

## PSI/Nature Structural Biology Knowledge Base (SBKB)

### September 2011 News

#### PSI:Biology in the Spotlight

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#### The PSI:Biology Network grows by two



The Protein Structure Initiative:Biology program announces that two more High-Throughput-Enabled Biology Partnerships have joined the Network.

The first new biology partnership is led by **George Phillips, Jr.** (University of Wisconsin (UW)-Madison) in collaboration with **Jon Thorsen**, **Michael Thomas**, **Craig Bingman**, **John Markley**, and **Brian Fox** (at UW-Madison) and **Ben Shen** (The Scripps Research Institute). Their biological project, "Enzyme Discovery for Natural Products", aims to identify and structurally characterize the natural enzymatic processes used by bacteria in order to design new cancer drug leads. Phillips explains, "Bacterial natural products have been and continue to be strong candidates for drug leads. These products can be further diversified when the enzymes that make them are characterized and their activities reused in other contexts." This study will be conducted with the help of the PSI MCSG.

The second new biological partnership is led by Michael Rout (Rockefeller University) in collaboration with John Aitchison (Seattle Biomedical Research Institute), Yuh-Min Chook (University of Texas Southwestern Medical Center), and Andrej Sali (University of California San Francisco). The project, entitled "Nucleocytoplasmic Transport: A Target for Cellular Control", will elucidate the structural basis for regulation of nuclear trafficking at the nuclear pore complex (NPC) with the continued help of the PSI center PSI NYSGRC. "The regulation of protein and nucleotide transport via NPC's is essential for normal cell function, and alterations in the nuclear transport system are associated with many human pathological conditions," describes Rout, "The targets of this analysis will be the interface of the NPC with its interacting proteins."

Considering the number of proteins potentially involved in these two studies, it was a natural choice for Rout, Phillips, and their colleagues to propose their projects to the PSI:Biology Network. Rout explains, "The PSI offers us an unparalleled opportunity to take advantage of a proven highly successful high-throughput pipeline to characterize key areas of the nuclear transport pathways at the atomic scale at unprecedented comprehensiveness and rapidity. This will provide crucial data for our integrative structure-function approaches, allowing us together to discover potential drug targets in a promising but largely unexplored area for therapeutic intervention." Phillips agrees, "The opportunity to efficiently connect structure to function in these new enzymes motivated us to seek the PSI partnership. It will

allow [our] researchers to focus more heavily on the biochemistry of the systems, and yet have access to structures that inform their function and potential redesign."

Steven Almo (Albert Einstein College of Medicine), director of the high-throughput center NYSGRC, is also enthusiastic about the questions presented by the partnerships since they allow for a broader understanding of basic biology. "The nuclear pore targets represent a challenging set of eukaryotic proteins and complexes. These targets provide new challenges associated with the co-expression of multi-domain proteins with regions of low complexity and multiple binding partners. Of note," explains Almo, "these targets provide the opportunity to leverage the extensive biochemical work from Rout and colleagues for identifying domain boundaries and interacting partners." The center plans to use diverse hybrid methods, including high resolution structure determination, SAXS, EM, crosslinking, co-IP and computational modeling in order to attain the greatest amount of structural information for this and all of their partnerships.

You too can become a future PSI biological partner enabled by one of the PSI's High-throughput or Membrane Protein Structure centers. The next round of applications is going on now; details available in [PAR-11-176](#).