

MAINE

INBRE

IDEA NETWORK OF BIOMEDICAL RESEARCH EXCELLENCE

Planktonic Crustaceans Feed Brain Research



THE CHRISTIE LAB ABOARD THE *INDIGO* COLLECTING COPEPODS NEAR MOUNT DESERT ROCK,
25 NAUTICAL MILES SOUTH OF BAR HARBOR

Greg Sousa, an INBRE Undergraduate Student Summer Fellow from Bates College, has learned what scientific discovery is all about while working with copepods – tiny crustaceans – at the Mount Desert Island Biological Laboratory (MDIBL). “Every finding we make is novel,” he explains. “It’s extremely exciting.”

As Sousa and his mentor, Dr. Andrew Christie of MDIBL and the University of Washington, are finding, copepods can help us better understand the workings of our nervous systems and may provide an evolutionary link between insects and decapod crustaceans such as lobsters and crabs. Although they go largely unnoticed at barely 2 millimeters long, copepods constitute ninety percent of ocean plankton. Of particular importance to the ecology of the North Atlantic is the copepod *Calanus finmarchicus* which is an essential part of the marine food chain.

Neurologists have long used the nervous systems of insects and crustaceans to study the hormonal control of behavior, providing insights into basic neurological functioning. Arthropod nervous systems are useful models because, being composed of thousands rather than billions of neurons, they are much easier to study than those of more complex organisms,

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DR. CHARLES IRVIN, DIRECTOR, VERMONT LUNG CENTER, AND DR. PATRICIA HAND, ADMINISTRATIVE DIRECTOR, MDIBL, AND PRINCIPAL INVESTIGATOR, MAINE INBRE (PHOTO COURTESY OF PATRICIA TEDESCO)

The Northeastern IDEa States' Regional Meeting in Burlington, Vermont, August 15 – 17, provided all of us with a great capstone to our summer. The conference, which showcased IDEa programs from Maine, Vermont, New Hampshire, Rhode Island and Delaware, drew over 200 participants. The two-day program was very rich in science, including more than ninety scientific presentations, creating a fertile environment for researchers to share their results and learn about each other's work.

We were pleased to see so many Maine INBRE and COBRE investigators representing our state's biomedical research. Fourteen INBRE participants from the Mount Desert Island Biological Laboratory, The Jackson Laboratory, Bates College and Colby College presented five platform presentations and six posters over the course of the two-day conference. Nine COBRE scientists from the Maine Medical Center Research Institute also presented their research.

The IDEa regional meeting provided us with opportunities and avenues to share our states' scientific resources with each other. As one outcome of the meeting, the Vermont INBRE is putting together a database of core facilities resources for the northeast so that investigators can find

tools and services that may not be available at their home institutions. We'll eagerly follow the progress of the database in the next few months.

There was also an important gathering of Bioinformatics Core representatives from the northeast states to discuss progress with NENI – the North East Network Initiative – a regional collaboration to improve access to upgraded networking capabilities. NENI's goals are: to improve regional internet connectivity to nationwide networks; to provide training and education for scientists and educators; to strengthen inter-institutional partnerships; to facilitate biomedical research collaborations; to enable access to distributed research resources; and to support NIH–INBRE, NIH–COBRE and NSF–EPSCoR Networks.

Representatives from each state discussed the status of the information technology infrastructure available to them and what our needs are – as individual states and as a collective. We're looking forward to the strength that this network will bring in building critical infrastructure for research and education as we move forward.

Research and education were at the heart of our summer. You'll read in this issue about some of the fantastic research

experiences our undergraduate students enjoyed over the last few months. Greg Sousa's fellowship work (*see cover story*) exemplifies the incredible mentorship that the highly collegial and collaborative atmosphere Maine researchers have created can provide. We saw at our annual Summer Student Symposium that the INBRE program has succeeded in providing many opportunities for students to learn scientific techniques at the bench, while also developing the presentation and publication skills they'll need to be successful.

Faculty researchers continued their very productive year this summer too, as you'll see in our publications listing on page seven. We were pleased to host colleagues from research institutions around Maine this summer at the MDI Biological Laboratory – including several from The University of Maine, UMaine-Augusta, and Colby College – as well as welcoming Dr. Glen Collier from the University of Oklahoma INBRE.

As fall begins, the Graduate School of Biomedical Sciences at UMaine enters its second year. We're pleased to be one of many partners that share the goals of providing more education, training and opportunities in biomedical science in Maine.

Best wishes,
Patricia Hand, PhD
Principal Investigator



OUTREACH CORE CO-DIRECTOR, MICHAEL MCKERNAN, DISCUSSES UNDERGRADUATE PROGRAMS OFFERED THROUGH MAINE INBRE (PHOTO COURTESY OF PATRICIA TEDESCO)

Summer Fellow, Katelyn Michaud, UM-Farmington '09

This summer I worked in Dr. Wesley Beamer's lab at The Jackson Laboratory on the molecular genetics of ovarian cancer in mice. The experience inside and outside the lab has been amazing.

The mouse model we use is similar to the ovarian cancer in humans called Juvenile Granulosa Cell Tumor (JGCT), which is an extremely rare tumor that affects girls under the age of 20. For the summer I have been doing candidate gene sequencing of two gene loci on the X chromosome. I have also been conducting immunohistochemistry comparisons of human JGCT and mouse JGCT tumor tissues for the androgen receptor.

We believe that these tumors need

androgen to rapidly grow. This study is important to human health because human JGCT is rare and only a few case studies have been conducted before in humans. Our mouse model allows us to study the tumors in mice and make comparisons to humans.

The summer program will benefit my future career significantly. My college has limited biomedical research opportunities, so to participate in a program like this has allowed me to experience and learn the hardships of biomedical research. After earning my bachelors degree, I plan to go on to medical school and earn my MD/PhD. I hope to conduct clinical and translational research in the field of oncology.

I am very interested in women's cancer research.

Thank you very much for the opportunity to conduct research at the Jackson Laboratory for the summer. I hope you can continue to fund students like me in the future.

Thank you again,



Katelyn Michaud, Gorham, Maine
University of Maine-Farmington '09

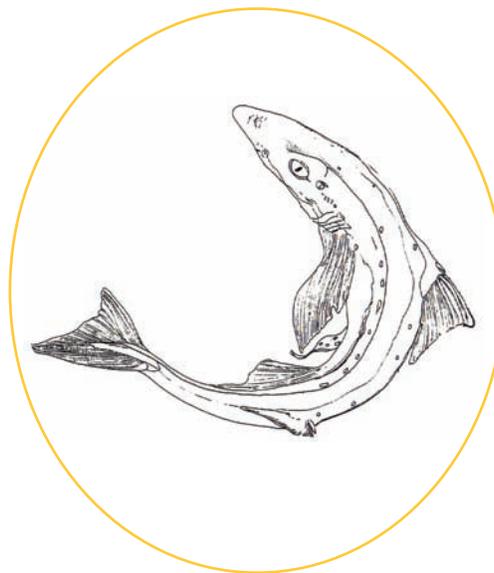
Squalus acanthias Genomics Study Becomes a Teaching Tool

Dogfish sharks (*Squalus acanthias*), long a valuable model for biomedical research, are becoming more difficult to find on the Maine coast. A new effort involving investigators from the College of the Atlantic (COA), the University of Maine and the Mount Desert Island Biological Laboratory (MDIBL), is studying the genotypes of captured sharks. The project will help scientists understand some of the causes behind the shark's dwindling population while providing a training ground for students to learn biomedical research techniques such as PCR assays and microsatellite analysis of genotypes.

Dr. Charles Wray, an evolutionary biologist, and staff of the laboratory of Dr. David Barnes, Associate Director of the Center for Marine Functional Genomics Studies at MDIBL, kicked off this project last March with a *Molecular Biology Research Techniques* class including students from the University of Maine-Machias and University of Maine-Farmington. The class examined the genetic structures of two dogfish families using three different microsatellite loci designed to help determine the inheritance of alleles.

This summer Dr. Christopher Lage, a population geneticist from

The University of Maine-Augusta, has continued to study the genetic structure of dogfish sharks in more depth, analyzing nine microsatellite loci in tissue samples from over 300 research specimens coming through MDIBL.



The work is important not just in understanding the reproductive biology of the species, but because it indicates how much genetic variation may occur between generations. Genetic variation provides a buffer for species against substantial climate change or disease by ensuring that

not all individuals carry similar genes which might make them all particularly susceptible to one threat or another. Another challenging factor in the population's stability is that the gestation period for dogfish sharks is almost two years – the longest of any vertebrate species – placing a higher importance on the success and viability of each litter. As Lage says, "other species have a refuge in fertility," with their more numerous and more frequent offspring ensuring the survival of the species.

Adding to this already delicate reproductive balance, dogfish travel in schools of like size and sex, with females sticking together – where predators or fishermen find one pregnant female they will find many, and potentially wipe out the offspring of two years' development.

This winter COA students will continue the study under the guidance of Dr. Wray and Dr. Chris Petersen of COA. The research will allow students to develop their molecular biology skills while monitoring the population of *Squalus acanthias* that has played such an important role in the study of transport-related diseases such as cystic fibrosis, as well as many other ailments from cataracts to cancer.

Summer Fellowship Students Share their Science

On August 2nd INBRE Summer Fellows from around Maine gathered at the Mount Desert Island Biological Laboratory to present the results of their season's projects. Students conducted research ranging from the role of calcium signaling receptor in chloride secretion, to the repair of LASIK corneas, and muscle fiber and myotome boundary morphogenesis in zebrafish.

The outdoor poster session was very impressive, and evidenced the time and effort students had spent on their projects. The interactive session attracted lots of viewers asking interesting, tough questions, and not one student was left standing idly. Fellowship participants fielded queries easily, with sophisticated answers.

As another part of the Student Symposium, some INBRE fellows also presented their work orally to an auditorium full of scientists and peers. Students gained valuable experience in presenting their research clearly in front of an audience, and in developing an effective Powerpoint presentation. The question and answer portion at the end of each talk made for stimulating insight for both the researchers and audience members.

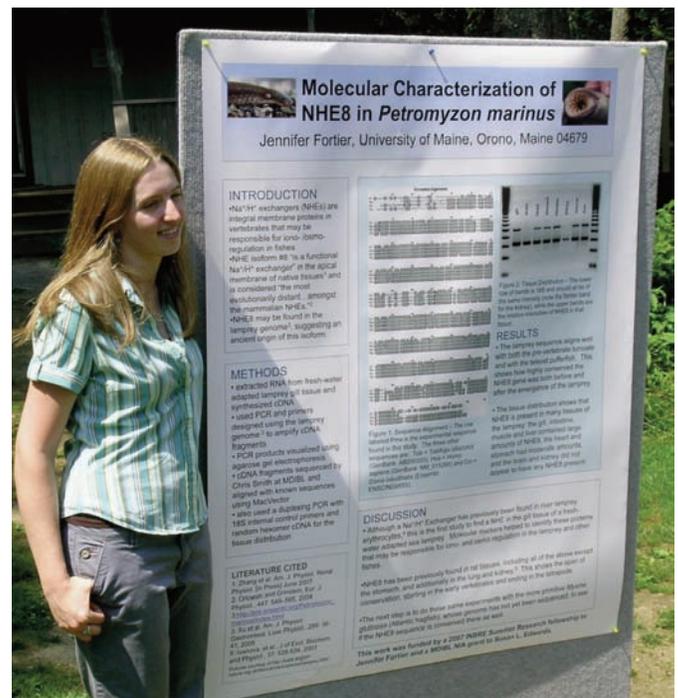
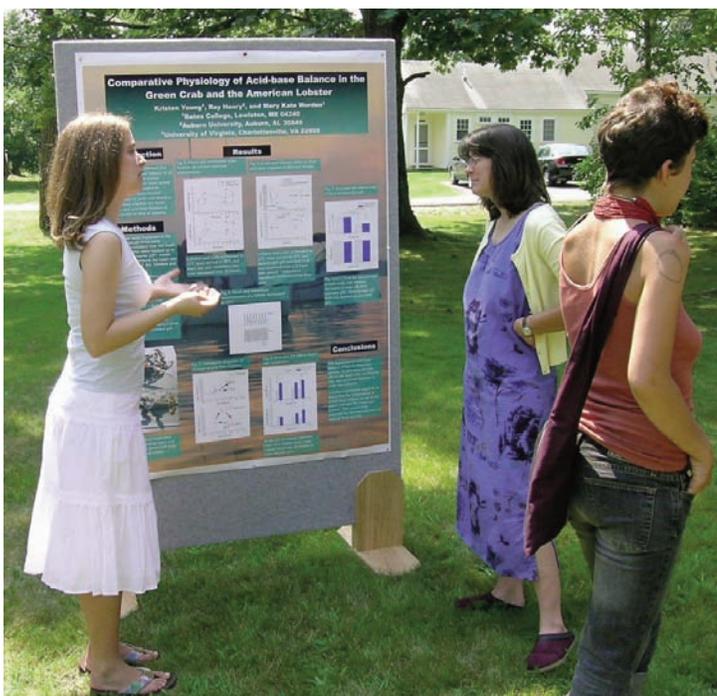


ABOVE: SCIENTISTS, STAFF AND STUDENTS GATHER AT THE OUTDOOR POSTER SESSION

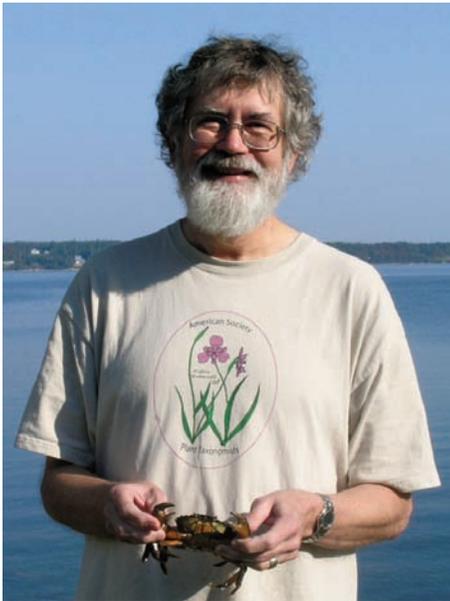
All of the INBRE fellows exhibited professionalism, organization and thoroughness in their presentations. This group of talented students demonstrated the strength of the Summer Fellows program and the valuable opportunity for in-depth research that it provides to undergraduates.

BELOW LEFT: INBRE FELLOW KRISTEN YOUNG OF BATES COLLEGE PRESENTED HER STUDY "COMPARATIVE PHYSIOLOGY OF THE ACID-BASE BALANCE IN THE GREEN CRAB AND THE AMERICAN LOBSTER" CONDUCTED UNDER MENTOR MARY KATE WORDEN, PHD

BELOW RIGHT: "MOLECULAR CHARACTERIZATION OF NHE8 IN *PETROMYZON MARINUS*" WAS THE RESEARCH FOCUS OF JENN FORTIER FROM THE UNIVERSITY OF MAINE, WHO WORKED WITH SUSAN EDWARDS, PHD



Visiting INBRE Scientist, Dr. Glen Collier



DR. GLENN COLLIER, MICROARRAY CORE DIRECTOR,
OKLAHOMA INBRE,
AT THE MDI BIOLOGICAL LABORATORY

This summer Maine welcomed Oklahoma INBRE Microarray Core Director, Dr. Glen Collier, PhD. His core facility at The University of Tulsa provides the only Affymetrix

GeneChip platform for the measurement of mRNA expression in the state designated for use by researchers throughout the area, as well as other molecular genetics services and consultation for researchers.

One of Collier's own research foci, as a specialist in molecular evolution and genetics, is the gene-enzyme system arginine kinase in *Drosophila* (fruitfly). Like the human enzyme creatine kinase (made notorious by supplements designed to enhance athletic performance), arginine kinase helps make energy available to cells. While arginine kinase is found in several tissues throughout the body of the fruitfly such as the ovary, muscles, and nerves, only one gene encodes the enzyme found in all these locations, whereas humans have multiple copies of the gene encoding creatine kinase each of which is expressed in a unique subset of tissues. Thus the genetic architecture of arginine kinase's diversity in *Drosophila* is very different from that of creatine kinase in vertebrates.

To explore the evolutionary history of this genetic structure further, Collier

spent the last two months at the MDI Biological Laboratory on a study of arginine kinase in the green crab (*Carcinus maenas*) as part of his sabbatical. As the sister group to the hexapoda (insects like *Drosophila*), the decapod crustaceans which include the green crabs could show evolutionary similarity, or indicate that a molecular divergence had occurred. Over the course of the summer Dr. Collier has identified multiple forms of the protein arginine kinase in tissues of the green crab, while thus far only locating one copy of the gene. Further tests will need to be done to determine the genetic basis of these multiple forms of arginine kinase.

Collier hopes to return to MDIBL in the spring to finish the study. Its findings could help scientists better understand gene diversification, and may have implications for gene therapy. In the meantime he's off to Costa Rica to study the larvae of a fruitfly relative which develop in the petals of flowers of a rainforest tree, a phenomenon he wants to examine first hand.

Graduate School of Biomedical Sciences Begins 2nd Year

As The University of Maine's Graduate School of Biomedical Sciences (GSBS) begins its second year, a new round of students are beginning their rotations at research laboratories across Maine. The UMaine program draws on close relationships between many of Maine's research and higher education institutions including The Jackson Laboratory, the Mount Desert Island Biological Laboratory (MDIBL), Maine Medical Center Research Institute, Maine Institute for Human Genetics and Health, the University of Southern Maine and the University of New England College of Osteopathic Medicine. This multi-institutional partnership brings over 80 combined faculty to the program, providing students with a rich base of teachers and mentors from diverse fields, including genomics, biophysics, molecular and cell biology, neuroscience, and the molecular mechanisms of disease.

Students can attend classes and interact with faculty virtually from their host institutions via a high-tech videoconferencing system. In addition to classes, students will complete three rotations in at least two different partner institution labs over the course of their studies.

The program provides a valuable in-state opportunity for Maine residents to pursue their studies in the biomedical sciences, but is also attracting students from other states and countries to come to Maine. Kim Brothers of Vermont is one participant who chose the program because of "the diversity of opportunities provided by the variety of sites for laboratory experiences." Brothers is doing her first rotation in the laboratory of Dr. Antonio Planchart, who holds a joint appointment at MDIBL and College of the Atlantic. Dr. Planchart, whose research is funded by INBRE, is working on a project which examines the effects of three different concentrations of

arsenic on the development of zebrafish embryos. This means Brothers is now studying toxicology, while the Master's degree she completed at the University of Southern Maine was in Immunology. Her next rotation will be in the lab of Dr. Carol Kim at The University of Maine, examining the role of the Cystic Fibrosis gene in *Pseudomonas* pathogenesis, again using the zebrafish as a model organism. Brothers is enthusiastic about the opportunity. "The GSBS program," she says, "promotes exposure to different areas of expertise."

Do you have INBRE news?

Please let us know about upcoming events, items of interest and your program accomplishments.

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New In Print

The collaborative research team involving Bowdoin College investigators **PATSY DICKINSON**, PhD, **ELIZABETH STEMMLER**, PhD, and **CHRISTOPHER CASHMAN**, as well as **ANDREW CHRISTIE**, PhD, MDI Biological Laboratory and the University of Washington, has published another paper on their work. "Direct tissue MALDI-FTMS profiling of individual *Cancer productus* sinus glands reveals that one of three distinct combinations of crustacean hyperglycemic hormone precursor-related peptide (CPRP) isoforms are present in individual crabs," authors EA Stemmler, YA Hsu, CR Cashman, DI Messinger, HO de la Iglesia, PS Dickinson and AE Christie, appears in *General and Comparative Endocrinology* (2007) 154(1-3):184-92.

Colby College researchers, **JULIE MILLARD**, PhD, and undergraduate **ADAM NEWMAN** '07 published "DNA Interstrand Cross-Linking by Epichlorohydrin," authors Romano, Keith P, AG Newman, RW Zahran, and JT Millard, in *Chemical Research in Toxicology*, 2007, 20: 832-838.

INBRE Junior Faculty members **CLARE BATES CONGDON**, PhD, and **CAROLYN MATTINGLY**, PhD, recently published two papers with collaborators from the University of Illinois. "An evaluation of information content as a metric for the inference of putative conserved non-coding regions in DNA sequence using a genetic algorithms approach," appears in the June 13 edition of *IEEE/ACM TCBB*, authors CB Congdon, J Aman, GM Nava, HR Gaskins, C Mattingly, 10.1109/TCBB.2007.1059.

The second paper, "Towards Interactive Visualization for Exploring Conserved Motifs in Non-coding DNA Sequence," authors CB Congdon, HR Gaskins, GM Nava, C Mattingly, is in *Proceedings of Frontiers in the Convergence of Bioscience and Information Technologies 2007* (FBIT 2007), IEEE Press, 2007.

INBRE Junior Faculty Researcher and MDIBL Investigator, **J DENRY SATO** was co-author on two papers published earlier this year. "Role of the glucocorticoid receptor and environmental arsenic in acclimation to seawater in killifish (*Fundulus heteroclitus*)," authors JR Shaw, K Gabor, E Hand, A Lankowsky, L Durant, R Thibodeau, CR Stanton, R Barnaby, B Coutermarsh, K Karlson, J. Sato, JW Hamilton and BA Stanton, was in the *American Journal of Physiology – Regulatory, Integrative and Comparative Physiology*, 292: R1052-1060.

The second paper, "Immunohistochemical expression of HbP17/FGFBP-1, FGF-2 and VEGF-A in head and neck tumorigenesis," authors S Begum, Y Zhang, T Shintani, S Toratani, JD Sato, and T Okamoto, was in *Oncology Reports* 17: 591-596.

IDeA Network of Biomedical Research Excellence

Research Institutions:

Mount Desert Island Biological
Laboratory
The Jackson Laboratory

Baccalaureate Institutions:

Bates College
Bowdoin College
Colby College
College of the Atlantic
The University of Maine

Outreach Baccalaureate Institutions:

University of Maine at Farmington
University of Maine at Machias

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Maine INBRE Program Coordinator:

David Barnes, Ph.D.

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Continued from page one: Planktonic crustaceans



INBRE FELLOW, GREG SOUSA (LEFT), WITH MENTOR DR. ANDREW CHRISTIE AT MDIBL'S ZEISS CONFOCAL

but still function similarly on many levels. In addition, comparing the nervous systems of insects, decapods, and their common ancestors teaches us about the evolution of nervous systems and neurohormones. For those reasons, and because little is known about copepod neurons and the hormones that govern them, Sousa and Christie set out to characterize the neurochemistry of the copepod nervous system.

Sousa started working in the Christie lab at MDIBL on an INBRE fellowship in the summer of 2006. In order to identify the neuropeptides – neurotransmitters which may be associated with specific behaviors – in *C. finmarchicus*, he learned how to dissect the copepod nervous system and conduct immunohistochemical labeling. Sousa mastered both techniques and began imaging his data using the confocal microscope system at the Lab. It was a steep learning curve, however, and Christie was surprised when Sousa was eager to pursue the project again during his second summer at MDIBL.

“The microdissection of the copepod was so tedious, and at times frustrating, that I wasn’t going to suggest Greg try it again,” Christie says, “but he has persisted and has done an amazing job.”

In fact, this summer Sousa and Christie prepared a paper that describes for the first time a copepod neuropeptidergic system. Their article on allatostatins, a family of peptides that govern developmental maturation and reproduction in arthropods, was accepted for publication in *General and Comparative Endocrinology* – a leading journal in the field of neuroendocrinology.

The project has also become a collaborative effort involving not only MDIBL, but several other INBRE institutions around Maine, including Bates College, Bowdoin College, and College of the Atlantic.

The project has also become a collaborative effort involving not only MDIBL and Sousa’s home institution, Bates College, but other Maine INBRE institutions, including College of the Atlantic (COA) and Bowdoin College. For instance, COA has a marine research station at Mount Desert Rock, 25 nautical miles offshore where baleen whales

feed on copepods. Captain Andrew Peterson has taken Sousa and Christie to those fertile collecting grounds in COA’s 40-foot vessel Indigo, which is equipped for plankton trawls.

Sousa will continue his copepod research as his senior research project at Bates College, working with Dr. Nancy Kleckner, Associate Professor of Biology. Bowdoin College researchers Dr. Patsy Dickinson and Dr. Elizabeth Stemmler – who have a long-standing collaboration with Dr. Christie, himself a Bowdoin graduate – will also mentor Sousa and provide access to their confocal microscope for imaging his fluorescently labeled nervous systems. Sousa will also use their Fourier transform mass spectrometer to determine the amino acid sequences and post-translation modifications of the copepod peptide hormones.

“Maine INBRE is very collegial,” says Christie, “we have wonderful relationships, and it has created a situation in which Greg can take a summer project he has been working on with me here at MDIBL back to his home institution, with no lack of scientific mentors.”

Sousa appreciates the opportunity he has had to learn from so many scientists and take the research further than he could have with a single ten-week internship. He had to learn a great deal about physiology and research techniques during his first summer, but during the second summer he could function more as an independent researcher. The INBRE program has allowed him to develop substantial relationships with the PIs at MDIBL and around Maine, hone his networking skills, and learn how projects are developed.

He’s looking forward to continuing his research back at Bates and will look for a job in a laboratory when he graduates in June 2008. Eventually, he plans to go to graduate school. Sousa is undecided about whether to pursue a Ph.D., an M.D., or both, but an advanced degree, biomedical research, and the thrill of discovery will definitely be part of his future.

Who we are

The Maine IDeA Network of Biomedical Research Excellence (INBRE) is an NCR/NIH-supported network of ten Maine institutions including Mount Desert Island Biological Laboratory (lead institution), Bates College, Bowdoin College, Colby College, College of the Atlantic, The Jackson Laboratory, and The University of Maine. Maine INBRE outreach institutions include The University of Maine at Farmington and The University of Maine at Machias.

The overall goal of the Maine INBRE is to strengthen Maine's capacity to conduct NIH competitive biomedical research. Maine's INBRE provides research support and core facilities to junior faculty, creates research and training opportunities for undergraduates, serves as a pipeline for undergraduate students to pursue health research careers and enhances the scientific and technical knowledge of Maine's workforce.



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