

# Translational Institute Unites Unlikely Partners at Penn

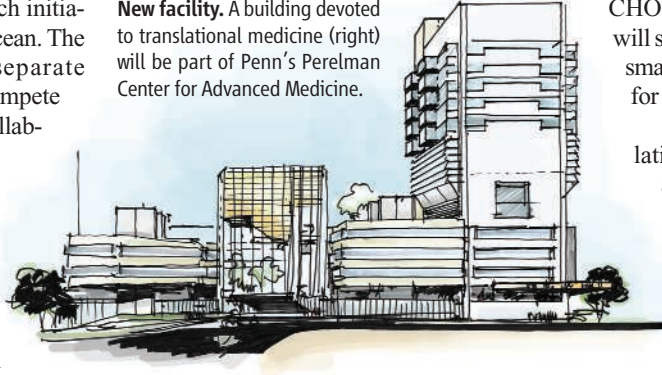
Translational research breaks barriers between the lab and the clinic and, at one institute, brings together some unlikely collaborators

The Hospital of the University of Pennsylvania and the Children's Hospital of Philadelphia (CHOP) sit side by side on the south edge of campus. But a few years ago, when they launched a joint translational research initiative, the separation loomed like an ocean. The two hospitals have completely separate finances, and their research arms compete with each other. So getting them to collaborate, says Penn pharmacology professor Garret FitzGerald, was like "Franco-German rapprochement."

FitzGerald is director of Penn's Institute for Translational Medicine and Therapeutics (ITMAT), launched in 2005 to unite and expand clinical and translational research programs across the Penn campus, including those at the two hospitals. Last year, Penn was one of a dozen institutions awarded a National Institutes of Health (NIH)-sponsored Clinical and Translational

Science Award (CTSA), a \$68 million, 5-year grant (see p. 966). Penn is investing \$30 million of its own money in the effort.

**New facility.** A building devoted to translational medicine (right) will be part of Penn's Perelman Center for Advanced Medicine.



Despite some "bumpy bits" during negotiations between Penn and CHOP, says FitzGerald, "[we] have worked more and more together, and this has gone extremely well."

## Establishing research and training

Building infrastructure to support translational investigators is key. "The previous model before was, you do the whole thing yourself," notes Carl June, director of translational research at the Abramson Cancer Center at Penn. But tougher regulatory requirements and more complex science now make that impossible. To help investigators, Penn employs clinical trial application specialists and has core facilities in everything from bioinformatics to proteomics, as well as a translational imaging center. Meanwhile, CHOP is constructing a new building that will support mouse model work—including small-animal imaging—which is essential for evaluating new cancer therapies.

Because the skills needed for translational science are so diverse, FitzGerald argues for a completely new "interdisciplinary" discipline. Penn offers a master's degree in translational research and a joint MTR-Ph.D. program. In addition, Penn has a grant from the Howard Hughes Medical Institute in Chevy Chase, Maryland, to develop courses to expose Ph.D. students to clinical research to inspire them to find cures for diseases.

In terms of research experience, Penn offers seven fellowships for translational

## EUROPEAN PROGRAMS OFFER TRANSLATIONAL TRAINING

Birgit Pless got her first glimpse of translational research in 2003 when, as a student working toward a master's degree, she did an internship at Berlin's Benjamin Franklin University Hospital. She spent the summer searching for new drugs for inflammatory bowel diseases. Once she had been dazzled by the bright promise of helping patients in their daily life, basic research paled.

But it wasn't until April of this year that she found another training opportunity in translational research. That was when she heard about the new, Frankfurt-based International Research Graduate School for Translational Biomedicine (FIRST), where she just enrolled this summer. "Only [FIRST] combined basic research with applied medicine and taught pharmaceutical basics," she says.

Translational research is fast becoming a priority in Europe. The European Commission set the tone by targeting most of its €6 billion health research budget for 2007–2013 at pan-European translational projects. Dedicated training programs such as FIRST are multiplying, but they remain few, vary greatly in approach, and are often works in progress. Three new European programs exemplify the range of approaches to training in translational research.

### Injecting medicine into basic science

The new Medical Research Council (MRC) Centre for Translational Research in Neuromuscular Disease, based at University College London (UCL) and Newcastle University, aims to provide a broad understanding of clinical context to influence research questions, says Michael Hanna, a neurologist at UCL's Institute of Neurology. The center, which will open its doors this October under Hanna's direction, received a £3.5 million grant from the

MRC to support its first 5 years, including the Ph.D. training of six biology students and two medical doctors.

Basic-science students will get direct contact with clinicians and patients at partner hospitals to pique their interest in research questions relevant to clinical care, Hanna says. Students will spend a year taking introductory courses on neuromuscular disorders and learning neuroscience techniques before starting a 3-year research project.

The two physicians will research a 3-year Ph.D. project in which they will work closer to patients than most basic scientists can, Hanna says. Hanna hopes to soon get more funding for training. "The intention will be to ... have a lot more [students] in the future," he says.

### A roundtrip, bench-to-bedside

In 2004, the University of Milan-Bicocca in Italy launched an international doctoral program in translational and molecular medicine called DIMET. DIMET connected the department of biotechnology and biosciences with the faculty of medicine so students could move easily between basic and applied biomedical research.

Some DIMET students' projects take a disease-driven approach, whereas others start with a basic finding and aim to develop clinical applications. Combining the two approaches is as fundamental for translational researchers as it is challenging, says DIMET coordinator Andrea Biondi, a clinician and cancer researcher at the university.

Some science students got to work at the interface between the lab and the clinic. After generating T cells against cytomegalovirus, medical

research, along with 12 offered through the CTSA, and five more fellowships through NIH T32 research training grants.

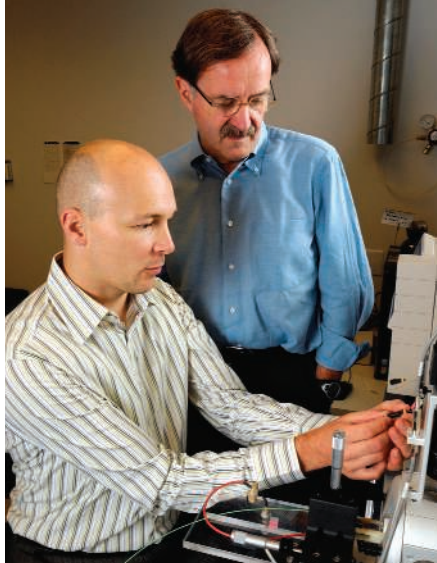
To encourage cross-disciplinary research, only researchers from different departments who haven't worked together can qualify for a \$150,000 transdisciplinary ITMAT seed grant. Six pairs of senior investigators won grants in the latest funding round.

Penn is trying to push translational research in nontraditional directions. One novel center is Personalized Medicine in Translation (PERMIT). This center will fund the expert staff and facilities needed to examine how genetic variants affect drug response and will give traditional clinical studies a new dimension by identifying which individuals are most likely to benefit or suffer side effects.

FitzGerald's own lab worked out the likely mechanism of Cox-2 inhibitor cardiac toxicity, and PERMIT is designed to detect and individualize such problems before drug launch, not after. FitzGerald is now probing why people differ in their response to all nonsteroidal anti-inflammatory drugs.

#### Cautions

As a postdoc in FitzGerald's lab, Tilo Grosser played a big role in the Cox-2 work. He is now



**Bench to bedside.** Assistant professor Tilo Grosser (left) and ITMAT Director Garret FitzGerald are bringing translational research to the forefront at Penn.

an assistant professor setting up his own lab at Penn, and he just applied for his first R01 grant. Grosser knows that a career in translational research is risky compared to basic science. "I am aware of the issues, particularly the [smaller] number of publications," he says. "These studies take a lot of time." Grosser points out that a single small clinical trial looking at drug-response variability could take 3 years, including patient screening and data analysis. And clinical research involves

sharing credit, which could also devalue his accomplishments.

"I have seen several instances since I've been at [Penn] where promising translational researchers had to go back and just do basic research in order to assure their promotion," says June. "That's not good." Grosser thinks that the breadth of clinical research opportunities at Penn, encompassing genomics, mechanistic work, and animal modeling, makes such career setbacks less likely.

Although tenure committees at Penn are still dominated by R01-type scientists, says FitzGerald, they are gradually taking into account the team contributions and lower publication rates among translational researchers. "That's an ongoing issue," June says.

Thomas Curran, a CHOP neurobiologist, cancer researcher, and ITMAT member, agrees that fears of failed clinical trials and nonexistent publications are real, but they shouldn't be career killers. "First, if you have all of those concerns, you're in the wrong job, because this is a risk-taking enterprise," he says. "Second, plan for success, never plan for failure. ... Come into it with the attitude [that] whatever you do, you're going to do the highest quality [work], and you're going to be successful—recognizing there's an element of doubt."

—KEN GARBER

Ken Garber is a freelance writer in Ann Arbor, Michigan.



**Head first.** Birgit Pless is among the first students to attend the Frankfurt-based International Research Graduate School for Translational Biomedicine.

biotechnologist Erica Dander, 26, wrote in collaboration with her multidisciplinary team a successful clinical trial protocol to test whether injecting the T cells could kill infected cells in transplant patients. Working at the nearby San Gerardo Hospital, she was "in the right environment to find help" with the protocol, she says.

The program's biggest limitation is its budget, Biondi says; it only receives a few thousand euros a year from the university, and most scholarships are raised by the participating professors. Still, DIMET will enroll 25 students for the next academic year. "We are just at the beginning, but we have seen from the first year a progressive increase in applications," Biondi says.

#### Promoting drug development

The FIRST program at the University of Frankfurt aims to address a lack of Ph.D. graduates who really understand the drug-development process, says Dieter Steinhilber, the coordinator of FIRST and a pharmacologist at the university's Institute of Pharmaceutical Chemistry.

Starting in October, scientists will learn about medical science and pharmacology while physicians and pharmacists study molecular and cellular biology. During the 3-year research program, students will also take courses on all the steps of drug development, including preclinical and clinical studies, regulatory affairs, and the marketing of medicines.

To form the program, the science and medicine faculties of the University of Frankfurt partnered with the private Georg Speyer Haus research institute and the Paul Ehrlich Institute, the federal health authority agency for biopharmaceuticals. They also count on pharmaceutical companies to provide additional expertise, traineeships, and €300,000 a year.

This money will complement the annual budget of about €1 million FIRST gathered from the university and the integration of two already-funded pilot Ph.D. programs. Starting in 2008, the university plans to recruit 20 basic scientists and 10 medical doctors each year, provided the German government decides in October to give additional support to the program.

"The opportunity for this career development is now," says Graham Lord, director of translational research development at the National Institute for Health Research Biomedical Research Centre at King's College London and Guy's and St. Thomas' hospitals. "I think the job opportunities that follow on that will be very substantial."

—ELISABETH PAIN

Elisabeth Pain is a contributing editor for ScienceCareers.org.