

Training New Researchers

Fellowship fosters clinical breakthroughs

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Translating Research into Clinical Breakthroughs

As a physician, there's little neurologist Trudy Pang, MD, can do to treat patients who suffer from epileptic seizures who are not candidates for epilepsy surgery. But, as a scientist, Pang is working to develop an early-warning and early-treatment mechanism that can help

individuals better prepare for these frightening events and possibly reduce their severity and duration.

“Some of these patients are confined to their homes because they have no warning that they’re about to have a seizure, they’re nearly always in danger of injuring themselves should a seizure occur,” says Pang. “Patients often come in with bruises and sometimes more serious injuries such as skull fractures and intracranial bleeding.”

Two years ago, while working primarily as a clinician seeing epilepsy patients, Pang’s scientific mentor, Steven Schachter, MD, suggested she apply to the Clinical Investigator Training Program (CITP), a two-year fellowship at BIDMC jointly administered by the Harvard-MIT Division of Science and Technology (HST). Although all entrants into the CITP are MDs, their backgrounds vary widely. Some



have primarily worked in a clinical setting with patients, others have spent most of their time in labs, while others have a mix of experiences.

Pang, who completed the program in June, pursued the CITP because it provided her with a tangible opportunity to conduct studies to develop treatments for patients who don’t respond to anti-convulsant medication. This includes one-quarter to one-third of epilepsy patients who suffer seizures – in severe cases, such as in pediatric patients, they may have as many as 20 or 30 seizures a day.

Today Pang is recruiting epilepsy patients for a pilot trial to test a non-invasive wearable seizure-detection system. The mechanism monitors a patient’s brain waves and can “sense” the beginning of an electrographic seizure. The goal is to develop an alarm system that then alerts the patient or the caregivers.

Where are they now?

“This may give patients a chance to move to a safe location before their seizure progresses or allow caregivers to administer other treatment,” says Pang, who is working with Schachter and engineers from the Massachusetts Institute of Technology to test the technology.

Additional applications being investigated will link an existing device called a vagus nerve stimulator (VNS) to the seizure detector, thereby possibly “switching off” the brain’s electrical currents that are responsible for seizures at the first sign of trouble.

The future of clinical and translational research

“The past 10 years have seen unprecedented scientific advances – with sequencing of the human genome coupled with advances in proteomics and bioinformatics – all of which have provided a wealth of new information to help speed drug discoveries and other patient therapies,” notes CITP Codirector Anthony Hollenberg, MD. “To take full advantage of these amazing new opportunities, we need to have clinical and translational researchers, skilled in both patient care and scientific discovery.”

Known by numerous monikers – physician-scientists, clinical researchers and clinical investigators – these individuals play a key role in BIDMC’s research enterprise, with more than 1,300 studies currently in progress. Approximately 500 clinical and translational investigators represent virtually every department throughout the medical center, and their work is supported by hundreds of research staff. They do much of the “bench-to-bedside” work that is at the heart of what distinguishes an academic teaching hospital from a general hospital.

“Clinical research tests a question in human beings,” explains BIDMC Chief Academic Officer Vikas Sukhatme, MD, PhD. “Unlike basic research in the laboratory, where a scientist may have conducted an experiment in a Petri dish or even begun working out a problem in a laboratory mouse model, in clinical research you are dealing with

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Volney Sheen, MD, PhD

CITP Class of 2003

Director, Epilepsy Service, BID-Needham Hospital
Assistant Professor of Neurology, Harvard Medical School

Sheen’s research centers on identifying the genetic, cellular and molecular mechanisms within neural stem cells that give rise to human neurological disorders.

Funded through federal grants, he has identified several genes responsible for a brain malformation called periventricular heterotopia, a source of developmental disorders. He is the recipient of the Doris Duke Clinical Scientist Development Award, the Ellison Foundation Award and the Beckman Young Investigator Award and has published more than 40 peer-reviewed articles in both clinical and basic science journals, including *The New England Journal of Medicine* and *Nature Genetics*.



Catherine M. Gordon, MD, MSc

CITP Class of 1998

Director, Children’s Hospital Bone Health Program
Senior Staff Physician, Divisions of Adolescent Medicine and Endocrinology, Children’s Hospital Boston
Associate Professor of Pediatrics, Harvard Medical School

Gordon’s primary research interest is the effect of nutrition and malnutrition on bone in children and adolescents. She has published widely in the areas of skeletal losses in young women with anorexia nervosa, cystic fibrosis, inflammatory bowel disease, and vitamin D deficiency. She has received independent funding and Department of Defense grants to carry out a clinical trial to investigate a new therapy to prevent bone loss in young women with anorexia nervosa.



Scott L. Rauch, MD

CITP Class of 1996

President and Psychiatrist-in-Chief, McLean Hospital
Chairman, Partners Psychiatry and Mental Health
Professor of Psychiatry, Harvard Medical School

Rauch has been a pioneer in research on the neurobiology and treatment of mood and anxiety disorders – contributing more than 300 publications to the scientific literature and winning numerous awards for his innovative work. He has served on a tandem of committees of the National Academy of Science, Institute of Medicine, producing expert reports on mental health consequences of the Gulf War, as well as the mental health needs of returning veterans and their families.



Farzaneh A. Sorond, MD, PhD

CITP Class of 2001

Associate Neurologist, Brigham and Women’s Hospital
Assistant Professor of Neurology, Harvard Medical School

In addition to her significant contributions to clinical teaching and patient care at the BWH, Sorond’s research is focused on expanding our understanding of cerebrovascular physiology in aging, cerebral hemorrhage and acute ischemic stroke through clinical research. She is funded through the National Institutes of Health and her research activities are in line with her clinical expertise serving as the model clinical investigator in that her clinical work provides the insights and stimuli for research projects.



people – and all of their real-life complexities – as you try to answer the question, ‘Does this scientific experiment work in human subjects?’”

One of a few such specialized clinical research training programs nationwide, the CITP has helped launch the careers of more than 150 clinical and translational researchers since its creation in 1993, according to Hollenberg, who codirects the program with its founder Robert Rubin, MD, of HST. Linda Bard, Program Manager, oversees CITP operations.

Each year the program provides 10 to 12 new participants from both BIDMC and other Harvard Longwood institutions with a comprehensive curriculum including statistical sciences, biomedical ethics and principles of pharmacology. It additionally provides fellows with two years salary, giving investigators the freedom and focus to be able to get their research projects off the ground. Successful graduates are awarded a Master’s Degree in Medical Science.

“Because I’m still at an early stage in my career, and because we’re currently in a difficult economic climate, research grants can be especially hard to come by,” says Pang. “The salary provided to me through the CITP offered me protected time to pursue my epilepsy research. Without that cushion, I probably would have had to sacrifice the research and concentrate only on seeing patients in the clinic.”

Since its inception, CITP has been funded by a grant from Pfizer, Inc. and in 2004, Merck & Co. joined Pfizer in supporting the program. “At a time when relationships between academic medicine and industry – pharmaceutical

companies, in particular – has come under intense scrutiny, it’s important to remember how important these partnerships can be,” notes Hollenberg, also an active researcher and Director, Interdisciplinary Research Strategy and Planning.

Training a new generation

Until recently, there has been little in the way of a “training pipeline” to produce physician-scientists, according to Steven Freedman, MD, PhD, gastroenterology, CITP Class of 1996.

“...in clinical research you are dealing with people – and all of their real-life complexities – as you try to answer the question, ‘Does this scientific experiment work in human subjects?’”

– BIDMC Chief Academic Officer
Vikas Sukhatme, MD, PhD

“Conducting patient-oriented research is a complex process. There are major regulatory issues to deal with, there are stringent guidelines to follow to ensure patient safety, and there are detailed protocols to follow from the FDA and from industry.” Today, in his roles as BIDMC’s Chief of Translational Research and Associate Dean for Clinical and Translational Research at Harvard Medical School (where he oversees the Catalyst research grant program), Freedman helps young clinical and translational researchers develop their careers.

For Paola Blanco, MD, who had been a basic scientist in Freedman’s laboratory studying the genetic mutations linked to both cystic fibrosis and pancreatitis, her path to the CITP fellowship took a different route from Pang’s.

“I knew about cell cultures, mouse models and hands-on laboratory benchwork,” explains Blanco. “I had learned basic science, how to run experiments and how to test hypotheses. But being in the clinic with Steve and seeing him dealing with patients who were suffering from chronic pancreatitis made me want to play a larger role as a clinical investigator.”

The CITP not only provided her with a breadth of experience that enhanced her laboratory skills, but also offered valuable exposure to numerous aspects of the drug development process.

“During a trip to the Pfizer headquarters, we spent a day learning how different drugs were developed, how they went through testing processes, how a drug’s marketing plan is developed.” Similarly, she adds, a separate CITP trip to the U.S. Food and Drug Administration (FDA) provided fellows with a firsthand look at government’s role in the process, including regulatory steps that have to occur before a new drug is launched.

As chief of BIDMC’s vast research enterprise, Vikas Sukhatme knows there are important discoveries on the horizon, many likely to come from CITP graduates as they continue to solve medicine’s most daunting puzzles. “These are the people who know what questions to ask,” says Sukhatme. “Their curiosity and innovation, combined with compassion and commitment will help us all make great progress in advancing patient care.”)



CITP Grad's Clinical Science Garneres Worldwide Attention

"Without the Clinical Investigator Training Program, this study never would have happened," says Endocrinologist Aaron Cypess, MD, PhD, Class of 2008.

The study he's referring to was published April 9 in *The New England Journal of Medicine*, and described how brown fat – a type of "good fat" known for its ability to increase metabolism – could lead to important new treatments for obesity. Brown fat is known to exist in infants to help them stay warm, but was assumed to disappear by adulthood. Cypess showed this was not the case.

"I applied for the fellowship because I wanted to take what I already knew about brown fat from working in the lab and somehow help patients," says Cypess. "And through the program, I learned the nuts and bolts of translational research; how to take information from the laboratory and apply it to human subjects – and then bring it back into the lab for further study."

With funding provided through CITP, Cypess was able to collaborate with a team led by Gerald M. Kolodny, MD, Chief of the Division of Nuclear Medicine at BIDMC, and study imaging scans of nearly 2,000 patients. They

learned that small deposits of brown fat were indeed "hiding" in the necks of adults. "We plan to find out if certain hormones can increase the amount of brown fat in the body as a way of turning these miniature calorie-burning furnaces into a new way to treat obesity and diabetes."

Cypess's study garnered worldwide media attention, including stories in *The New York Times*, *Washington Post* and a host of leading print and broadcast outlets, including a report on NBC Nightly News with Brian Williams. It's the kind of rare attention too few scientists ever receive.)