



Photo Harold Shapiro

Director's Corner

One of the reasons I accepted the position as director of YCCI when we opened our doors eight years ago was the commitment to education that is part of our mission and about which I continue to remain passionate.

We have worked hard during the intervening years to create programs that nurture the next generation of clinical and translational researchers, and provide the training they need to succeed in today's complex and competitive research environment. We have begun to see the fruits of our efforts as our first groups of Scholars have transitioned into productive research careers. I am especially proud of the fact that they are now active mentors, guiding and encouraging their younger colleagues to follow in their footsteps.

Besides the educational programs that have been created or expanded under the YCCI umbrella, I'm excited about our interactions with such programs as the master's degree in chronic disease epidemiology in the School of Public Health, which provides in-depth training in research methodology and is a valuable component of Yale's educational offerings in conducting high-quality research.

Our efforts culminated in a well-attended gathering for researchers at the third annual All-Scholar Day Retreat, which took place at the beginning of April. Our keynote speaker was **Christopher P. Austin, M.D.**, director of the National Center for Advancing Translational Sciences (NCATS), who shared his experiences in industry and at the National Institutes of Health, and who is committed to promoting collaboration from within the NIH and with external institutions to speed the development of medical advances.

There are many educational opportunities for investigators interested in pursuing research or improving the quality of their research endeavors. I hope you'll avail yourself of all we have to offer.

Robert Sherwin, M.D.
YCCI Director

Training the Next Generation of Clinical and Translational Researchers

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When YCCI was established in 2006, one of our key goals was to attract promising students, fellows, and junior faculty members to careers in clinical and translational research, and offer them the training necessary to work effectively in today's complex research environment. While YCCI has grown and expanded in the intervening years, our focus on education has remained unwavering.

To help support YCCI's efforts to provide a home for training the next generation of clinical and translational researchers, we are pleased to welcome **Lloyd Cantley, M.D.**, who joins **Eugene Shapiro, M.D.**, as co-director for education. Cantley is C.N.H. Long Professor of Medicine (Nephrology) and professor of cellular and molecular physiology; and vice chair for research in the Department of Internal Medicine. He is an outstanding basic scientist, whose research focuses on kidney epithelial cell development and repair; changes that occur during tubule formation; and the role of the innate immune response to kidney injury. He is also an exceptional mentor who has trained over 30 graduate students, medical students, and postdoctoral fellows in his laboratory as well as numerous undergraduate students.



Photo Terry Dagradi

"I believe that inspiring the next generation of physician-scientists, and providing them with the proper foundation to succeed in the current academic environment, is one of the most important responsibilities we face in academia today," said Cantley. "YCCI provides a perfect platform to achieve these two missions, and I feel lucky to be named as the co-director for education and to be able to work with Doctors Shapiro and Sherwin to foster this environment at Yale."

The education leadership team oversees training programs that YCCI has developed, enhanced, or expanded. These include: the YCCI Scholars Program; the Investigative Medicine Program; the TL1 Predoctoral Training Program; the Robert Wood Johnson Foundation Clinical Scholars Program; and training programs for research staff.

The Scholars Program is a YCCI initiative that has been particularly successful. To date, 88 Scholars from 18 programs and departments across the health campus have received salary and research support through the program, which also includes

mentorship and training in the conduct of clinical research. YCCI Scholars have published over 1,000 papers and received \$157 million in independent funding. Over 90 percent of Scholar alumni remain active in research.

The Investigative Medicine Program — one of a handful of such programs in the country — is a unique doctoral program for physicians who have completed their clinical training. YCCI support also allows about a dozen medical students each year to take a year off to work on a research project. These investments in the next generation of investigators are critical to the School of Medicine's mission of sustaining research excellence. ☺

Lloyd Cantley, M.D.

Visit <http://yci.yale.edu/education/index.aspx> to learn more about our educational programs.

2013 YCCI Junior Faculty Scholars

Photos Photo & Design at Yale University



Alan Anticevic, Ph.D.
Assistant Professor of Psychiatry and of Psychology

In an effort to understand cortical dysfunction in schizophrenia, Alan is conducting research to test the hypothesis that disturbances in the cortical microcircuitry resulting from disruptions of the **NMDA** glutamate receptor may contribute to perceptual and cognitive disturbances in patients.



David Assis, M.D.
Instructor in Medicine (Digestive Diseases)

David is conducting research to determine whether macrophage migration inhibitory factor (**MIF**) polymorphisms and the relationship of **MIF** to its receptor **CD74** play a role in the pathophysiology of autoimmune hepatitis.



E. Jennifer Edelman, M.D.A., M.H.S., FACOG
Assistant Professor of Medicine (General Medicine)

Jennifer is studying the immunosuppressive effects of prescription opioids among **HIV**-infected patients who are often prescribed these drugs, with the goal of developing interventions to promote safer opioid prescribing in these patients.



Aileen Garipey, M.D., M.P.H.
Assistant Professor of Obstetrics, Gynecology, and Reproductive Sciences and Assistant Clinical Professor of Nursing

Aileen is investigating the relationship between pregnancy intention, depression, and preterm birth in order to develop new interventions and prevention strategies that mitigate the risk of preterm birth.



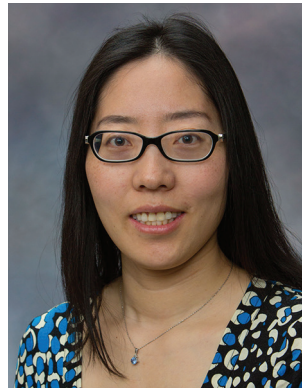
Hanna Stevens, M.D., Ph.D.
Assistant Professor in the Yale Child Study Center

Hanna is assessing how prenatal stress interacts with genetic risk and postnatal environment to determine the risk of **ADHD** by comparing the known timing of different aspects of neurobiological development in children to that found in the mouse model.



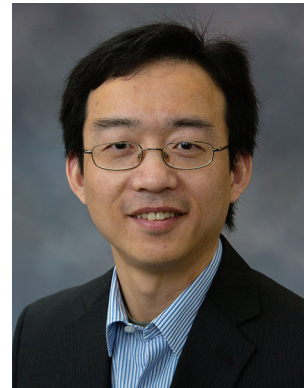
Jeffrey Testani, M.D., M.T.R.
Assistant Professor of Medicine (Cardiology)

Jeffrey is conducting research to better understand and evaluate the mechanisms of diuretic resistance in acute decompensated heart failure, which has a 50 percent rehospitalization rate within six months of treatment.



Bingqing Zhou, Ph.D.
Assistant Professor of Public Health (Biostatistics)

Bingqing is working on a project to develop novel competing risks methodology to estimate more accurately the risks of graft failure and death following kidney transplantation, in order to optimize the process of kidney allocation and improve post-transplantation management.



Jiangbing Zhou, Ph.D.
Assistant Professor of Neurosurgery and of Biomedical Engineering

Jiangbing is working on a project to synthesize tumor-responsive nanoparticles for systemic drug delivery to brain tumors, and to evaluate the therapeutic effects of novel drugs targeting brain cancer stem cells in order to develop new treatment options for glioblastoma multiforme.

Scholar News

Joseph Contessa, M.D., Ph.D., 2010 YCCI Scholar, was awarded a research scholar grant from the American Cancer Society for "Targeting N-linked glycosylation in non-small cell lung cancer."

Charles Dela Cruz, M.D., Ph.D., 2011 YCCI Scholar; and **Mathieu Lemaire, M.D.**, Investigative Medicine Program student, were selected to serve as associate scientific advisors of the journal *Science Translational Medicine*.

Stephanie Eisenbarth, M.D., Ph.D., 2011 Scholar, received the American Society for Clinical Investigation Young Physician Scientist Award at the society's 2014 meeting.

Raimund Herzog, M.D., M.H.S., 2009 YCCI Scholar, received an R03 small research grant for "Human Brain Ketone Metabolism in Type 1 Diabetes and Hypoglycemia."



Lucia Jilaveanu, M.D., Ph.D.
Associate Research Scientist
in Medicine (Medical Oncology)

Lucia is conducting research on the mediators of brain metastases in metastatic melanoma that involves screening a number of candidate genes upregulated in specimens from patients with early brain metastases, and developing a biomarker model that predicts metastasis to the brain.



Christoph Juchem, Ph.D.
Assistant Professor of Diagnostic
Radiology and of Neurology

Christoph is conducting a study that applies magnetic resonance spectroscopic imaging (MRSI) methods to quantify and detect glutathione and other neurochemicals in the brain, in order to better understand the role of neuroprotection in multiple sclerosis.



Kasia Lipska, M.D., M.H.S.
Instructor in Medicine
(Endocrinology)

Kasia is conducting a study to examine severe hypoglycemia occurring in the course of type 2 diabetes treatment, particularly in older patients, in order to help guide the design of interventions to mitigate the risk.

Research Highlight: PCare4NHV

There is a lack of understanding of adult primary care resources in New Haven, which has a growing population of Medicaid patients as a result of the expansion of this program under the Affordable Care Act.

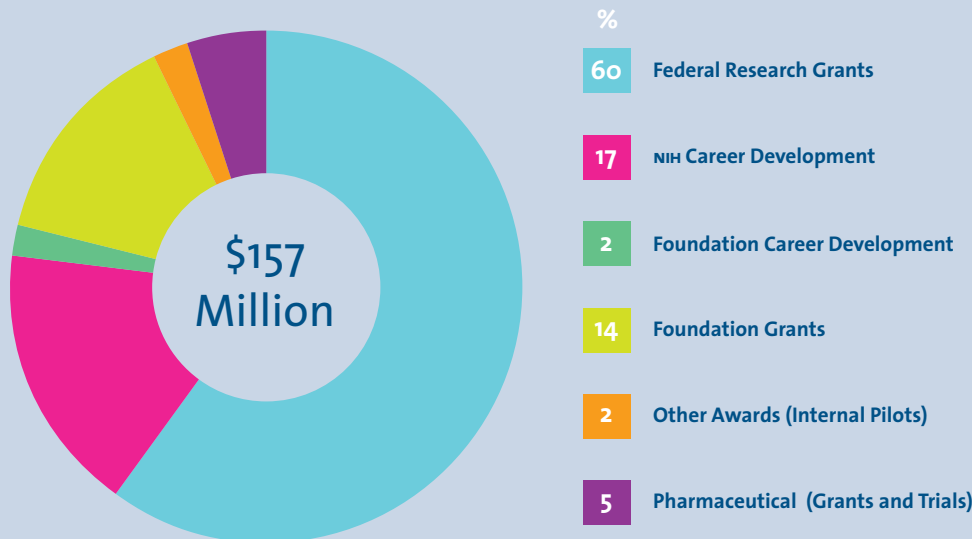
As part of their training in the Robert Wood Johnson Foundation (RWJF) Clinical Scholars program, a group of Yale investigators set out to better understand access to primary care in New Haven and surrounding communities through a community-based participatory research project.

Jason Lott, M.D.; **Arjun Venkatesh, M.D., M.B.A.**; **Jennifer Voorhees, M.D.**; and **Ilse Wiechers, M.D.**, worked with five community organizations to develop a 78-item survey of factors that affect access to adult primary care. They collected data from over 90 percent of the 98 adult primary care sites in New Haven and four surrounding towns.

The results reveal both barriers and opportunities in access to primary care. Only about half of primary care providers accept new Medicaid patients and the majority require photo ID, a barrier for many patients. The majority of practices uses electronic health records and has entries that are wheelchair-accessible, but only a third has a counter height that is wheelchair-accessible.

The scope of the project includes sharing the results in meetings with the participating community organizations; delivering feedback to individual practices; producing a report for the community; and using the data and advocacy efforts to obtain funding for further research. It also has the potential to serve as a model for a statewide primary care assessment. The group hopes to create an online resource catalogue and administer a similar survey to pediatric practices in the community.

\$157 Million in Independent Funding Generated by YCCI Scholars



Over 1,000 papers published.

Young-Shin Kim, M.D., M.S., M.P.H., Ph.D., 2009 YCCI Scholar; and **Andrew Goodman, Ph.D., 2012 YCCI Scholar**, were honored as recipients of the Presidential Early Career Awards for Scientists and Engineers, the highest honor bestowed by the United States government on science and engineering professionals in the early stages of their independent research careers.

In August, **James McPartland, Ph.D., 2006 YCCI Scholar**, will receive the American Psychological Association's Division of Intellectual and Developmental Disabilities Sara S. Sparrow Early Career Research Award. The award is given biennially to an individual who has made substantial contributions to the understanding of intellectual or developmental disabilities as reflected in his or her published and presented works.

Frederick Shic, Ph.D., 2012 YCCI Scholar, was awarded an R21 research grant from the National Institute of Mental Health for "Gaze modification strategies for toddlers with ASD."

James Yu, M.D., 2012 YCCI Scholar; and **E. Vincent Faustino, M.D., 2012 YCCI Scholar**, received a Master of Health Science Research degree in May. A total of six YCCI Scholars have now received this degree since the program's inception in 2009.

Events Calendar

Research-in-Progress Meetings

These meetings feature presentations from YCCI Scholars and Investigative Medicine Program students, as well as trainees from the Medical Research Scholars Program (MRSF). We encourage all faculty and staff to attend.

The meeting listed below will take place at noon in TACN203. (Lunch is provided)

June 23

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

Coffee and Conversation

Third Wednesday of each month

8:00 a.m., Cohen Auditorium
(Coffee at 7:30 a.m.)

Lunch and Learn

Second Thursday of each month

Noon, Cohen Auditorium
(Lunch is provided).

For the schedules for Coffee and Conversation and the Lunch and Learn series, please visit: <http://ycci.yale.edu/education/stafftrain/index.aspx>

To register, visit: www.yale.edu/training; browse courses by course owner; then select CTSA/YCCI; select Clinical Trials.

For more information:
e-mail **LaToya Howard** at: latoya.howard@yale.edu
or call, 203.737.3661



Jessica Illuzzi, M.D., M.S.

Jessica Illuzzi, M.D., M.S. '06, had a strong background in basic science and treating patients, but felt that she lacked the clinical research skills needed to address the issues she was interested in exploring. "There were unanswered questions in my field and I didn't have the tools to do that type of research," said Illuzzi, associate professor of obstetrics, gynecology, and reproductive sciences.

To deepen her skill set, Illuzzi pursued a Master of Science in Chronic Disease Epidemiology (CDE) at the Yale School of Public Health. This program offers rigorous training in research methodology, helping investigators develop skills in such areas as trial design, advanced biostatistical methods, and epidemiology.

"We're finding that increasingly, clinical investigators need to have training in things like how to do clinical trials, or confidence in genetic epidemiology if they're going to be doing genetics," said Susan Mayne, Ph.D., the C.-E.A. Winslow Professor of Epidemiology and chair of the department of chronic disease epidemiology. The curriculum ranges from introductory level to more sophisticated courses in methods that clinical investigators need to master.

The program is particularly well suited to clinical fellows or junior faculty, including YCCI Scholars, who often fund the tuition through a κ award.

Marney White, Ph.D., M.S. '09, who included the M.S. tuition in her κ application, noted that the education component of her proposal was very well received. Unlike auditing classes, an approach sometimes used for κ awards, the master's degree in CDE offers

in-depth training through a solid and structured didactic approach.

Students may tailor electives to their own interests in addition to completing core courses in data analysis, epidemiology, developing a research proposal, and research ethics. White, associate professor of psychiatry and of epidemiology (chronic diseases), who specializes in eating and weight disorders, chose electives in nutrition and food policy. She attended the program part time, taking several years to get her degree, although it can be completed in one year of intensive full-time study.

Alumni note that the program has made a significant difference in their ability to conduct research, providing quantitative skills and informing new avenues of pursuit. "It really equipped me with the basic steps necessary to understand trial design and epidemiology better," said 2008 YCCI Scholar R. Douglas Bruce, M.D., M.A., M.Sc. '08, assistant professor of medicine (AIDS) and of epidemiology (microbial diseases), whose research focuses on pharmacology and operations. These skills can be especially important for new investigators, because they don't necessarily have the funding to support a statistician, for example. "If you're always waiting for someone else to analyze the data for you, you're very limited on how quickly you can do things and how much you can do," said Illuzzi.

Earlier in her career, Illuzzi was focused on how to prevent the transmission of Group B streptococcus from mothers to newborns during birth. While she was enrolled in the master's in CDE program, she conducted a systematic review of the literature based on a course she took in evidence-based medicine. She was subsequently the first investigator to publish

Photo Robert Usak



Susan Mayne, Ph.D.

Research Methods

findings that questioned the Centers for Disease Control and Prevention protocol for prevention of neonatal Group B streptococcal disease. She went on to receive **NIH** funding to investigate the topic further and published several additional articles. Illuzzi then proceeded to try to determine the cause of rising cesarean rates in the United States. She conducted a large study at Yale-New Haven Hospital, looking at 30,000 births over 7 years and analyzed factors that contributed to the increase. Her study, which found that the increase in primary cesarean delivery was due to labor arrest disorders and non-reassuring fetal status, was one of the first published reports of this finding. It prompted the American Congress of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine to investigate the issue; it has been widely cited by subsequent studies; and has led to increased attention on reducing primary cesarean delivery rates.

“I couldn’t have done any of that research without the degree,” said Illuzzi, who had never taken statistics before enrolling in the program. At the time she finished the program, she was one of the few faculty members in her department with skills in statistical methods and programming, and was often asked to collaborate with colleagues. She contributed to a series of publications on gynecologic oncology and other areas, and is currently embarking on a cost-effectiveness analysis of the impact of high cesarean rates on health care costs across the country.

This spring, the department of chronic disease epidemiology offered a mini-course on concepts and applications of health outcomes research, an area that is experiencing tremendous growth.

“This is the way things are moving in the future, so Yale needs to be well positioned to train investigators to do that work,” said Mayne. The three-lecture course, taught by **Shiyi Wang, M.D., Ph.D.**, assistant professor of epidemiology (chronic diseases), filled up within two days. “There’s enormous demand for rigorous research methodology training, and we’re trying to build programs that help supply that demand,” said Mayne. 🌟

“There’s enormous demand for rigorous research methodology training, and we’re trying to build programs that help supply that demand.”

YCCI’s QA Team is Growing



Alyssa Gateman, M.P.H., CCRP

In an effort to ensure the high quality of clinical research at Yale, **YCCI** is expanding its **QA** staff with the addition of **Alyssa Gateman, M.P.H., CCRP**, who will join Yale on July 1. She will be working with **Susan Anderson, R.N., B.S.N., M.F.A.**, **YCCI** associate director for quality assurance and training, to support quality initiatives for clinical research across the medical campus.

Gateman is a recognized and respected **QA** expert who brings a wealth of experience to Yale’s **QA** team. She joins Yale from the Dana-Farber/Harvard Cancer Center (**DF/HCC**), where she most recently served as director of the Quality Assurance Office for Clinical Trials (**QACT**). Throughout her 14-year tenure at Dana-Farber, she provided oversight of all protocol registration,

data collection design of investigator-initiated clinical trials, and management of the internal auditing program. As director of the **QACT**, she provided leadership and management for the Data and Safety Monitoring Committee, Multi-Center Review Committee, Audit Committee, Clinical Investigations Leadership Committee, and Clinical Operations Committee (responsible for development of **DF/HCC** policies and procedures). She was directly involved with the Dana-Farber/Harvard Cancer Center’s participation in the **NCI**’s Cancer Center Support Grant as well as in a pilot initiative for the Clinical Trial Reporting Program (**CTRP**).

“We’re really excited to have Alyssa join our team,” said Anderson. “She has great experience having worked in quality assurance at Dana Farber that will be enormously helpful in our **QA** program, which spans Yale’s entire research enterprise.”

Gateman is the latest hire in **YCCI**’s efforts to build its **QA** program to support clinical research at Yale. The center will continue to augment its **QA** staff in the months ahead to support Yale’s growing clinical research portfolio. 🌟

Scholar Retreat Highlights Importance of Team Science and Training

Yale students, trainees, and faculty from across the medical campus attended the third annual All-Scholar Day Retreat sponsored by **YCCI** on April 1 at the Anlyan Center.

Following a poster session, **Christopher P. Austin, M.D.**, director of the National Center for Advancing Translational Sciences (**NCATS**), spoke to attendees on the role of **NCATS** in catalyzing translational innovation. “Translation is a team sport,” Austin said in his presentation, which stressed the need for collaboration, from both programs within the National Institutes of Health and those in external institutions, in order to speed the development of new treatments.

Austin’s role at **NCATS** brings together his work as a neurologist and his position at Merck, where he observed a team-based approach and a culture of deliverables in discovering novel targets and drugs but perceived a lack of deep biology to support research. The fact that people are unhealthier and that funders of research – both public and private – are impatient, points to a need to improve the translation of discoveries in the lab to benefit human health.



Christopher P. Austin, M.D.



Erin DeBiasi, M.D., clinical fellow in medicine, explains her research to Thomas J. Lynch, M.D., director of Yale Cancer Center.

Photo: Rob Lisak

The number of new drugs approved by the **FDA** per billion dollars spent on research and development has halved roughly every nine years since 1950, Austin said. **NCATS**’ mission is to bring together methods, technologies, and tools to tangibly improve human health across a wide range of diseases. Examples of translational problems requiring a team approach include predictive toxicology; the efficacy of data interoperability; clinical trial networks; **BHRs** for research; and adaptive clinical trial designs.

NCATS seeks to fulfill its mission through the **CTSA** program, the Rare Disease Research and Therapeutics program, technology programs to re-engineer translational science, innovative training programs, the development of a robust academic discipline of translational research, and new models for engaging and partnering with communities. “**NCATS** has just begun to transform itself and its programs to benefit patients,” said Austin.

Richard Flavell, Ph.D., F.R.S., founding chair of the Department of Immunobiology, presented on the role of inflammasomes in health, microbial imbalance, and disease. Flavell explained research conducted by immunobiologists at Yale and other institutions

that elucidates how altered microbiota in the gut is implicated in the pathogenesis of diabetes, rheumatoid arthritis, obesity, inflammation-induced cancer, and other diseases. This research sheds light on how diet, gut bacteria, and inflammation interact with one’s genotype in a cycle that leads to a wide variety of systemic diseases.

The number of new drugs approved by the **FDA** per billion dollars spent on research and development has halved roughly every nine years since 1950.

Other presenters included:

- **Ellen Hoffman, M.D.**, associate research scientist in the Yale Child Study Center and a trainee in the Investigative Medicine Program, who presented her research on zebrafish to examine neuropathways in autism. She is using a new genetic engineering technology to knock out newly discovered autism genes and small-molecule screening to identify common pathways and relevant drugs.
- **Serene Chen**, a student at Yale School of Medicine in the **TL1** program, who spent a year working on Variation in Recovery: Role of Gender on Outcomes of Young **AMI** Patients (**VIRGO**). **VIRGO** is a study examining heart disease in women aged 55 and under, a group that has about twice the risk of dying from a heart attack than men of similar age.
- **Meagan Moore, M.D., Ph.D.**, postdoctoral fellow in internal medicine (pulmonary and critical care), who presented research on the role of the protein receptor Plexin **C1** in pulmonary fibrosis – a disease that is both difficult to treat and unpredictable.

In his closing remarks, **YCCI** director **Robert S. Sherwin, M.D.**, noted that **YCCI**’s success in training scientists capable of bridging the gap between basic science and clinical care is illustrated by the results of its educational programs. The 88 **YCCI** Scholars who have been awarded research and salary support since the program’s inception in 2006 have received \$157 million in independent funding and published over 1,000 papers. Furthermore, about 90 percent of **YCCI** Scholars and Investigative Medicine alumni have remained in academic medicine. ☺