Training Tomorrow’s Investigators

YCCI is committed to training the next generation of clinical and translational researchers by offering robust educational programs that provide the support and expertise young investigators need to launch their careers. This effort has involved crossing boundaries and opening dialogues across the entire university to ensure that tomorrow’s investigators have the tools and training they need to conduct innovative research.

The Scholar Program highlights YCCI’s initiative under the Clinical and Translational Science Award to educate junior faculty members. YCCI Scholars benefit not just from salary and research support, but also from mentorship, research infrastructure, research-related courses, and opportunities to interact with other Scholars and investigators across the institution.

Since the program was established in 2006, there have been 105 Scholar awards. YCCI Scholars have applied successfully for $240 million of independent grant funding, including 47 Individual K Career Development Awards and 43 R01 awards; and have published more than 1,800 papers. Of the program’s graduates, more than 90% have remained in academic medicine, while five have continued their research careers in the pharmaceutical industry.

Scholar applications undergo a rigorous review process similar to an NIH study section. The review committee comprises senior investigators who are selected on the basis of their diverse expertise in research and their experience in fostering the career development of young investigators. This process accords with the program’s vision, which is to support Scholars across the entire spectrum of research. Recently, Scholar applications have been divided into two separate cohorts to ensure the continuous support of clinical/community-based outcomes research and translational projects. Applications from these two groups are reviewed by different committees whose membership reflects the appropriate expertise required for different types of research.

Scholars credit YCCI with launching their research careers, allowing them to investigate new areas, and supplying much-needed expertise in areas in which they lacked experience. For many, the monthly Research-in-Progress meetings are an opportunity to forge interdisciplinary collaborations, while courses in such subjects as grant writing produce tangible results.

“The Scholar award was the big foot in the door,” said 2006 YCCI Scholar Richard Kibbey, MD, PhD, associate professor of medicine (endocrinology) and of cellular and molecular physiology. “It allowed me to generate a lot of the preliminary data as well as manuscripts I would need to apply for additional funding, and made me a much better candidate.”

Scholars universally agree that mentorship has been a major factor in their success. Mentors are senior faculty members with strong research portfolios who have the opportunity to undergo mentoring training offered by YCCI. “Mentorship has been the key at all stages,” said 2007 YCCI Scholar Elijah Paintsil, MD, associate professor of pediatrics (infectious diseases) and of epidemiology (microbial diseases).
FORMER SCHOLARS USE AWARD AS A SPRINGBOARD TO EXPAND THEIR RESEARCH

Marcella Nunez-Smith, MD, MHS  2006 YCCI Scholar

Associate Professor of Medicine (General Medicine) and of Epidemiology (Chronic Diseases)
YCCI Deputy Director of Health Equity Research and Workforce Development

Growing up in St. Thomas, U.S. Virgin Islands, an area with a shortage of health professionals, Marcella Nunez-Smith, MD, MHS, remembers countless stories of loved ones and members of her community who struggled with their health or died prematurely. That experience led her to pursue a career in medicine and conduct research that focuses on vulnerable populations and their interactions with health care systems.

Ever since her arrival at Yale as a fellow in the Robert Wood Johnson Foundation (RWJF) Clinical Scholars Program, Nunez-Smith has been on a mission to develop ways of addressing health and health care inequities wherever they are: in patient settings, in the health care workforce, and in medical education. As a 2006 YCCI Scholar, she gathered preliminary data for what is now known as PreDict (Patient-Reported Experiences of Discrimination in Care Tool). PreDict is a tool that assesses the patient care experience and measures hospital performance with the goal of improving the quality of care delivery.

“The Scholar award was tremendously helpful because it allowed me to launch a line of inquiry that was new, and then provided me with the resources to complete the preliminary work that allowed us to be competitive for major NIH grants,” she said.

Nunez-Smith went on to develop the Eastern Caribbean Health Outcomes Research Network (ECHORN), a collaborative multimillion-dollar research study funded by the National Institute on Minority Health and Health Disparities (NIMHD). ECHORN examines the risk factors and prevalence of cancer, diabetes, and heart disease in the eastern Caribbean, a region for which such data are lacking.

Both ECHORN and PreDict – which has spurred several related projects undertaken by Nunez-Smith’s mentees – are now incorporated into the Equity Research and Innovation Center (ERIC), where she serves as director. ERIC builds on the local, national, and global experience of Nunez-Smith and 60 team members who are involved in research aimed at narrowing health and health care inequities, as well as disparities in the health care workforce and medical education.

As a former YCCI Scholar, Nunez-Smith appreciates the benefits of mentorship and serves as an academic advisor to Yale School of Medicine students. She also continues her involvement with the RWJF as a core faculty member of the Clinical Scholars Program and co-director of Community Research Initiatives. “I’m working towards synergy across all of these programs so they’re not siloed,” she said.

“The idea is to think about core elements of knowledge for our faculty for population health and health equity, and engage stakeholders in our work.”

Elijah Paintsil, MBChB  2007 YCCI Scholar

Associate Professor of Pediatrics (Infectious Disease), of Epidemiology (Microbial Diseases), and of Pharmacology

In 1998, the HIV epidemic was in full force in Ghana, but Elijah Paintsil, MBChB, had no treatment to offer his patients. He came to the United States on a mission to acquire research expertise and find solutions to treat AIDS and other infectious diseases.

Already a practicing physician, Paintsil had to repeat his residency training before he came to Yale to pursue a fellowship in pediatric infectious diseases. His 2007 YCCI Scholar award helped support his research on the high rate of hepatitis C in intravenous drug users. He showed that the virus can live more than 60 days in used syringes. This finding led to collaboration with colleagues at the School of Public Health to investigate disinfectants and other means of reducing infection rates.

“The Scholar award provided me with the needed time, mentorship, and research support to successfully navigate through an academic physician-scientist career,” he said. It allowed him to compete for an NIH Career Development Award and seamlessly transition to an R01 award.

Paintsil makes ample use of such YCCI-supported resources as data analysis, study design, and magnetic resonance spectroscopy. During his term as a Scholar, YCCI’s focus on interdisciplinary research through the monthly Research-in-Progress seminars spurred him to consider conducting research overseas.

In New Haven, he had seen that pediatric HIV patients who were now adults were not complying with their medication regimen. He suspected that one reason for this negligence was that they weren’t being told their diagnosis. In Ghana, many thought that children with HIV would not live to adulthood; not surprisingly, only 21 percent of them knew their diagnosis. Paintsil designed an intervention using a culturally sensitive, adaptive approach for caregivers to disclose HIV information in an age-appropriate and personalized way. He is currently conducting a large multicenter trial in Ghana to determine whether this intervention will make a difference.

In his lab, Paintsil is investigating the side effects that almost half of those on antiretroviral therapy experience. His group has identified a mitochondrial protein in the blood that could serve as a biomarker of toxicity, negating the need for guesswork or a biopsy. The ability to conduct research in basic science and public health has been invaluable to Paintsil’s work. “It wouldn’t have been possible without the facilities YCCI has put in place,” he said.
Yawei Zhang, MD, PhD, MPH 2008 YCCI Scholar
Associate Professor of Epidemiology (Environmental Health)

For Yawei Zhang, MD, PhD, MPH, a grant from YCCI has flourished into an ongoing collaboration. As a YCCI Scholar in 2008, Zhang sought to examine the fetal origins hypothesis, which connects perinatal nutritional deficiencies to cardiovascular disease, diabetes, and cancer in later life. She looked at how expectant mothers’ intake of one-carbon nutrients, such as folate, had an impact on the methylation status of DNA, which is vital to gene expression during fetal development.

Zhang used her preliminary data, which confirmed her hypothesis that folate intake has an effect on methylation, to develop a larger-scale birth cohort study of 10,500 mother-and-baby pairs in partnership with the Gansu Provincial Maternity and Child Care Hospital in Lanzhou, China. The study was expanded to include research on the impact of air pollution, passive smoking, and many other environmental and lifestyle factors, as well as gene-environment interactions on newborns. The city of Lanzhou has some of the worst air pollution in China; and according to Zhang, approximately 30% of pregnant women are regularly exposed to secondhand smoke even though the negative effects of passive smoking on fetal development are known in China.

The partnership led to a mutually beneficial relationship. While Gansu Hospital provides ongoing funding for the birth cohort study, Zhang has brought more than 30 physician-researchers from the hospital to her lab at Yale for research training.

Zhang’s work caught the attention of the Chinese government, which has lent further support to her study. Shanxi Province awarded her a grant to establish an additional birth cohort study in the city of Taiyuan. “Air pollution and passive smoking are hot topics in China right now,” she said. “There have been very few studies conducted in the Chinese population in these areas.”

Many other areas of China are also establishing birth cohort studies; Zhang is helping to foster this vital research by sharing her expertise not only with the scholars she trains at Yale, but also with researchers in China. Zhang is sharing her questionnaires with other researchers who are establishing a cohort study consortium, which, she hopes, will lead to additional studies on key health issues in China.
While much is known about the genetic basis of cancer, less has been known about the role of the immune system in its progression until recently. Oscar Colegio, MD, PhD, aims to change that by studying tumor immunology to unravel how the immune response can lead to tumor growth.

His research is linked to his clinical work caring for solid-organ transplant recipients who are on an immunosuppressant regimen and therefore have a one-hundredfold increased risk of squamous cell carcinoma. His 2010 Scholar project focused on the role of macrophages, cells in the innate immune system that are found in all tumors. His hypothesis that communication between cancer cells and macrophages led to their activation and increased tumor growth proved to be correct.

Working in collaboration with his mentor, Ruslan Medzhitov, PhD, the David W. Wallace Professor of Immunobiology, Colegio went on to discover that lactic acid, a byproduct of cancer cell metabolism that has largely been overlooked, transforms macrophages into abettors of tumor growth. He has also found that certain key enzymes within macrophages are critical for supporting tumor progression, and is currently exploring whether their inhibition can lead to tumor regression.

Colegio’s collaborations with the Yale-New Haven Transplantation Center and Yale Cancer Center illustrate the benefits of crossing boundaries to train the next generation of investigators. Moving from mouse models to human cells, he is excited about the possible wider implications of his findings in developing cancer therapies that target macrophages or inhibit enzymes that play a role in tumor growth.

According to Colegio, the education and access to facilities afforded by the Scholar award have had a profound impact on his research. A sample grant he wrote during the grant writing course led to an award from the National Cancer Institute, which funds his current work. He has also received biostatistical support from the Yale Center for Analytical Sciences, and has found the Research-in-Progress seminars to be very helpful. “YCCI has provided very practical concrete support that is essential for investigators to have as they move their research forward,” he said. As his research progresses, he continues to turn to YCCI. “I keep going back to YCCI for all sorts of resources,” he said.

Kelly Cosgrove, PhD 2009 YCCI Scholar
Associate Professor of Psychiatry, of Diagnostic Radiology, and of Neurobiology

When it comes to smoking, men and women have differing behaviors, reasons for using tobacco, and responses to treatment. According to research conducted by Kelly Cosgrove, PhD, some of these differences may be explained by the effect smoking has on their brains.

Cosgrove uses positron emission tomography (PET) and single-photon emission computed tomography (SPECT) scans to gain insights into the brains of people after they’ve stopped using alcohol and tobacco. Her work has shown that smoking cigarettes activates a different dopamine-driven response in men compared to women.

“A lot of smoking cessation treatments are directed at nicotine’s action in the brain, but nicotine reinforcement is not what’s activated in women,” she said. “So we need to switch gears from replacing nicotine or targeting those pathways and focus more on the reasons women smoke.”

Trained as a clinical psychologist who worked with individuals suffering from drug addiction, Cosgrove was driven to conduct research in order to find more effective ways of helping her patients recover and avoid relapse. As a YCCI Scholar, she found that it takes up to 12 weeks after someone quits smoking for the number of nicotine receptors they’ve developed to decrease. This finding suggests that smokers may need long-term support to kick the habit. The award helped her start her research portfolio, which continues to grow and for which she utilizes such YCCI-supported resources as the Magnetic Resonance Research Center and Core lab.

Her recent work has shown that smoking interferes with the recovery of receptors for the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) during alcohol withdrawal. “A lot of times people don’t tease apart differences between alcohol-dependent smokers and nonsmokers,” she said. When she investigated these differences, she found that smoking seems to interfere with the neuroadaptations that happen during the first month of alcohol withdrawal. This difference may make it harder for smokers to stop drinking, and highlights the need for clinicians to consider the clinical implications of encouraging alcohol and tobacco cessation at the same time. “When I help people quit smoking, I ask them not to drink, because as soon as they drink, they’ll want to smoke,” she said. “Why wouldn’t we say the same thing for the reverse?”

Oscar Colegio, MD, PhD 2010 YCCI Scholar
Assistant Professor of Dermatology

Kelly Cosgrove, PhD 2009 YCCI Scholar
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“Detecting early-stage cancer via a simple blood test is one of the holy grails in oncology,” says Abhijit Patel, M.D., Ph.D. For many types of cancer, the probability of achieving a cure is much higher if the tumor is detected before it has had a chance to spread. Through the study of tumor-derived DNA fragments in blood, Patel hopes to move cancer care closer to attaining this goal.

As a 2010 YCCI scholar, and in ongoing work in his lab, Patel has been focused on developing technology to measure tiny amounts of DNA shed into the bloodstream from dying cancer cells. Scientists can zero in on these DNA fragments because they contain mutation signatures that are highly tumor-specific.

Using tumor DNA as a biomarker could expand a physician’s capacity to detect and treat cancer. “Tumor DNA is so cancer-specific, you are extremely unlikely to get false positive results in a healthy person—so that makes it very attractive as a marker for screening,” Patel said. The “liquid biopsy,” as this type of blood test is sometimes called, can also be used to determine the mutation profile of a patient’s tumor noninvasively in order to personalize therapy. Moreover, the test can be used to closely monitor changes in mutations over time so that therapy can be modified without having to resort to frequent invasive biopsies.

Currently, Patel is continuing his work to improve the sensitivity of existing technology to detect even smaller amounts of genetic material. He has continued his collaboration with YCCI through his use of its biospecimen software platform, which helps his team bank and track the thousands of blood samples he collects through collaborations with several other researchers and physicians from across Yale. He also has taken advantage of the next-generation DNA sequencing facility at Yale’s West Campus as well as the biostatistical support offered through the Yale Center for Analytical Sciences. As he progresses in his research career, he continues to take advantage of the support available from the YCCI-supported core facilities that are critical to his work.

Abhijit Patel, MD, PhD 2010 YCCI Scholar
Assistant Professor of Therapeutic Radiology

How the immune system goes awry to cause disease has long intrigued Stephanie Eisenbarth, MD, PhD. To solve this puzzle, she used her 2011 Scholar award to focus on the basic task of characterizing the immune response in healthy subjects. While many questions in immunology have been answered using mouse models, Eisenbarth is applying these findings to humans.

Studying the normal immune system has led her to study how dendritic cells – which act as messengers between the innate and adaptive immune systems – work. Her main area of interest is understanding and predicting why approximately 10 percent of the individuals vaccinated fail to respond. Dendritic cells act as a sort of field marshal for the immune system, regulating what it sees and therefore responds to. By focusing on how these cells function, Eisenbarth hopes to be able to devise methods to better target them and increase the vaccine response rate.

The Scholar award was one of the first major awards Eisenbarth received when she started her lab. “That kind of seed money is really critical,” she said. “It helps you get established.” Since then she has gone on to receive other funding, including a Hartwell Biomedical Research Award and a Clinical Scientist Development Award from the Doris Duke Charitable Foundation. She is poised to conduct more intricate research examining how peripheral blood monocytes move through an artificial tissue-like matrix in vitro. “It’s a very complex process that’s fundamental to initiating vaccine immunity,” she said. Because immune cells don’t react well to being frozen, Eisenbarth has established what she terms a “living biorepository” that enables her to call upon healthy subjects to donate a blood sample up to eight times a year. YCCI has been instrumental in helping her recruit subjects. The program has grown exponentially and has been so successful that Eisenbarth is collaborating with YCCI to expand it and make it available to other investigators. She has contributed protocols and other research expertise, while YCCI has helped establish the database infrastructure via OnCore, Yale’s clinical research management system. YCCI is also marketing the biorepository through ads that are linked to its Help Us Discover campaign – an effort that will directly benefit Eisenbarth’s research, as well as that of other researchers.

Besides blood, Eisenbarth is collecting stool samples for the biorepository in order to investigate the role of gut microbes in regulating the immune response. The ability to obtain multiple samples from the same subject over time is crucial to her research and has benefited from her collaboration with YCCI. “Research is a team effort,” she said. “Working with YCCI has facilitated our success.”

Stephanie Eisenbarth, MD, PhD 2011 YCCI Scholar
Assistant Professor of Laboratory Medicine, of Immunobiology, and of Medicine (Immunology)
MEET YCCI’S EDUCATION PROGRAM LEADERSHIP

Robert Sherwin, MD
YCCI Director, Associate Dean for Clinical and Translational Sciences

Throughout my career, I have been committed to nurturing the next generation of investigators. As director of YCCI and PI of the CTSA, I remain passionate about pursuing this goal. As YCCI celebrates its tenth anniversary, I am pleased by the ways in which our support has helped to expand and enhance Yale’s existing educational programs. I am especially proud of our Scholars program and the training and mentorship it provides to help launch the careers of tomorrow’s researchers. Looking ahead, training members of our research community and expanding Yale’s cadre of exceptional young investigators will remain one of our highest priorities.

Lloyd Cantley, MD
Co-director, Education

Lloyd Cantley, MD, is a noted nephrologist who studies the mechanisms of renal tubule formation and repair. He has mentored about 40 trainees in his lab, where he studies the mechanisms by which kidney cell regeneration occurs following acute kidney injury in order to develop therapies to enhance this process. His goal is to identify pathways that would be logical targets for drug therapy to either accelerate normal repair in the case of acute kidney injury, or block repair pathways in polycystic kidney disease or chronic kidney disease. From the beginning of Cantley’s career, he has enthusiastically pursued teaching and mentoring. As a fellow at Harvard University, he taught medical students; today, in addition to his appointment as co-director of education, he teaches physiology case conferences to first-year medical students. He views his role at YCCI as mentoring on a larger scale, in which he has the opportunity to guide young investigators on becoming successful researchers. He is interested in the approach young faculty members take in answering research questions, and relishes the chance to offer a fresh perspective on their work.

Eugene Shapiro, MD
Co-director, Education

An experienced clinical epidemiologist in pediatric infectious diseases, Eugene Shapiro, MD, is especially interested in vaccines and in Lyme disease. He is currently involved in studies of the effectiveness of the HPV vaccine in clinical practice. This work includes qualitative research to discover why uptake of the vaccine is low in the United States, as well as a case-control study to evaluate the vaccine’s effectiveness by age at the time of vaccination and the number of doses given. As a researcher who has had continuous NIH funding since 1983 and has mentored hundreds of young researchers, Shapiro is ideally suited to lead YCCI’s educational program. His interest in mentoring extends beyond mentoring younger colleagues. He was an author of a report on the results of a national trial of the effectiveness of a curriculum to train mentors. Despite the significant time commitment involved in mentoring, typically little attention is given to training faculty for this vital role. The response to the training program was so positive that Shapiro and Patrick O’Connor, MD, associate director of YCCI’s community research core, continue to co-teach a yearly course on mentoring for Yale faculty.

Rajita Sinha, PhD
Co-director, Education

Rajita Sinha, PhD, is internationally known for her pioneering research on the neural and biobehavioral mechanisms linking stress to addiction. She directs the Yale Stress Center, started with one of the largest interdisciplinary Consortium grants from the National Institutes of Health, to study the effects of stress and self-control on addictive behaviors and chronic disease. The collaborative research conducted at the center by Sinha and other scientists is multidisciplinary. The Stress Center is developing and testing interventions to reverse the toxic effects of stress and the loss of self-control that drive addictive behaviors. Sinha is examining the role of long-term stress and repeated stress exposures in alcohol and substance dependence to develop new therapies to reduce compulsive motivation to use alcohol and drugs of abuse. She brings her interdisciplinary focus to her role as co-director of education, where she seeks to increase the diversity of trainees and mentors, and provides guidance in connecting trainees to colleagues in different disciplines. She enjoys helping young investigators shape their ideas into scientific hypotheses, and watching them get hooked on research.
Joseph Craft, MD
Director, Investigative Medicine Program

Joseph Craft, MD, is an internationally recognized expert on the pathogenesis of systemic autoimmune diseases, investigating both animal models of these diseases as well as patients in the clinic. He has been funded by the NIH since 1985 and is a past NIH MERIT Awardee.

Since 2004, Craft has directed the Investigative Medicine Program, which awards a PhD to physicians training in either laboratory-based or clinically-based patient-oriented research. He has served as a mentor to dozens of postdoctoral fellows, graduate students, medical students, and rheumatology fellows, many of whom have taken positions in academia or industry.

John Forrest, Jr., MD
Director, Multidisciplinary Pre-Doctoral Training Program in Translational Research

John Forrest, Jr., MD, is a highly respected investigator with NIH R01 funding in the area of hormonal regulation of ion transport. He has published more than 150 articles in peer-reviewed journals.

Forrest has served as director of the Office of Student Research at the School of Medicine for over 30 years and is program director of the Medical Student Research Program, which funds clinical research training for medical, nursing, and biomedical engineering students. Yale is one of the few medical schools to require a dissertation based on original research, a tradition that the program helps support.

Cary Gross, MD
Director, National Clinical Scholars Program

Cary Gross, MD, is co-director of the RWJF Clinical Scholars Program and will direct the newly launched National Clinical Scholars Program at Yale. The new program will train nurses and physicians to serve as scholars, leaders, and innovators who will improve health care, community health, and public policy.

Gross’s research focuses on disconnections between evidence generated from clinical research and the needs of patients in the real world. He has received NIH-funded grants to explore barriers to clinical trial enrollment, the impact of non-cancer illnesses on older persons with cancer, and the dissemination of new cancer screening and treatment modalities into clinical practice.

Barbara Kazmierczak, PhD, MD
Director, MD-PhD Program

Barbara Kazmierczak, PhD, MD, directs Yale’s MD-PhD program, which draws upon the flexibility of the School of Medicine’s MD program and the breadth and depth of graduate education at Yale to allow MD-PhD candidates to customize their educational paths.

Kazmierczak studies how such environmental or commensal organisms as *Pseudomonas aeruginosa* and *Staphylococcus aureus* can become pathogens capable of causing severe life-threatening infections. She is also exploring how the use of antibiotics alters the composition of the gastrointestinal microbiome and the consequences to an individual’s ability to mount immune responses to vaccines and to infectious pathogens.
Gustavo Angarita-Africano, MD
Instructor in Psychiatry
Glutamate-Glutamine Cycling (VCYC) During Cocaine Abstinence Using 13C-MRS

Deepa Camenga, MD, MHS
Instructor of Pediatrics (Adolescent Medicine)
Text Messaging to Augment Physician Advice for Smoking Cessation in a College Health Clinic

Stuart Campbell, PhD
Assistant Professor of Biomedical Engineering & Physiology
Establishing Feasibility of an In Vitro Assay for Cardiomyopathy Inheritance

Forrest Crawford, PhD
Assistant Professor of Public Health (Biostatistics) and of Ecology and Evolutionary Biology
Estimation of Disease Rates in Hidden Populations

Marcelo Dietrich, MD, PhD
Assistant Professor of Comparative Medicine and of Neurobiology
Hunger-Promoting AGRP Neurons and Their Cellular Substrates in the Etiology of Anorexia Nervosa

Jason Gerrard, MD, PhD
Assistant Professor of Neurosurgery and of Neurobiology
How and Where Do Seizures Happen? A Systems Neuroscience Approach to Understanding Epileptogenesis in Epilepsy Patients and a Novel Animal Model in Parallel

Emily Gilmore, MD
Assistant Professor of Neurology
Using Noninvasive Electroencephalography and Cerebral Oximetry Monitoring to Understand Brain Physiology in Critically Ill Patients with Sepsis

Shangqin Guo, PhD
Assistant Professor of Cell Biology
A New Model for Cancer Cell-of-Origin

James Hansen, MD
Assistant Professor of Therapeutic Radiology
Optimizing a Lupus Autoantibody for Targeted Cancer Therapy
Janice Hwang, MD  
Instructor in Medicine (Endocrinology)  
Investigating Fructose Production in the Central Nervous System via the Polyol Pathway in Patients with Obesity and Type 2 Diabetes Mellitus

Daniel Weinberger, PhD  
Assistant Professor of Public Health (Microbial Diseases)  
Predicting Patterns of Pneumococcal Serotype Replacement among Adults Using Experimental and Epidemiological Data

Melissa Knauert, MD, PhD  
Instructor in Medicine (Pulmonary)  
Circadian Misalignment in Critically Ill Patients

Grace Kong, PhD  
Associate Research Scientist in Psychiatry  
Interactive Mobile Phone Intervention to Reinforce Smoking Cessation for Underserved Adolescent Smokers

Neil Romberg, MD  
Assistant Professor of Immunology  
Characterization of the Immune Deficient and Autoimmune Features of Smith-Magenis Syndrome

Monica Ordway, PhD, APRN, PNP-BC  
Assistant Professor of Nursing (Acute Care)  
Associations of Socioeconomic Adversity and Sleep with Allostatic Load Among Toddlers

Xiting Yan, PhD  
Assistant Professor of Medicine (Pulmonary)  
Computational Analysis of Longitudinal Blood and Airway Gene Expression Data to Define Endophenotypes of Asthma

Brian Shuch, MD  
Assistant Professor of Urology and of Diagnostic Radiology; Assistant Professor of Radiology  
Tumor Heterogeneity in the Small Renal Mass: Biomarker Approaches to Limit Overtreatment
MENTORING THE NEXT GENERATION

The YCCI Society of Mentors is a group of experienced researchers and mentors who are committed to helping YCCI Scholars succeed. Below are selected senior faculty members who are helping to guide the next generation of clinical and translational scientists.

Gail D’Onofrio, MD, MS
Professor of Emergency Medicine, Chair Of The Department Of Emergency Medicine

“Academic faculty members need to be very proactive in their career trajectory,” said Gail D’Onofrio, MD, MS, professor of emergency medicine and chair of the department of emergency medicine. “They need someone to help them navigate the academic waters. It’s an active process.”

D’Onofrio has extensive experience mentoring dozens of young investigators from multiple disciplines at Yale and other institutions. She is Co-PI with Patrick O’Connor, MD, on a training grant from the National Institute on Drug Abuse (NIDA) to train Fellows from such fields as emergency medicine, internal medicine, obstetrics/gynecology, and pediatrics to become independent investigators focusing on drug abuse, addiction, and HIV prevention in general medical settings. She also leads grants from the Substance Abuse and Mental Health Services Administration (SAMHSA) to train primary care residents and students in the professions of medicine, nursing, social work, and counseling. Her mentees include researchers from fellow-CTSA sites New York University and the University of North Carolina.

As a mentor, D’Onofrio has a hands-on approach to helping junior colleagues align their interests with fundable research proposals, write grants, establish a professional network at Yale and in the wider community, and balance professional activities with scholarship. D’Onofrio is a national expert on heart disease in women and internationally known for her work in screening emergency department patients for alcohol and other drug use. A recent study published in the Journal of the American Medical Association was the first-known randomized trial comparing three treatment strategies for opioid-dependent patients receiving emergency care. Eighty percent of those treated with buprenorphine in the emergency department were engaged in treatment 30 days later and were less likely to use illicit opioids. D’Onofrio, Co-PI David Fiellin, MD, and other colleagues are currently developing plans to expand this treatment model to multiple sites. D’Onofrio is committed to expanding the cadre of clinical researchers at Yale University. Working with Yale-New Haven Hospital — the fourth largest hospital in the United States — she said “we have the opportunity to enroll patients with a wide range of diseases and to work with community and outreach programs to improve the health of the public. Centralized CTSA-supported resources are critical to these efforts.”

Thomas Gill, MD
Humana Foundation Professor of Medicine (Geriatrics) and Professor of Epidemiology (Chronic Diseases) and of Investigative Medicine

As an increasing number of people live active lives well into their seventies, eighties, and beyond, geriatric physicians are charged with helping their elderly patients live not only longer but healthier lives. In his research and clinical practice, Thomas Gill, MD, Humana Foundation Professor of Medicine (Geriatrics) and director of the Yale Program on Aging, addresses this challenge by drawing upon the wealth of knowledge from his clinical practice to inform his research.

Gill’s research focuses on the mechanisms of the aging process and the impact of the inevitable decline in function—and the increase in disability—in older patients. His ongoing study, the Yale Precipitating Events Project, which began in 1998, has been closely monitoring a large cohort of elderly patients over more than 17 years, and has shed new light on the resiliency of older people to recover from debilitating events that can frequently occur in daily life. The study has changed both the way in which family and professional caregivers view disability in the elderly, and ways to manage it. An earlier clinical trial led by Gill showed that home-based physical therapy, or “prehabilitation,” is an effective strategy for preventing injury and stopping the effects of decline before they start. Gill is currently leading a large multisite clinical trial that is evaluating the effectiveness of an evidence-based intervention to reduce the risk of serious fall injuries among vulnerable older persons.

Gill began his career at Yale as a Robert Wood Johnson Clinical Scholar in 1991. As a clinician, he sees the results of his research play out in the lives of the patients he treats, and finds new questions to ask as well. To him, research and clinical training go hand in hand. He encourages his clinically trained mentees to “take advantage of their clinical knowledge and experience when framing their research questions and hypotheses,” in order to distinguish themselves in their chosen fields.
With treatments constantly improving and patients living longer, HIV is now considered a chronic disease, and affects people in all walks of life, including many elderly. However, this wasn’t always the case. Amy Justice, MD, PhD, professor of medicine and public health, as well as chief of general internal medicine at Connecticut’s VA, began conceptualizing HIV as a chronic disease in 1997, when combination antiretroviral therapy began to take off. This was fully ten years before many in the field adopted the same way of thinking.

As it was clear those with HIV would be living longer, Justice realized the importance of studying the impact of the disease on patients as they aged. That same year, Justice began the now-renowned Veterans Aging Cohort Study (VACS). In the past 18 years, VACS has followed more than 50,000 HIV-positive veterans who are matched to 100,000 HIV-negative veterans to determine how HIV, which like many chronic diseases that take their toll on all systems of the body, affects medical and psychiatric health simultaneously. There are several smaller studies nested within the larger sample that include survey data, a tissue repository, and more in-depth evaluations of pulmonary and cardiac disease. Through the study, Justice has chronicled the shifting outcomes of chronic HIV infection, and seeks to use the disease as a model for better understanding of chronic diseases of all varieties.

VACS was recently funded as a consortium by the National Institute of Alcohol Abuse and Alcoholism. The consortium will have a particular focus on how alcohol and substance abuse affects the long-term health of people living with HIV.

For Justice, the mentor/mentee relationship is a mutually beneficial one. While she imparts guidance to her mentees, she says, “[they] see holes in arguments that may no longer be obvious when you’ve been working with something for a long time. It certainly keeps you on your toes.”

Complex but common mental illnesses such as schizophrenia, alcoholism, and depression continue to challenge scientists who seek ever better treatments for patients. John H. Krystal, MD, Robert L. McNeil, Jr. Professor of Psychiatry, professor of neurobiology, and chair of the Department of Psychiatry, has made a career of delving into molecular levels of the brain to better understand how these psychiatric disorders function, and finding novel treatments for them in order to improve the lives of patients and their families.

One of these novel treatments, for which Krystal is well known, made use of ketamine, infamously known as “Special K.” Krystal and a team of investigators successfully used the drug in the 1990s to safely and transiently produce in healthy people symptoms and disturbances in brain function associated with schizophrenia, and to probe the neurobiology of alcohol intoxication and alcoholism. His laboratory then discovered the rapid antidepressant properties of ketamine in humans. Ketamine is now administered widely for treatment-resistant symptoms of depression, and one form of ketamine is now in Phase III clinical trials.

Krystal has mentored several YCCI Scholars who study how the mechanisms of the brain at the molecular level affect behavior, relating to such disorders as cocaine addiction, mood disorders, delusional disorder, and schizophrenia. “I learned very early on,” he said, of the days when he was a mentee himself, “to ask the important question, rather than the easy question, and then to design the most powerful experiment that could destroy it: what we used to call the ‘killer experiment.’ If the hypothesis could withstand these kinds of tests, then it might be more powerful.” Krystal believes that it is an important part of the scientific process to mentor young investigators, and pass on the lessons he has learned. “In some way, the way I can best have an impact on my field is by training people who will be future innovators.”

**Amy Justice, MD, PhD**

Professor of Medicine (General Medicine) and of Public Health (Health Policy)

**John H. Krystal, MD**

Robert L. McNeil, Jr. Professor of Psychiatry and Professor of Neurobiology
Biorepository Study

Someday they will thank you for the few minutes you gave today.

Your clinical samples are important components of medical research. A new program will bring thousands of samples together so researchers can more easily develop life-saving treatments. Volunteering is as quick and easy as giving blood or other clinical samples. Your donation will be held completely secure and your information in the strictest of confidence.

Compensation will be provided.
To learn more, visit www.yalestudies.org or call 1-877-y-studies.

Supported by National Institute of Allergy and Infectious Disease and National Institutes of Health
HIC # 003704933

Clinical Cancer Trials

Yale Cancer Center, one of only 41 comprehensive Cancer Centers in the country designated by the National Cancer Institute, harnesses the resources of the Yale School of Medicine and Yale-New Haven Hospital in order to advance cancer research and develop effective therapies for cancer treatment. None of these advances would be possible if people like you weren’t willing to take part in clinical trials. Our portfolio includes over 100 active trials, providing options beyond the standard care for patients with most cancers.

By participating in a study, you can help Yale continue its tradition of advancing medical knowledge. For more information about cancer trials, visit www.yalecancercenter.org or call (203) 785-5702

Type 2 Diabetes & Weight Loss Brain Imaging Study

Do you have type 2 diabetes? Do you want to lose weight?

You can play an important role in research by volunteering for a study that will look at the effects of an 8-week weight loss diet on reduced blood sugar and brain responses to food images.

If you are 30 to 58 years of age, have type 2 diabetes, and are above normal weight, you may be eligible to participate. The study involves:

- Screening history, physical exam, and blood work
- Infusions of insulin and glucose and MRI scan
- 8-week weight loss diet, with a once a day free meal replacement
- Free diet consultation

We are also looking for non-diabetic volunteers to participate.

Compensation up to $750
To learn more or make an appointment, contact: 1-877-978-8343 or helpusdiscover@yale.edu

Supported by the National Institute on Aging
HIC #0108012609

IBS Study

Do you suffer from Irritable Bowel Syndrome (IBS)?

If you are 18 to 70 years of age and have been suffering with active irritable bowel syndrome, you may be eligible to participate in a four week individualized diet. This study requires follow-up visits at four and eight weeks.

Compensation of $200 for participation.
For more information or to see if you qualify for the study, please call Theresa Weiss at (203) 737-1391 or email theresa.weiss@yale.edu

Supported by Cell Sciences System Corporation
HIC #1404013784

To find out more about trials at Yale, visit our website, www.yalestudies.org. Or call 1-877-y-studies for more information.
Yale has hundreds of clinical studies under way for a wide variety of conditions. None of them would be possible without volunteers who were willing to take part in clinical studies. Volunteers like you are the only way for medical breakthroughs to reach the public. Please consider participating in a clinical study and helping Yale continue its tradition of advancing medical knowledge.

Research Studies at the Yale Child Study Center

Are you concerned about your infant’s or toddler’s development?
Do you have concerns that your infant or toddler may have an Autism Spectrum Disorder (ASD) or developmental delay? Take part in a research study that examines early childhood development and helps to answer these questions. Parents often find the visits highly informative and helpful. Research from these studies may lead to the development of new methods to diagnose and treat ASD and related disorders in young children.

For more information and to learn if your child is eligible, please contact us at (203) 764-5933 or visit www.medicine.yale.edu/childstudy/yescog/index.aspx

Walk Study

Are you able to walk for 6 minutes?

Play an important role in research by volunteering for this free and confidential study that focuses on walking speed and quality of life.

If you are 50 to 60 years of age and are able to walk for 6 minutes without help from another person (walkers and canes are okay), you may be eligible to participate. This will involve study visit lasting 90 to 120 minutes and blood pressure screening at no cost to you. Slow walkers are welcome and encouraged to call.

Compensation of $50

To learn more or see if you are eligible to participate, call (203) 737-7401 or email 6minutewalk@yale.edu

Supported by Precision Health Economics

Children’s Air Pollution Study (CAPS)

Does your child have asthma?

Millions of children suffer with asthma. Please join us in studying how cleaner indoor air can help.

If you have a 5 to 11 year old child with asthma, you may be eligible to participate in an 18-week clinical trial of indoor air cleaners. The study involves a brief phone screening, sampling of your home’s indoor air, and home visits every 6 weeks to install a new air cleaner and collect information on your child’s asthma symptoms and medication use.

Compensation of $200 for full 18-week study

To learn more or to see if you are eligible, contact (203) 737-6469 or email CAPS@yale.edu. Visit our website for more information: www.yale.edu/cpsee/CAPS.html

Supported by National Institute of Environmental Health Sciences

Alcohol Reduction Study

Do you drink too much when you’re stressed?
The Yale Stress Center is looking for individuals who are 18 to 60 years old who are looking to participate in an alcohol research study.

Compensation up to $790

To learn more or make an appointment, please call 1-888-Y-STRESS or email stress@yale.edu or visit www.yal_estress.org

Supported by National Institute on Alcohol Abuse and Alcoholism

Neurofeedback for Tourette Syndrome Study

Does your child have chronic tics or Tourette Syndrome?

Your child can play an important role in research by volunteering for this free and confidential study that will evaluate biofeedback as a new treatment option.

If your child is between 11 and 19 years old and has a tic disorder or Tourette Syndrome, they may be eligible to participate. The study will entail 7 MRI scans over a 4 week period.

Compensation up to $600. Travel reimbursement available for one-way distance over 30 miles.

To learn more or see if your child is eligible, please contact Christopher Walsh at (203) 737-6055 or email christopher.walsh@yale.edu

Supported by Department of Veterans Affairs; National Center for Research Resources; National Institute of Biomedical Imaging and Bioengineering; National Institute of Mental Health; National Institutes of Health; Yale University School of Medicine

Binge Eating Study

Are you overweight and do you binge eat?

If you are 21 to 65 years old, currently overweight, binge eat or sometimes feel out of control while eating or upset about eating, and do not take antidepressants, you may be eligible to participate in a new study of a medication treatment for binge eating.

Compensation up to $100

To learn more or see if you are eligible to participate, call (203) 737-4299 or visit yalepower.wordpress.com/current-research

Supported by National Institute of Diabetes and Digestive & Kidney Diseases
The Center for Biomedical and Interventional Technology (CBIT), YCCI’s newest emerging core, is dedicated to catalyzing biomedical technology development and commercialization at Yale. Education is built into CBIT’s activities of facilitating team formation across schools and institutions to find solutions to unmet clinical needs. CBIT is training students and faculty to become innovators through activities that encompass the School of Medicine, the School of Management, and the School of Engineering & Applied Science. CBIT’s unique relationship with Yale-New Haven Hospital and connection to more than 150 mentors at the Yale Entrepreneurial Institute and in industry offers unprecedented opportunities to learn how to develop medical devices and technology that benefit patients. “CBIT is creating a culture of innovation that spans the entire university and even the state,” said Peter Schulam, MD, PhD, director of Yale Cancer Center and chair of the department of urology, who co-founded CBIT with W. Mark Saltzman, PhD, Goizueta Foundation Professor of Biomedical Engineering, Chemical and Environmental Engineering and Physiology. CBIT regularly hosts Clinician Pitch Nights in which students, staff, and faculty from across the medical campus and university gather to listen to five-minute pitches by clinicians on novel solutions to clinical problems. Their purpose is to form interdisciplinary teams that collaborate to develop and commercialize these ideas to improve patients’ experiences. A Pitch Night held last spring partnered School of Management students with projects that were awarded Stage 1 funding under a new pilot award mechanism created by CBIT and YCCI. Ten faculty members, clinicians, and scientists from the Yale School of Medicine, Yale-New Haven Hospital, and the Yale School of Engineering & Applied Science presented their ideas to an audience of over 60 who attended the event. The response to the call for proposals under the new mechanism illustrates the untapped potential that CBIT is leveraging. CBIT received 40 Stage 1 proposals, 17 of which were awarded $1,500 to further develop their projects, and 18 Stage 2 proposals for as many as four awards of up to $50,000 each. The awards are used to fund prototype activity, preclinical and clinical evaluation, and to create a strong business strategy for commercialization of biomedical technologies – efforts that involve teams of students from the various schools. The more than 50 projects that have emerged from CBIT’s work with clinical and engineering departments include: • A swallowing assist device for stroke patients. • A simpler and less painful method of performing bone marrow biopsies. • A novel device for treating sleep apnea. • A device to diagnose motor weakness in real time for ischemic stroke patients. • A safer, more reliable “smart shunt” for patients with hydrocephalus. CBIT also sponsors biomedical innovation coursework in medical device design and innovation, and new ventures in health care designed to tackle real-world clinical needs and bring solutions to market. Other events include lectures that provide practical advice on such topics as conducting market analysis, obtaining funding, and getting a medical device through the FDA, which helps promising technology companies get off the ground. CBIT has also hosted a series of Healthcare Hackathons—three-day events held to find solutions to a range of health care problems—which have been widely attended. All these activities highlight CBIT’s commitment to educating tomorrow’s clinicians, engineers and entrepreneurs. Said Schulam: “We’re training people to be innovators.”
YCCI supports the Venture Creation Consultant (VCC) program, a valuable resource offered through the Yale Entrepreneurial Institute (YEI) that provides specialized expertise for advancing new Yale ventures.

This select group of graduate and professional student consultants brings significant business expertise to YEI startups in such areas as biomedical engineering, market research, and software development. Over a period of about six weeks, pairs of VCCs consult on projects and then present their findings to the client. The VCCs are led this year by Nancy Tao, a fifth-year PhD candidate in the Department of Chemistry who is developing molecules that amplify the immune response against HIV in collaboration with scientists at Bristol-Myers Squibb. Below are four successful VCC startup projects supported by YEI and YCCI:

**KnackTime Interactive (Medical School – Faculty)**
KnackTime makes video games that teach critical life skills, addressing such issues as HIV, drug and alcohol abuse, obesity, and bullying. Its first game, PlayForward: Elm City Stories is focused on HIV/STI prevention and won the 2013 Gold Medal in the Healthcare/Medical category of the International Serious Play Awards. The goal is to provide a version for schools distributed via counselors, and an app version of the game that parents and mentors can download.

KnackTime is led by Lynn Fiellin, MD, associate professor of medicine at the Yale School of Medicine (YSM); Ben Sawyer, cofounder of DigitalMill; Kimberly Hieftje, PhD, associate research scientist at YSM; Lindsay Duncan, PhD, assistant professor in the department of kinesiology and physical education at McGill University; and Tyra Pendergrass, MEM, who received her Masters of Environmental Management degree from Yale.

**Improvement for Implantable Devices (CBIT)**
Pramod Bonde, MD, associate professor of surgery, is working on game-changing technologies for left ventricular assist devices (LVADs) for patients with heart failure. This technology is expected to expand the patient population several-fold. The team is led by Bonde, who is also surgical director of Mechanical Circulatory Support and principal investigator of the Bonde Artificial Heart Lab.

**Wellinks (Yale College)**
Wellinks (formerly 109 Design) is a wearable health technology company commercializing a device that attaches to scoliosis braces and collects data on how patients wear them. The startup is also developing a smartphone app that lets patients, parents, and doctors easily track brace data. The startup received $100,000 from the YEI Innovation Fund as well as support from the UConn Proof of Concept Fund. It was also named one of Inc. Magazine’s “50 Emerging Global Entrepreneurs to Watch” and one of the “11 Best Spine Technologies of 2014” by Spine Magazine, as well as a “Connecticut Tech Company to Watch” by the Connecticut Technology Council. Wellinks was cofounded by Levi DeLuke (YC '14), Sebastian Monzon (YC '14) and Ellen Su (YC '13).

**Thoracostomy Chest Tube Insertion Tool (CBIT)**
Juan Pablo Arroyo, MD, PhD, and his team are developing an improvement to a chest tube insertion device used by surgeons when they are draining fluid from a collapsed lung. Many physicians have difficulty inserting these tubes, which leads to medical complications. This team is led by Arroyo, a postdoctoral fellow in the Department of Genetics.

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By Brita Belli
YCCI 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. We encourage all faculty and staff to attend.

November 9 and 23, December 14
noon, lunch is provided
TACN203
Please visit the YCCI website to find the list of presenters and projects.

Investigative Medicine Program Information Sessions
November 10, 4 p.m.
TAC S447

Society of Clinical Research Associates (SoCRA) Exam Prep Course
November 2, 8 a.m. – 5 p.m.;
November 3, 8 a.m. – 12 p.m.
Cohen Auditorium
Preparation for Certification for Clinical Research Professionals exam, which will be administered on November 3 in the Cohen Auditorium

Coffee and Conversation
YCCI Coffee and Conversation: “Regulatory Binders: Preparation and Maintenance”
Susan Anderson
November 17
9 a.m. – 10:30 a.m.
Cohen Auditorium
These monthly presentations on topics related to clinical research operations are open to all Yale faculty and research staff.

Lunch and Learn
YCCI Lunch and Learn: “Biorepositories”
Stephanie Eisenbarth, MD, PhD
David Rimm, MD, PhD
November 12, noon – 1:30 p.m.
YCCI Lunch and Learn: “Holiday Program”
December 10, noon – 1:30 p.m.
Cohen Auditorium
These monthly sessions address broader research issues and are open to all Yale faculty and research staff. Lunch is provided.

For schedules and registration information for training events, visit http://ycci.yale.edu/education/stafftrain/.

Training Tomorrow’s Investigators continued from page 1

“The YCCI atmosphere provides a pool of secondary mentors with diverse and complementary expertise that benefits junior faculty members. The mentors are accessible, approachable, and dedicated.”

In addition to the Scholars program, YCCI has partnered with the Robert Wood Johnson Foundation (RWJF) Clinical Scholars Program to create a cadre of YCCI Community Research Scholars with training in community-based research. In response to the projected closing of the RWJF Clinical Scholars Program in 2016, Yale joined forces with fellow RWJF and CTSA sites at the University of California, Los Angeles; the University of Michigan; and the University of Pennsylvania to launch the National Clinical Scholars Program.

Like the RWJF program, the new program will educate clinicians to serve as scholars, leaders and innovators who will improve health care, community health, and public policy as well as maintain close ties with YCCI. “We could not be more excited about offering this training program,” said Cary Gross, MD, co-director of the Yale RWJF program. “As the health system is rapidly evolving, there are tremendous opportunities for physicians and nurses to not only translate research into action, but to also provide leadership from within the system that can improve health in our communities and across the nation.”

Offering Residents an Entry into Research
As a former YCCI Scholar who has benefited from the guidance of senior colleagues, Charles Dela Cruz, MD, PhD, assistant professor of medicine (pulmonary) is committed to working with medical students, residents, and fellows who are interested in pursuing careers in research. “I’m a big proponent of fostering physician scientists, which are a dying breed given the number of years of training required and the limitations of funding,” he said.

Dela Cruz is lending a hand with the Residency Distinction Projects, a new initiative that is the brainchild of Mark Siegel, MD, professor of medicine (pulmonary) and program director of the traditional internal medicine residency. The program is intended to provide additional opportunities and robust support – including educational activities and career advice – for residents with interests in education, global health, public policy, quality improvement, or investigation. It will include the creation of a mentorship database, a journal club, and various events to discuss career pathways. The current Research in Residency program will be an essential component of the Investigation Distinction Project, which will offer credit for the additional effort required to bring research projects to fruition.

Dela Cruz is helping to chair the Investigation Distinction Project for internal medicine residents. With John McGinnis (chief resident of internal medicine), he is one of the leaders of a working group for those interested in research. “It’s a group with a shared interest in research that we can foster, even though time in residency is very limited,” he said. The working group brings residents together to provide guidance and fill gaps for tomorrow’s future clinician scientists. Dela Cruz is also working with YCCI to involve aspiring researchers in such educational activities offered by the Center as the semimonthly Research-in-Progress lectures and the annual Scholar Day.

These events provide participants with opportunities to learn about research taking place at Yale, network with investigators, and find out about such practical matters as grant writing. Open to all faculty and staff, these events will be particularly valuable for busy residents who are thinking of pursuing research.