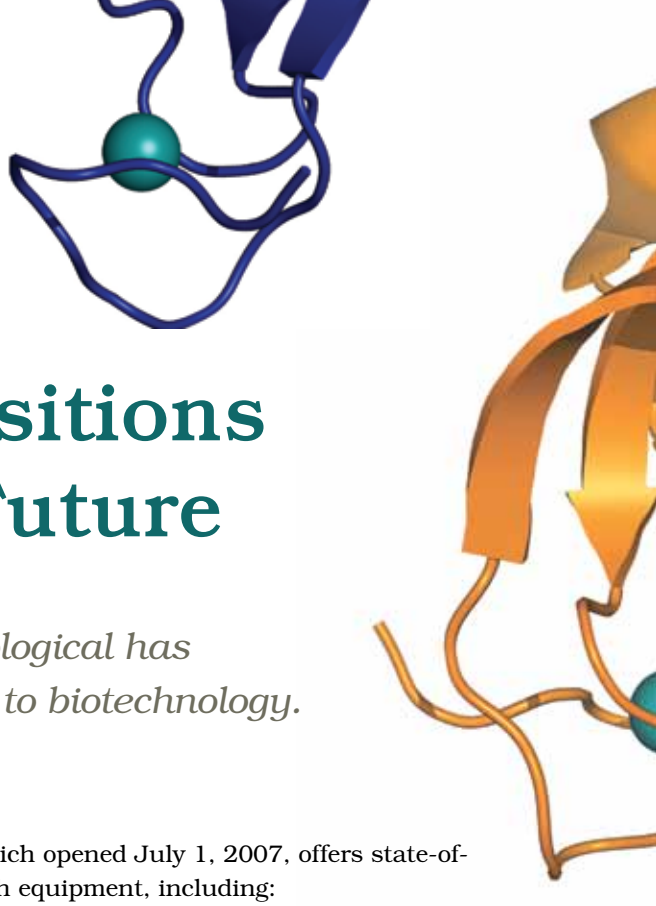
WHAT IS X-RAY CRYSTALLOGRAPHY?

X-ray crystallography is a method of determining the structure of a crystal; an advantageous method when studying large molecules like proteins. Determining the structure of a protein provides insight into its function and interactions with other molecules.

First, a pure, imperfection-free crystal of the target protein is made and mounted. Then a concentrated beam of X-rays hits the crystal as it slowly rotates on a platform. The diffracted beams cause a specific pattern of "reflections" on a detection film. A well-known X-ray diffraction pattern made by Rosalind Franklin was used by Watson and Crick to infer DNA's double helix structure.

Using X-ray crystallography to determine protein structure became a part of proteomics in the 1950s, with the modeling of sperm whale myoglobin protein. Today, X-ray crystallography is a standard method for studying protein interactions (see Spotlight, page 11).

Specific diffraction patterns and mathematical computer modeling software are used to make an electron density map of the protein (see On the Cover, page 2). Electron density maps, in turn, are used to determine the 3-D structure of the target protein. A protein's structure is critical information when studying its interactions and function.



CORE STRENGTH:

Proteomics Center Positions Rhode Island for the Future

Our ability to understand and manipulate the biological has increased dramatically in recent decades thanks to biotechnology.

By: Sam Costello

Biotechnology has affected nearly every aspect of our lives, from increased farm yields to new drugs to treat cancer, diabetes, and HIV/AIDS. Biotechnology's impact isn't limited to health and environment; it's also economic. BioWorld, an industry publication, reports that from 2003-2007, biotech companies received over US $100 billion in financing.

The biotech sector is forecast for continued growth, and, if a group of Rhode Island scientists, businesspeople, and politicians have their way, the Ocean State will flourish along with it.

A WELL-EQUIPPED FACILITY

A major building block of the state's biotech strategy is the RI NSF EPSCoR Proteomics Center. Located in a Brown University building in Providence, the facility could transform biotech research in Rhode Island.

Development of the facility was spurred by researchers who needed specialized equipment, according to Edward Hawrot, associate dean of the program in biology at Brown University.

"We realized that there really wasn't any place in the state of Rhode Island where this instrumentation was being assembled," says Hawrot, who is also a co-program director for Rhode Island NSF EPSCoR.

The majority of the facility's instruments were purchased using RI NSF EPSCoR's founding grant. Additional funding came from the Rhode Island Science and Technology Advisory Council, the Rhode Island Research Alliance, and Brown.

The facility, which opened July 1, 2007, offers state-of-the-art research equipment, including:

- Circular Dichroism Spectroscopy J-815
- Microcal VP-DSC (Differential Scanning Calorimetry)
- Isothermal Titration Calorimetry
- Surface Plasmon Resonance - Biacore T100
- Thermo LTQ Mass Spectrometer.

With such advanced equipment nearby, researchers from across the state are bringing their work – and their students – to the Proteomics Center. And though the facility is located at Brown, it is becoming a hub for the entire state's scientific community.

Buffer solutions are a key component to performing proteomic experiments in the center.

FROM MARINE RESEARCH TO DRUG DEVELOPMENT

The facility supports diverse research, from investigating heart drugs to antibiotic resistance, from phytoplankton behavior to cancer.

In addition to promoting research, the facility was also created with an eye towards economic development.

"We felt that a proteomics center might eventually be of use to companies interested in developing biopharmaceuticals," says Hawrot, adding that the facility contributes "critical baseline knowledge that pharmaceutical companies can build on to use in drug development."

Rebecca Page, a professor in the department of molecular biology, cell biology and biochemistry at Brown, is doing just that kind of work.

Page and her team (including Breann Brown, page 11) study protein interactions that affect biofilm formation from *E. coli*, which causes antibiotic resistance that reduces drug effectiveness.

"All the drugs that (people) take interact with proteins," Page says. "What pharmaceutical companies want to know is how drugs interact."

Research at the facility isn't limited to the pharmaceutical. It's also used in one of Rhode Island's traditional strengths and RI NSF EPSCoR's major focus: marine life sciences.

Among those researchers is Tatiana Rynearson, assistant professor of oceanography at the University of Rhode Island's Graduate School of Oceanography. Rynearson uses proteomics to investigate how phytoplankton – a fundamental part of the marine food web - respond to stress.

For John Williams, a chemistry professor at Rhode Island College, the proximity of the facility is particularly appealing, since it puts advanced tools in the hands of researchers and students who wouldn't otherwise have access to them.

Williams, whose research focuses on reducing the side effects of breast cancer drugs while maintaining their effectiveness, also says the facility prepares students for competitive graduate-degree and job environments.

Hawrot agrees: "We can have graduate students and undergraduates get hands-on experience with the instrumentation .... that's an important advantage."

TRAINING TOMORROW'S RESEARCHERS AND WORKERS

For Rhode Island to become a biotechnology hub, it will need well-trained students and employees. Thanks to the emphasis on hands-on research in RI NSF EPSCoR-supported programs, undergrad and graduate students across the state get substantial direct laboratory experience.

Real-world training is crucial, according to RIC's Williams.

"They're competing with students that have done research, that have some real hardcore, hands-on scientific background, and if they didn't have that, they would be disadvantaged in their applications," he says.

Employers appreciate this experience, he adds.

"We get this feedback all the time: 'This person actually knew what they were doing when they got here.'"

Dr. Rebecca Page explaining the value of the Proteomics Center to Rep. David Obey (D-WI), chairman of the U.S. House Appropriations Committee, and Rep. Patrick Kennedy (D-RI) during their Knowledge District tour in November. Photo by Frank Mullen

ECONOMIC DEVELOPMENT THROUGH RESEARCH

Not only does the facility help students attain better graduate placement and jobs, it keeps research dollars in state.

Before the facility opened, researchers sent their samples – and dollars – to labs in Boston, California, even Canada. With a facility in Providence, research dollars are kept in state.

Beyond serving local researchers, the facility could attract established companies, incubate start-ups, and attract government funding. This is a major goal of Providence's plan to transform the Jewelry District (where the Proteomics Center is located) into a campus-style Knowledge District.

That plan, which aims to make Providence a leader in biotech research and innovation, attracted former House majority leader Richard Gephardt, Rhode Island Representative Patrick Kennedy, and Providence Mayor David Cicilline to forum at the facility in December 2009.

At that event, Gephardt discussed National Institutes of Health plans to develop biotech research hubs.

"I think they want 60 or so," Gephardt said, according to the Providence Journal. "So, clearly, Providence and Rhode Island would be one of those. We have lots of problems, we have lots of research, we have lots of diseases. So we need places like Rhode Island to be one of those centers of excellence in research."

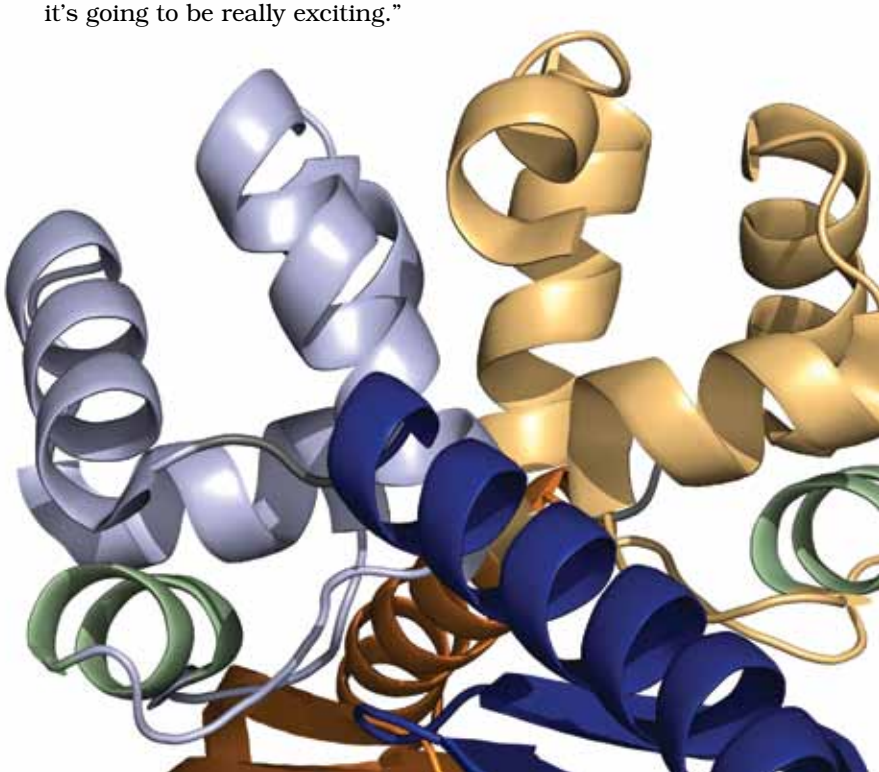
AN EXCITING FUTURE

With the Proteomics Center gathering a community of researchers, the next step is to spread the word and engage even more scientists, say Hawrot and James Clifton, the facility manager.

"The important thing is to get more people aware of what we can do for them and get more people in," says Clifton.

As that happens, researchers will be able "to apply the power of the technology here to any question that a researcher is interested in," according to Hawrot.

Brown's Rebecca Page is hopeful. The City of Providence "wants to make this a place that's not only enriched with academic research, but also industrial research," she says. "If this area becomes a center for biotechnology, it's going to be really exciting."



Engaging Students in STEM: EPSCoR & ETS

RI NSF EPSCoR recently partnered with the Rhode Island Educational Talent Search (ETS), a Community College of Rhode Island (CCRI) program, to engage Rhode Island middle and high school students in science and technology programs.

Dr. Beth Zielinski guiding ETS students through hands on forensics lab at Brown University.

A federally funded Department of Education TRIO program, ETS provides academic assistance and opportunities to middle and high school students to encourage them to graduate from high school and go on to college. ETS serves 750 students enrolled in 11 target middle and high schools in Central Falls, East Providence, Providence, and Woonsocket school districts.

Trained ETS counselors at all participating schools offer grade appropriate study-skill development and standardized-test preparation, information and one-on-one assistance on the college admissions and financial aid process, and career counseling. ETS students go on cultural field trips and college tours (like the visits with EPSCoR). ETS also provides crucial support: assisting students in securing financial aid through scholarships and application waivers.

The EPSCoR and ETS relationship has led to three college visits so far this academic year with more planned. In addition, future visits will engage more middle school students. This fall semester, seventy five high school students from Mount Pleasant, East Providence, Central Falls, Woonsocket, Hope, and Central High Schools visited Brown University, the University of Rhode Island, and Roger Williams University to spend a day immersed in college life and life science activities. Hands on lab activities have included forensics, molecular biology, and physiology topics.

›› more

ETS students extracting DNA during hands on lab at Brown University.

» in the lab

In November, students participated in a hands-on lab activity facilitated by Professor of Biotechnology and Medicine Dr. Beth Zielinski, toured campus and ate lunch at a dining hall in the heart of College Hill during their visit to Brown University.

Topics in Dr. Zielinski's courses range from stem cells to artificial body parts, and are enlivened by pop culture references to SpongeBob SquarePants and the OctoMom. Prior to Brown, Dr. Zielinski completed a post-doctoral fellowship for a laboratory that developed tissue-engineered artificial muscle for the study of atrophy in the aging populations and astronauts subject to zero gravity while on space missions. She also worked at the University of Rhode Island in their Biotechnology Manufacturing Program.

Participating ETS students had biology interests ranging from swine-flu vaccines to stem cells and DNA, which led to an experiment and a memento of the day.

Building on the students' interest in DNA, Dr. Zeilinksi discussed her work on forensic evidence with the Providence Police Department.

"When you leave, I could swab all the seats and determine where each one of you sat from skin and hair samples," she told the students.

This idea excited the students and provided a segue into information about DNA needed for the lab activity.

DNA provides the groundwork for an organism's characteristics. All cells in a body contain the same set of DNA – blood, hair, saliva, etc. In lab, the students swished water in their mouths and spit epithelial (skin) cells from their cheeks into a test tube. To get to the DNA in the cells, both the cell membrane and the nucleic membrane first had to be broken. Then, to get pure DNA, enzymes were used to separate out the attached proteins.

Usually, DNA is in a loose configuration and only condenses during replication. Ethanol (alcohol) was used in the lab to separate the DNA so it could be seen by the naked eye. Then the students got a souvenir to take home: their DNA in a necklace.

"It's kind of creepy, but it's fun! Very Angelina Jolie and Billy Bob Thornton," Dr. Zeilinksi says.

An important lesson for the students to take away from this experience that applies to all learning - especially science - was not to do anything unless you know why you are doing it, said Dr. Zeilinksi.

"Otherwise, you take away nothing," she reminded them.

Tim Pelletier, Outreach Coordinator at the Biotech Center at CCRI, emphasized that a wide variety of interests apply to biotechnology - not just laboratory science. Some other interests include graphic design, writing, computers, modeling, television and radio, and even freelancing. Biotechnology is a field with sustainable, high-paying jobs. Throughout the lab activity, Dr. Zielinski stressed the fact that almost anything in science requires biotechnology.

These visits and others supported by RI NSF EPSCoR and ETS will continue to advance STEM interests in middle and high school students from Rhode Island.

spotlight

Breann Brown, RI NSF EPSCoR Graduate Student

Originally from a suburb of Washington, D.C., Breann Brown came to Rhode Island to study proteomics at Brown University. Currently in her fourth year of doctoral research in the lab of Dr. Rebecca Page, she has the freedom to develop and carry out experiments that have led to published papers, as well as direct access to a mentor for guidance.

Breann Brown at her workspace in the Page lab.

In Page's lab, Brown is working on two research projects, both using X-ray crystallography (see Explainer, page 5), and regularly uses equipment at the RI NSF EPSCoR Proteomics Center.

The first project, for which she uses the facility's isothermal titration calorimeter to study protein interactions, looks at proteins in brain cells to determine how they interact with other proteins, which may provide insight into how they work.

"Determining how this protein functions will provide important information that may be useful for developing novel therapeutics for diseases such as drug addiction and schizophrenia," she says.

Through this research, Brown optimized a protocol for protein production that is suitable for structural studies. This work was published in the technical methods journal *Protein Expression and Purification*.

Her second project studies *E. coli* proteins in bacterial biofilms - communities of bacterial cells that adhere to a surface. Biofilms are responsible for the majority of infections and are notoriously resistant to antibiotics, a key function of the proteins Brown studies. Understanding how they work may be useful for developing new pharmaceuticals.

Brown determined the structure of a protein with a new folding pattern, as well as its structure when it reacts with another protein in a complex. These structures reveal the mechanism by which *E. coli* cell processes may change in the presence of antibiotics leading to resistance. For this research, Brown uses the circular dichroism spectrometer to determine whether binding proteins are folded – a critical preliminary step, since unfolded proteins typically do not crystallize. The results were recently published in the widely read *Public Library of Science Pathogens*.

In addition to her publications, Brown has presented her research at conferences including the Rhode Island Research Symposium, the Mid-Atlantic Macromolecular Crystallography Meeting, and the American Crystallographic Association Meeting.

Brown has always enjoyed science: "I enjoy learning about various laboratory techniques and instrumentation and then using them to apply to my projects. I would like to use the tools I am learning now and build on them."

But research isn't her only focus; she also enjoys working directly with young scientists.

"They keep you on your toes. Their questions help me realize what I know and what I don't," she says.

She mainly teaches students how to effectively communicate their research through proposal development, poster presentation, and scientific writing. She has been both a Senior Scholar through the Brown University Initiative to Maximize Student Diversity and a Graduate Student Advisor for the Leadership Alliance Summer Research Early Identification Program.

Her advice to young scientists is not to get discouraged.

"Science is very difficult by itself and sometimes other factors add to it. Confidence in yourself and your abilities is important no matter what other people may think."

RI NSF EPSCoR

Experimental Program to Stimulate Competitive Research

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Rhode Island's collaborative research network is represented by the state's two standing governance and advisory committees:

RI Science and Technology Advisory Council (STAC) provides oversight and governance for the program. Its government-appointed membership includes key leadership from government, local industry and institutions of higher learning. STAC ensures that RI NSF EPSCoR-funded programs are integrated and aligned with the state's research infrastructure and economic development objectives.

RI NSF EPSCoR Advisory Council serves in an advisory capacity to the RI NSF EPSCoR program and STAC. The Council is composed of individuals representing Rhode Island institutions of higher education who have expertise in life-science research, K-16 education initiatives and workforce development.

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