

## **University of Pittsburgh Announces the Creation of a Program to Develop Therapeutics for Huntington's Disease based on Quantitative Systems Pharmacology (QSP)**

**Pittsburgh, February 11, 2014.** The University of Pittsburgh Drug Discovery Institute (UPDDI), the University of Pittsburgh Brain Institute, the Department of Neurological Surgery and the Department of Computational and Systems Biology announced today the creation of a program to create therapeutics aimed at Huntington's disease using the tools of quantitative systems pharmacology (QSP).

Huntington's disease is a progressive, fatal, highly penetrant genetic disorder characterized by motor, emotional and cognitive dysfunction. Although the causal gene has been identified there is currently no treatment that can delay onset or slow progression. Progress in understanding the molecular pathogenesis of Huntington's disease that could provide insights critical for the development of novel therapies has been hampered by the lack of suitable experimental and computational tools and their systematic application to enable data-driven modeling of disease progression. To overcome this barrier, a QSP approach has been implemented to model Huntington's disease progression as a set of interdependent, dysregulated pathways. Well-characterized small molecule probes will be used to understand how the aberrant pathways "conspire" at various stages of the disease. Although Alzheimer's and Parkinson's diseases are more common than Huntington's, the genetic basis for Alzheimer's and Parkinson's has not been established. However, these disorders have a number of pathophysiological hallmarks in common with Huntington's. Thus, progress in elucidating the molecular pathology of Huntington's disease through QSP may lead to the identification of novel therapies for a wide range of neurodegenerative diseases. The program integrates the fields of clinical medicine, neuroscience, computational and systems biology, pharmacology, chemistry and medicinal chemistry.

"The overall mission of the new University of Pittsburgh Brain Institute is to unlock the mysteries of normal and abnormal brain function and then, use this new information to develop novel treatments and cures for brain disorders. To meet this goal requires the creation of new resources-- technical, intellectual and financial. The Drug Discovery Institute will clearly be one of the key resources for the Institute. The application of QSP to Huntington's disease therapeutics and the collaborative effort this entails is just the type of research program that the Brain Institute intends to promote and support.", stated Dr. Peter Strick, Director of the Brain Institute.

"The application of QSP allows us to harness clinical data to develop relevant experimental and computational models to probe disease progression and to guide the development of therapeutics", stated Dr. Andrew Stern, Director of Novel Therapeutics in the UPDDI.

"Integration of our computational and experimental work at multiple scales is an important way we may come up with new therapeutic strategies for diseases like Huntington's and more complex neurodegenerative diseases like Alzheimer's and Parkinson's", stated Dr. Ivet Bahar, Chair, Department of Computational and Systems Biology.

### **About the UPDDI:**

The University of Pittsburgh Drug Discovery Institute has implemented Quantitative Systems Pharmacology (QSP) as a major theme in developing therapeutics and companion diagnostics for many disease areas, but with a focus on cancer, neurodegenerative diseases and infectious diseases. The UPDDI integrates investigators from many fields in academia and industry including clinical medicine,

disease biology, pharmacology, computational and systems biology, chemistry and medicinal chemistry to pursue a powerful and cost-effective path to discovery and development, see [www.upddi.pitt.edu](http://www.upddi.pitt.edu).

#### **About the UPBI:**

The launch of a federal “BRAIN” Initiative by the White House reflects the public’s recognition of the critical importance of brain science. This bold new research effort aims to revolutionize the study of the human mind and to discover new ways to treat, cure and even prevent brain disorders. The neuroscience community at the University of Pittsburgh is uniquely situated to take a leading role in this formidable challenge. Pittsburgh is where Salk developed a vaccine against Polio which prevented the virus from damaging neurons in the spinal cord, brainstem and cerebral cortex; it is where the gamma knife for minimally invasive brain surgery was first introduced to neurosurgeons in North America; where Pittsburgh Compound B was developed for early detection of Alzheimer’s Disease; and where a Brain-Computer Interface first enabled a paralyzed woman to control a robotic arm and feed herself. The research expertise at the University of Pittsburgh is ideally suited to take brain science and neuro-clinical care to the next level.

The new Brain Institute will coordinate strategic planning for research in neuroscience; develop and oversee essential research resources; and unify the University’s fund-raising efforts in the area of brain research. As a consequence, it will enrich the neuro-related centers of excellence that already exist. The Institute will encourage collaboration between basic and clinical scientists to facilitate the translation of new results into novel treatments. In addition, the Institute will promote the development of new initiatives that enable the University to continue to be a leader in this area of research. Finally, the Institute will bring to bear the full resources of the University to attack some of the major health and scientific concerns of our time.

#### **About the Department of Neurological Surgery:**

The Department of Neurological Surgery at the University of Pittsburgh was founded more than 75 years ago with a strong commitment to patient care, education and research. Today, the department is one of the largest neurosurgical academic providers in the United States performing approximately 11,000 procedures annually. Our neurosurgeons recognize that each individual patient has a unique problem that requires carefully developed treatment options, sometimes surgical, sometimes not. Our facilities include the most technologically-advanced equipment—modern surgical microscopes, advanced image-guided brain and spine navigational tools, state-of-the-art monitoring techniques—improving patient outcomes by reducing operative complications. Our physicians are leaders in their field, pioneering advancements in brain, spine, neck and peripheral nerve care. Treatment is provided through our centers of excellence, each focusing on a specific disease and treatment technique. Our doctors and researchers also perform unique, federally-funded research into methods for improving clinical outcomes; they continually develop new tools and techniques to improve the status of patients with potentially life-threatening illnesses. In addition, we provide the most advanced training to future and current neurosurgeons from the United States and abroad, with a residency program that is internationally renowned, and professional-level training courses that attract medical personnel from around the globe, see [www.neurosurgery.pitt.edu](http://www.neurosurgery.pitt.edu).

#### **About the Department of Computational and Systems Biology:**

Computational and Systems Biology (CSB) encompasses an interdisciplinary approach that harnesses the power of computation and systems-level analyses to formulate and solve complex biological problems. The research programs within CSB also synergize and collaborate with the extensive basic and clinical

research programs at the University of Pittsburgh and across the globe. Foremost among these is our close partnership with the UPDDI and their focus on QSP, which combines multi-scale computations with molecular and systems pharmacology to accelerate drug discovery. Concomitant with our research foci, CSB is also a leader in educating and training all levels of emerging and nascent scientists in computational and systems biology, who will continue this work and identify and tackle next-generation biological problems, see [www.csb.pitt.edu](http://www.csb.pitt.edu).

**About the University of Pittsburgh School of Medicine:**

As one of the nation's leading academic centers for biomedical research, the University of Pittsburgh School of Medicine integrates advanced technology with basic science across a broad range of disciplines in a continuous quest to harness the power of new knowledge and improve the human condition. Likewise, the School of Medicine is equally committed to advancing the quality and strength of its medical and graduate education programs, for which it is recognized as an innovative leader, and to training highly skilled, compassionate clinicians and creative scientists well-equipped to engage in world-class research. The School of Medicine is the academic partner of [UPMC](http://UPMC), which has collaborated with the University to raise the standard of medical excellence in Pittsburgh and to position health care as a driving force behind the region's economy. For more information about the School of Medicine, see [www.medschool.pitt.edu](http://www.medschool.pitt.edu).