

Photo by William Sacco

## Education Program Issue

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As YCCI moves into the next five years of its Clinical and Translational Science Award (CTSA), we have a good opportunity to highlight one of our foundational programs: Education and Training. Addressing one of the primary missions of the Center, this program offers clinical and translational research training and career development opportunities for students and investigators at all levels.

One of our overarching goals has been to provide mentoring and guidance to young investigators. During the past year, we participated in a 16-site CTSA randomized mentoring trial spearheaded by the University of Wisconsin. Mentors were assigned to either an intervention group that took part in five two-hour training sessions or a control group that received no training. The sessions were led by **Eugene Shapiro, MD**; **Patrick O'Connor, MD**, newly appointed associate director of YCCI's T3 translational research core; and **Jo Handelsman, PhD**, who recently received the Presidential Award for Excellence in Science, Mathematics, and Engineering Mentoring.

Despite the significant time commitment involved in mentoring, very little attention is usually given to training faculty for this important role. Participants in the intervention group responded enthusiastically to the opportunity to interact with peers and discuss strategies for dealing with issues that arise. Although the results of the trial have not yet been published, the response was so positive that YCCI will be offering the training sessions to anyone who is interested beginning in fall 2012.

The past year has also seen the expansion of the successful Research-in-Progress meetings to include trainees from the Medical Research Scholars Program (MRSP), an initiative from Yale's Combined Program in Biological and Biomedical Sciences (BBS) aimed at helping graduate students in the life sciences enter careers in medical research. These meetings are an opportunity for trainees to present their research and receive feedback in an open environment conducive to discussion.

We've also incorporated ethics topics into these meetings, inviting experts to lead general discussions that apply to a wide range of research areas as well as to address specific concerns related to a particular research project.

Year Six of the CTSA grant is off to an equally productive start, with an international meeting of scholars and mentors at a workshop held at the

### From the Education Co-Directors

We're very proud of the progress YCCI has made in its first five years.

We've attracted and trained an impressive group of Scholars who have great potential for successful careers in clinical and translational research. Recent changes to the rules for the K program have given us the ability to appoint more Scholars through cost-sharing with various departments. This measure has given us the potential to expand the number of trainees under this productive initiative. It offers an excellent opportunity to obtain both salary and research support, and fund more advanced training and mentorship at a time when competition for dwindling research dollars is keen. We look forward to reviewing this year's proposals.

This issue of the newsletter profiles trainees in each of our programs and introduces a few new initiatives in addition to the newest Scholar appointees. You'll also find the schedule for our bimonthly Research-in-Progress meetings, which continue to be well attended and stimulating. They're a great chance to learn about current research projects over lunch.

We look forward to this next five years, when in addition to building on the success we have had, we will broaden our outreach to a larger community and integrate with other Yale and non-Yale career development and training programs. We also hope to further develop the multidisciplinary nature of our training programs by increasing both the exposure of basic scientists to translational research and their presence in our programs.

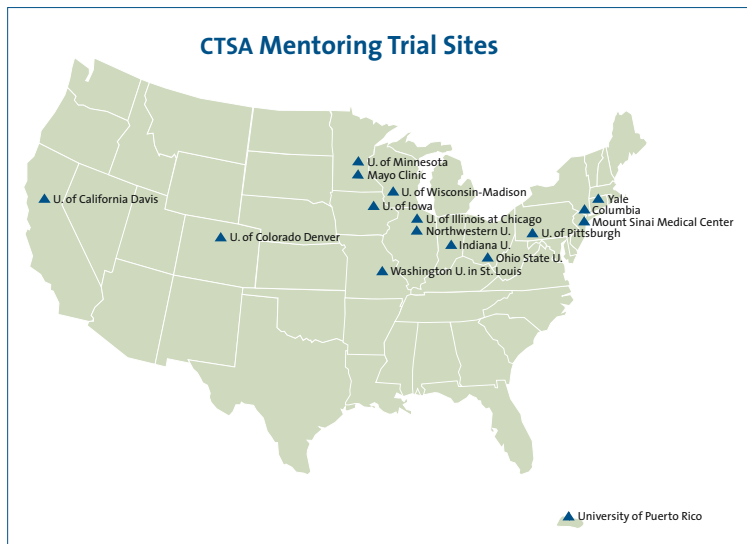
We encourage you to find out more about what YCCI offers by exploring our website to learn more about courses and events that may be right for you.

Wellcome Trust in London and the first-time expansion of our annual scholar retreat program to include an event for all trainees in the Schools of Medicine, Nursing, and Public Health (see articles on page 6). We hope that many of you will avail yourselves of these opportunities, and we look forward to your participation.

Eugene Shapiro, MD

Judy Cho, MD  
YCCI Co-Directors of Education

### CTSA Mentoring Trial Sites



# 2011 YCCI Junior Faculty Scholars

Scholar Photos by Carl Kaufman



**Renata Belfort De Aguiar, MD, PhD**  
*Instructor in Medicine (Endocrinology)*

Renata is conducting a study on the effect of glucose fluctuations on eating behavior and brain activation in order to gain new insights into the pathogenesis of obesity.



**Sandy Chang, MD, MHS**  
*Instructor in Medicine (Geriatrics)*

Sandy is evaluating the association of coexisting chronic diseases, geriatric conditions and impairments with the severity of COPD in older adults in order to improve health outcomes.



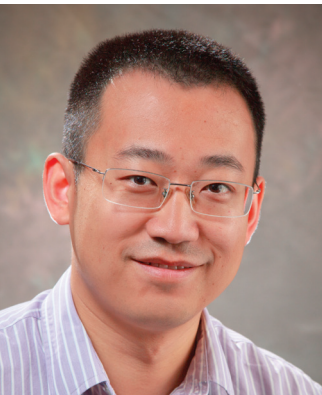
**Charles Dela Cruz, MD, PhD**  
*Assistant Professor of Medicine (Pulmonary and Critical Care)*

Charles is investigating the mechanisms that explain the exaggerated responses to viral infections found in COPD patients exposed to cigarette smoke.



**Stephanie C. Eisenbarth, MD, PhD**  
*Instructor in Laboratory Medicine*

Stephanie is seeking to identify new innate immune receptors that regulate effective vaccine immunity. These receptors may represent potent therapeutic targets for enhancing vaccination or inhibiting ongoing T cell activation in autoimmunity.



**Chi Liu, PhD**  
*Associate Research Scientist in Diagnostic Radiology*

Chi is developing techniques to improve the quantification of myocardial blood flow that can be used in such diagnostic imaging systems as Yale's state-of-the-art SPECT/CT system.



**Don X. Nguyen, PhD**  
*Assistant Professor of Pathology*

Don is working on a project to identify biomarkers to identify, isolate, and characterize metastatic stem cells in lung adenocarcinoma.



**Jennifer Sherr, MD**  
*Instructor in Pediatrics (Endocrinology)*

Jennifer is conducting a study to determine whether liraglutide, a long-acting GLP-1 analog approved for type 2 diabetes, reduces or eliminates early postmeal hyperglycemia and late postmeal hypoglycemia in type 1 diabetes patients using the insulin pump.



**Qin Yan, PhD**  
*Assistant Professor of Pathology*

Qin is exploring the roles of the enzyme PLU1 in resistance to Herceptin (a breast cancer drug), and will perform a high-throughput screening for its small molecule inhibitors. PLU1 is a potential target for cancer therapy; however, no specific PLU1 inhibitors have yet been identified.

## Scholar News

**Marcella Nunez Smith, MHS, MD, 2006 YCCI Scholar**, was awarded a five-year, \$5.3 million grant from the National Institute on Minority Health and Health Disparities to study the risk factors and prevalence of heart disease, cancer, and diabetes in the eastern Caribbean.

**Erica Herzog, MD, PhD, IMP Alumna and 2007 Junior Faculty for Clinical and Translational Research Pilot Awardee**, received a Ro1 grant for "Novel immunologic effects of semaphorin 7A in IPF."

**Eda Cengiz, MD, 2010 YCCI Scholar**, recently received a JDRF award to test the insulin infusion site warming device at a higher temperature.

**Joseph Contessa, MD, PhD, 2010 YCCI Scholar**, received an Ro3 small research grant for "A bioluminescent screen for inhibitors of N-linked glycosylation."



**Ania Magdalena Jastreboff, MD, PhD**  
*Instructor in Medicine (Endocrinology)*

Ania is using functional magnetic resonance imaging (fMRI) to characterize neural responses to visual food cues in severely obese adolescents before and after bariatric surgery.



**Hedy Kober, PhD**  
*Assistant Professor of Psychiatry*

Hedy is conducting a study to test whether cocaine-dependent individuals are able to use cognitive strategies to regulate their cravings and identify the neural mechanisms that underlie their regulation.



**Melissa Langhan, MD**  
*Assistant Professor of Pediatrics (Emergency Medicine)*

Melissa is evaluating whether capnography, a continuous noninvasive method of monitoring ventilatory status, will improve the recognition of hypoventilation and apnea in moderately sedated pediatric patients.

### CTSAs Now Under NCATS

An appropriations bill for FY 2012 that was signed into law in December includes funding for the NIH as well as specific language creating the National Center for Advancing Translational Sciences (NCATS). The CTSA program is now part of NCATS along with other programs slated for the new center. NCATS has a critical mission — to speed the discovery of next-generation methods and technologies to enhance the development, testing, and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions. The CTSAs will be a vital part of that mission.

As a reminder, the CTSA must be cited in your resulting publications, and the new citation is: This publication was made possible by CTSA Grant Number UL1 RR024139 or KL2 RR024138 or TL1 RR024137 (as appropriate) from the National Center for Research Resources (NCRR) and the National Center for Advancing Translational Science (NCATS), components of the National Institutes of Health (NIH), and NIH Roadmap for Medical Research. Its contents are solely the responsibility of the authors and do not necessarily represent the official view of NIH.

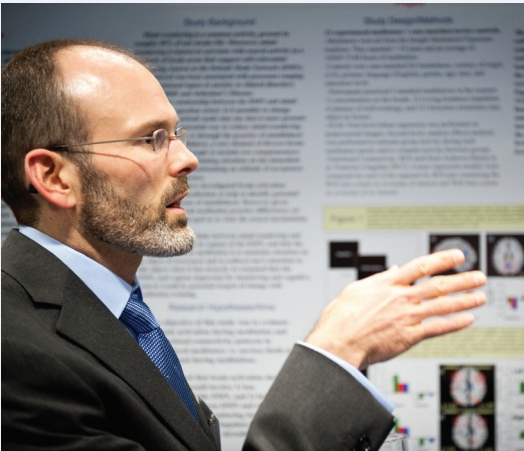
### Past Scholar Investigates Meditation to Understand Mental Illness

Understanding how meditation works will aid investigation into a host of diseases, according to 2008 YCCI Scholar **Judson Brewer, MD, PhD**. Brewer was the lead author of a study published in November in the *Proceedings of the National Academy of Sciences*, which found that experienced meditators seem to be able to switch off areas of the brain associated with such psychiatric disorders as autism and schizophrenia.

Using functional magnetic resonance imaging (fMRI) scans on both novice and experienced meditators as they practiced three different meditation techniques, Brewer found that regardless of the type of meditation practiced, those with experience had decreased activity in areas of the brain called the default mode network. This network, which consists of the medial prefrontal and posterior cingulate cortex, has been implicated in lapses of attention, such disorders as anxiety and attention deficit-hyperactivity disorder, and the buildup of beta-amyloid plaques in Alzheimer's disease.

The scans also showed that when the default mode network was active, brain regions associated with self-monitoring and cognitive control were co-activated in experienced meditators, indicating that they are constantly keeping their minds from wandering. In pathological forms, these thought-wandering patterns are associated with such diseases as autism and schizophrenia.

"The hallmark of many forms of mental illness is a preoccupation with one's own thoughts, a condition meditation seems to affect," said Brewer. "This gives us some nice cues as to the neural mechanisms of how it might be working clinically."



Wellcome Images

**Abhijit Patel, PhD, MD, 2010 YCCI Scholar**, received a Junior Faculty Career Research Training Award from the American Society for Radiation Oncology for his project, "Ultrasensitive measurement of tumor DNA in blood as a biomarker of radiation response."

**Yibing Qyang, PhD, 2010 YCCI Scholar**, received a \$375,000 grant from the Connecticut Stem Cell Program for his project "Pulsatile tissue-engineered grafts for surgical correction of single ventricle cardiac anomalies."

**Jennifer Sherr, MD, PhD, and Ania Jastreboff, MD, PhD, 2011 YCCI Scholars**, graduated from the IMP Program in December 2011.

**Yawei Zhang, MD, PhD, MPH, 2008 YCCI Scholar**, received a Ko2 award for "Air pollution and fetal growth in China."

# PROFILE

## Investigative Medicine Program (IMP)

Yale's innovative Investigative Medicine Program awards a PhD degree in investigative medicine to physicians training in either laboratory- or clinically-based patient-oriented research. The IMP has been expanded under the Clinical and Translational Science Award (CTSA) to include scholars in nursing, public health, biomedical engineering, and the biological and biomedical sciences. IMP also serves as a vehicle for integrating student training; many other individuals (medical, nursing, and graduate students; residents; international scholars; and clinical fellows and junior faculty members, some of whom are YCCI Scholars) take courses offered by the IMP each year.

### Exploring Rare Mutations to Understand Kidney Disease

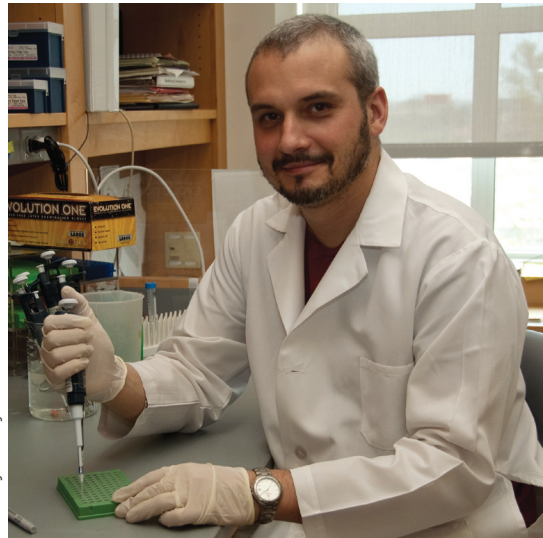


Photo by Lindsay Borthwick

Throughout his medical career, **Mathieu Lemaire, MSc, MDCM**, has been fascinated by genomic science and renal physiology. Those two interests led him to Yale's Investigative Medicine Program and the lab of **Richard Lifton, MD, PhD**. The idea of combining doctoral training in translational research with his medical training appeals to him because it allows him to study diseases in his own patients, moving from the bedside to the bench and back to the bedside.

Trained as a pediatric nephrologist, Lemaire is uniquely positioned to diagnose and treat such serious but rare inherited kidney conditions as

Dent's disease, which is characterized by defective functioning of the proximal renal tubules. Children with the disease are unable to absorb such critical components needed for proper growth and bone health, as salts, amino acids, and proteins. Two genes are implicated in Dent's disease – *CLCN5* and *OCRL* – but while studying the literature on the disease, Lemaire noticed that a number of the patients in published cohorts didn't have a mutation in either gene.

It turned out that about 30 percent of these patients lacked the mutations. This finding suggests that there may be unknown disease-causing genes implicated in this disease. In his IMP thesis project, Lemaire is using whole-exome capture to study the DNA of approximately 80 unrelated patients from the United States, Europe, and Asia without *CLCN5* or *OCRL-1* mutations. He hopes to find a set of patients that have not only a similar phenotype, but also mutations in the same gene. Although the work is more challenging than he anticipated, it has been worthwhile – he has found a handful of convincing novel candidate genes.

Elucidating the underlying genetic basis of Dent's disease may prove helpful in terms of treatment, but its usefulness goes beyond this rare disease. This approach has the potential to shed light on the pathophysiology of the proximal renal tubules, as well as other rare diseases that affect nephron segments and are commonly seen in pediatric nephrology. Lemaire is also working on a genomic project on essential hypertension, which has wider implications for the health of the general public. "It's a nice complement to work on both common and rare diseases," he said.

Lemaire was drawn to the Investigative Medicine Program in 2009 because of its structure and collaborative nature. "For most people, doing clinical work doesn't give you the confidence to be a functional scientist," he said. He finds that regular meetings with his committee members who are experts in their fields adds value to his training, as does the IMP curriculum, which includes courses in grant writing and other aspects of clinical and translational research. What may be most appealing, however, are the skills he's acquiring that will allow him to help his young patients. "To know the underlying cause of a disease, even if there's not a cure, is incredibly reassuring for a family," he said. 🌟

### YCCI RWJ Community Research Scholars

Yale is one of four sites in the country to provide research training through the Robert Wood Johnson (RWJ) Foundation Clinical Scholars Program, a two-year fellowship program that seeks to develop health leaders and influence the quality of health care. The program consists of a core curriculum that has been used for over 30 years but was expanded in 2005 to include a community-based research component in response to an increasing demand by funding agencies and policy makers for research to develop new interventions that demonstrate widespread community involvement.

As a result of the growing interest in this training as central to translating research into practice, YCCI asked the RWJ Clinical Scholars Program to offer its community-based participatory research (CBPR) course to other investigators on the health campus beginning in 2010, creating a cadre of YCCI Community Research Scholars.

The course covers the basic principles and processes of the CBPR approach, such as how to incorporate quantitative and qualitative research methodologies into CBPR; it also includes community outreach visits. To date, 13 trainees from the Schools of Medicine (including two medical students), Nursing, and Public Health have completed the course. So far, the response has been enthusiastic. Trainees have said they appreciated being exposed to CBPR mentors and resources, and have been motivated to pursue research projects using approaches gleaned from the course. For more information about this program, please contact [georgina.lucas@yale.edu](mailto:georgina.lucas@yale.edu) or [marjorie.rosenthal@yale.edu](mailto:marjorie.rosenthal@yale.edu).



Photo By Harold Shapiro

# PROFILE

## TL1 Training Program

The TL1 training program provides expanded clinical and translational training for predoctoral medical, nursing, MD/PhD, and biomedical engineering students. The program supports one-year clinical research projects and includes an intensive training core. It also provides training for medical students for short-term clinical research projects.

Yale students supported by the TL1 training grant have achieved a remarkable record of scientific productivity. In all, during or shortly after medical school, 77 students have co-authored 148 full-length publications; 63 students have presented abstracts; 68 students have presented 78 posters and oral presentations; and 37 students have completed a Yale MD thesis.

### Understanding How Immune Cells May Facilitate Cancer

Witnessing the suffering of close family members led **Mona Sadeghpour, MD '12**, to pursue a career in medicine, but her time at Yale has expanded that interest to encompass research as well.

She views YCCI's TL1 training program as a unique opportunity. "I wanted to develop the analytical skills necessary to do research, from asking a good question to being able to answer that question, to troubleshooting a project when there are problems," she said.

Having completed four years of medical school, Sadeghpour is now spending her fifth year doing research. An affinity for oncodermatology and the desire to work with a strong mentor led her to the lab of **Michael Girardi, MD**. Her research involves investigating the role of Langerhans cells – immune cells found in the epidermis – in UV-induced skin cancers.

Emerging evidence from mouse models in Girardi's lab indicates that instead of fighting cancer, Langerhans cells may facilitate chemical-induced carcinogenesis. Based on this finding, Sadeghpour decided to investigate the role of these cells in UV-induced carcinogenesis.

"Figuring out how these cells are contributing to carcinogenesis will enhance our understanding of the versatile response that the immune system can play when it comes in contact with mutagenic environmental exposures," Sadeghpour said. She hopes her research will enhance the understanding of factors in the immune system that play a role in tumor promotion pathways versus tumor clearance; and that it will guide novel strategies to prevent the emergence of skin cancer in mutated keratinocytes.

Sadeghpour believes that the TL1 program complements the medical school experience and can make a world of difference for young doctors hoping to pursue clinical and translational research. "Spending a whole year in the lab doing research really teaches you the language of science and allows you to be able to communicate effectively," she said. 🌐



Photos by Carl Kaufman



Mona Sadeghpour and her mentor, Michael Girardi, MD.

### New Role in YCCI's Educational Programs



Photo by Carl Kaufman

To help support the mission of training the next generation of clinical and translational investigators, YCCI has enhanced its management support of the program. **Nicholas Licht** has assumed increased responsibilities that include overseeing the integration of all the components of the education program, managing the YCCI Scholars program, and marshaling and leveraging available resources to help advance the program's mission. Licht has spent the last three years providing administrative support to the program and its co-directors **Eugene Shapiro, MD**, and **Judy Cho, MD**, as well as to the Office of the YCCI Director, **Robert Sherwin, MD**. Licht's familiarity with YCCI's education initiatives and the expertise he has gained will serve him well in his new job. "We were looking for a new level of operational support to integrate our educational programs and we're thrilled that Nick will be playing a more active role toward that end," said Shapiro. Licht has relocated to YCCI's offices at 2 Church Street South.

### Research-in-Progress Presentations

These bimonthly meetings feature presentations from YCCI and IMP Scholars as well as trainees from the Medical Research Scholars Program (MRSP).

We encourage all faculty and staff to attend. All meetings take place at noon; lunch is provided.

Please visit our website at <http://ycci.yale.edu/index.aspx> to find the list of locations, presenters, and projects.

# Workshop Lays Groundwork for International Collaboration

Scientific advances in neuroscience and genetics may be on the verge of producing fundamental transformations in psychiatry. Combined with a shortage of psychiatry trainees, these changes amount to a turning point for the field.

To address these challenge, investigators from Yale, Cambridge University, and University College London met with leaders from the Wellcome Trust in London in October. The purpose of the workshop was to explore how global institutional partnerships might facilitate the development of a new generation of clinical academics in neuroscience and mental health.

It emerged during the meeting that the United Kingdom faces major shortages of psychiatry trainees comparable to or greater than those in the United States. Common research themes across the departments of the participating institutions also highlighted opportunities for synergies in terms of research. “I think what emerged was a pretty clear interest on the part of the three institutions to work together to develop a new model for treating psychiatrists, both in regard to enriching the experience of their training and providing a path for science research-oriented psychiatrists to be facilitated in their career development,” said **John Krystal, MD, Robert L. McNeil Jr. Professor of Psychiatry**, who chaired one of the sessions.

Wellcome Images



Chris Pittenger, YCCI Scholar and Assistant Professor of Psychiatry, discusses his poster presentation at the Wellcome Trust meeting with another attendee.

At a subsequent meeting in conjunction with the Society for Neuroscience, the National Institute of Mental Health also expressed interest in the idea of developing a collaborative training model for psychiatrists. “We came away feeling that the work Yale has done over the last several decades in advancing neuroscience and making that a core mission of our department is considered to be a model and fairly unique in psychiatry,” said Krystal. 🌐

## Expanded Event for All Scholars

Every year, YCCI participates in a Scholar Day with a fellow CTSA site, Rockefeller University, to provide Junior Faculty Scholars with the opportunity to learn from experienced researchers as well from one another.

This year YCCI is expanding this concept to a larger community in an effort to broaden the experience and the population it serves. On March 9, we will be hosting an event for all Yale Scholars at the TAC Auditorium that is open to all trainees in the Schools of Medicine, Nursing, and Public Health.

The event will feature presentations, panel discussions relevant to clinical research, a poster session featuring the work of Yale Scholars and the following speakers:

- **James Anderson, MD, PhD**, Director of the NIH Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI), which plans and implements trans-NIH initiatives supported by the Common Fund and coordinates research related to AIDS, the behavioral and social sciences, women’s health, and disease prevention.
- **Richard Lifton, MD, PhD**, Sterling Professor of Genetics and professor of medicine (nephrology), who will speak about the molecular genetics of common diseases.
- **Victor Schuster, MD**, chair of the department of medicine at Albert Einstein College of Medicine, who will speak about career development in academic research.

We hope that opening our umbrella to include Scholars from across Yale’s medical campus will encourage interdisciplinary collaboration and increased opportunities for clinical and translational research. Please visit <http://ycci.yale.edu/news/scholardayretreat> for details about this event. 🌐



Photos by Robert Lisak

Judy Cho moderates a panel on “Developing ‘Bench-to-Bedside’ Collaborative Relationship” with Nina Papavasiliou (Rockefeller University), Iddo Ben-Dov (Rockefeller University), and Sarah Huen (Yale University) at last year’s collaborative Yale-Rockefeller Scholar Day.

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