Chemistry Faculty & Research News
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- **C06 NIH $5.9 million stimulus award** to Boston University will reinforce its Life Science research infrastructure on the Charles River Campus by renovating space on the 4th floor in the East Wing of the Metcalf Science and Engineering Center Department of Chemistry space. Started in April 2010, the one-year effort will renovate 6,700 square feet of laboratory and office space to create four laboratory modules for state-of-the-art research in synthetic organic chemistry and supporting laboratory space for analytical chemistry. The flexible laboratory layout will enable technology-facilitated medicinal chemistry. Complementary faculty and meeting space will be developed to fully support real and virtual conferencing that facilitates engagement and collaboration among research scientists on the Charles River and Medical campuses as well as sites outside of BU. These renovations of four research laboratories will provide the infrastructure for the chemical sciences to realize BU's biomedical research vision, which has been constrained by outdated and inflexible infrastructure available in the Metcalf Center for Science and Engineering (renovated in 1983). It will bolster BU's leadership position in translational science by providing a robust environment for multidisciplinary research efforts bridging chemistry and biology. This NIH facilities renovation award is the first federally funded renovation grant on the CRC in BU's history.

- Work by **John Porco** cited in **C&E News**, May 17, 2010, "Silver Spurs Cycloadditions: Nanoparticles make their debut as catalysts for organic synthesis in a Diels-Alder reaction."

- This **NIH 4-year, 1.6 million award** (2010 to 2014) is funding **John Porco**, **Chemistry**, and his **collaborators to investigate the Biomimetic Synthesis of Complex Natural Products**. For the chemistry studies he is collaborating Professor Linda Doerrer, BU Chemistry, Professor Eric N. Jacobsen, Harvard University, and Professor William B. Tolman, University of Minnesota. For biology studies, the collaborators are Dr. John A. Beutler, Molecular Targets Development Program (MTDP), National Cancer Institute and Professor Jerry Pelletier, Department of Oncology, McGill University. Work involves 4 graduate students. Chemical synthesis of natural products inspired by their biogenesis is appealing because they can lead to the formulation of biosynthetic hypotheses and the inventions of new synthetic methodology with which to access synthetic targets. The overall goal of this highly successful investigation (12 publications, 2 patents) funded by the NIH is to develop and refine biomimetic syntheses using copper-mediated enantioselective oxidation processes; photochemical cycloaddition employing excited state intramolecular proton transfer (ESIPT); and asymmetric reactions of acylphloroglucinols. Professor Porco and colleagues are applying these methodologies to the chemical synthesis of complex natural products including bisorbicillinol, sorbicillactone A, aglaiastatin, ponapensin, and myrtucommulones A and B. Professor Linda Doerrer is performing mechanistic investigations to understand copper-mediated enantioselective oxygenase and oxidase processes and also develops catalytic, asymmetric oxidation processes. Likewise, a continuing collaboration with Professor Eric N. Jacobsen and coworkers (Harvard University) seeks to identify chiral thiourea photocatalysts for asymmetric photocycloadditions. Collaborations are also in place with biological collaborators including Dr. John A. Beutler (Molecular Targets Development Program, National Cancer Institute) and Professor Jerry Pelletier (McGill University) to evaluate compounds as anticancer agents and

protein translation inhibitors. The syntheses of complex natural products and derivatives facilitate the identification of novel, bioactive molecules with great potential to serve as novel pharmacological tools and cytotoxic agents for treatment of various prevalent human malignancies, including human cancers. For example, the Pelletier group found that the rocaglate natural product silvestrol synthesized by the Porco group could reverse chemoresistance in tumors containing lesions in the PI3Kinase/Akt pathway or overexpressing eIF4E. In addition, they determined that silvestrol exhibits significant anticancer activity in human breast and prostate cancer xenograft models, and that this is associated with increased apoptosis, decreased proliferation, and inhibition of angiogenesis ("Antitumor activity and mechanism of action of the cyclpenta[b]benzofuran, silvestol" Cencic, R., Carrier, M., Galicia- Vazquez, G., Bordeleau, M.E., Sukarieh, R., Bourdeau, A., Brem, B., Teodore, J.G., Gerger, H., Tremblay, M.L., Porco, J.A Jr., Pelletier, J. PloS ONE 2009 4(4):e5223.) It appears that silvestrol targets translation initiation to cause preferential inhibition of weakly initiating mRNAs. The Porco laboratory has recently identifiedrocaglate analogues that are approaching the potency of silvestrol as a protein translation inhibitor.

- **Pinghua Liu** - Mechanistic studies of enzymes in isoprenoid biosynthesis -The goal of this **NIH-funded project** ($1.9 mission over 5 years - 2010-2015) is to characterize the mechanism of a key enzyme in the deoyxylulose biosynthetic pathway as well as identify its key partner proteins. This pathway, identified only in bacteria and plants, produces the required compounds for isoprenoid synthesis. The results of this work could eventually lead to new broad-spectrum antibiotics or toward more efficient bioengineering based isoprenoid production. The work has developed an enzyme preparation that is many times more active than those previously reported, providing a crucial piece to illuminating enzymes. These isoprenoid biosynthetic studies will guide the development of mechanism- based inhibitors of the DXP pathway enzymes, which can be used as broad-spectrum antibiotics. The public health benefit will result from the development of effective new treatments for drug-resistant strains of pathogens (e.g., tuberculosis), currently of increasing concern worldwide.

- **Karen Allen** - Bridge Project: Functional Assignment in HAD Superfamily Phsphotransferases. Karen Allen is leading the HAD Bridge Project of the **NIH U54 award to the University of Illinois** entitled "Collaborative Center for an Enzyme Function Initiative," ($25 million over 4 years, John Gerlt, PI). Known as "GLUE Grants," these prestigious awards provide resources to currently funded scientists to form research teams to tackle complex biomedical problems that are beyond the means of any one research group. This consortium will facilitate the discovery of in vitro enzymatic and in vivo metabolic/physiological functions of unknown enzymes discovered in genome projects. The consortium is organized around five Bridging Projects and seven Cores. Professor Allen and her collaborator, Professor Debra Dunaway-Mariano, University of New Mexico, were invited to lead the HAD Bridge Project based on their 15 years of investigations on the chemical and catalytic mechanisms of the phosphotransferases in the haloalkanoic acid dehalogenase (HAD) superfamily of proteins ("Mechanism and Function in HAD Phosphotransferases," NIH R01 GM061099. Their work has successfully uncovered and confirmed the structural determinants of substrate specificity in all three subfamilies of the superfamily and are using this knowledge to predict the substrates for enzymes of unknown function, identifying the associated metabolic pathways of at least six members from various bacterial species. The HAD efforts will be greatly extended, enhanced, and enabled by the other Cores and Bridging Projects of the consortium, including the Protein Core, the EN and AH Bridges, Sequence/Genome Analysis Core,

Microbiology Core, Computation Core, and the Structure Core. In turn, the HAD Bridge Project, will afford comprehensive kinetic and mechanistic expertise to provide test cases for and utilize the facilities and expertise of the Cores.

- **Adrian Whitty** - Quantitative Analysis of RET Receptor Activation and Signaling. This five-year, **$2 million NIH R01 Award**. Growth factors (GFs) are messenger proteins that mediate the signals between cells that regulate critical functions such as cell growth, maturation, and death. In comparison with other medicinally important protein classes (enzymes, ion channels and G protein-coupled receptors) little is known about how GF receptors perform their function. This project aims to address this important knowledge gap by using the GF receptor RET, which is important in sustaining the survival of a key population of nerve cells in the spinal cord, as a model system to elucidate how GF/GF receptor interactions are coupled to intracellular signaling and to the resulting cellular response. If successful, the new knowledge and experimental methods it will deliver will contribute to innovative and improved approaches to discovering and developing drugs that target GFs and their receptors.

- **Bjoern Reinhard** Receives NSF CAREER Award - **The National Science Foundation Faculty Early CAREER awards** are presented to teacher-scholars who are "most likely to become the academic leaders of the 21st century." The Department is proud to announce that this year, Bjoern Reinhard has received this important award for his proposed research on "Frequency Domain Plasmon Fluctuation Spectroscopy For Single Biopolymer Mechanical Sensing." In this work, he plans to develop novel plasmon fluctuation spectroscopy with which to characterize the mechanical properties of individual biopolymers with unlimited observation time. By transitioning from a time to a frequency domain analysis, his plasmon fluctuation spectroscopy will provide insight into the structural properties of short DNAs, RNAs, and their protein complexes on the single molecule level. This research is part of his Nano-Bio Interface Lab, which aims to design, implement, and characterize new tools for imaging and manipulation of "hard" (inorganic) and "soft" (biological) materials with the ultimate goal of generating reliable tools that can provide insights into fundamental biological processes on a single molecule level. In addition, Bjoern's project will offer high school, undergraduate, and graduate students the opportunity to participate in an exciting collaborative research and education program. Dr. Reinhard plans to invite undergraduates and interested high school students who have completed his NanoCamp to obtain hands-on research experience in interdisciplinary research.

- **Chemistry Faculty Receive Boston University's Top Teaching and Advising Awards** -Boston University has again recognized Chemistry's distinction in teaching and advising by conferring a 2010 Metcalf Award for Excellence in Teaching on **John Caradonna** and the 2009/2010 Templeton Prize for Excellence in Student Advising on **Binyomin Abrams**. Student's have found John Caradonna's teaching to be the most remarkable and enriching academic experience of their undergraduate careers. In "exit interviews" with graduating seniors, Professor Caradonna was consistently recognized as one of the most respected and valued faculty members in the Department of Chemistry. When asked to recall their very best experiences as chemistry majors, many students named their time in his CH232 Inorganic Chemistry course as a truly inspiring educational experience. His contributions to Chemistry's educational mission also include great teaching in first-year Chemistry courses and in graduate program, his work as a mentor to undergraduate and graduate research students,

his strong voice for excellence and rigor in our academic programs, and his leadership as Director of Undergraduate Studies. John Caradonna is the fifth Chemistry faculty member to receive a Metcalf. Previous recipients have included Al Prock (1978), John Snyder (1989), Morton Hoffman (1994, Cup and Prize) and John Straub (2005). BINYOMIN ABRAMS, is a Chemistry Lecturer who does research in molecular dynamics and teaches introductory chemistry for both concentrators and non-concentrators. He is also well-known among his students for his half-hour advising appointments, which usually, but not always, take place in his office at the appointed time, but may also take place whenever a student has a question that needs a "thoughtful and well-informed answer," whether about which Chemistry classes to take, plans for grad school, or even general academic interests. Binyomin Abrams has received this prize in his FIRST YEAR serving as an academic advisor! He is the third Chemistry faculty member in a row to receive this honor. Previous recipients have included **John Snyder** (2009) and **Sean Elliott** (2008).