# Columbia Medicine

Columbia University College of Physicians & Surgeons

**2012 ANNUAL REPORT** 



### • DEAN'S MESSAGE

his past year – 2011-2012, or Fiscal 2012 in academic shorthand – has been a remarkable year, notable for the faculty and students, our substantial growth in the resources needed to advance our missions, and formulation of a visionary plan to build on our achievements and progress as we look forward to 2020. This "2020 Vision" is our theme as we turn the page on Fiscal 2012 and begin the work of making the next year even better than the last.

In numbers alone, 2012 was a banner year. We successfully executed our three-year financial turnaround plan and emerged stronger than ever. Research funding to P&S from the NIH increased by 5 percent even while the overall NIH budget was flat. Our 10 percent two-year growth in NIH

funding is the highest among top-ranked medical schools. Clinical revenue for our ColumbiaDoctors Faculty Practice Organization increased by more than 8 percent. In education, the yield for our entering medical school class – the percentage of accepted students who enrolled – was the highest in 35 years.

Perhaps most impressive of all, we achieved a goal that is a testament to the loyalty of our P&S community in its broadest sense: 2012 marked the most successful fundraising year in the history of our medical school, with more than \$206 million in new commitments, a figure that outpaced last year's record. This year's success is due in part to a \$40 million gift from Herbert and Florence Irving to continue their support of the Herbert Irving Comprehensive Cancer Center and further build on their generous legacy to our medical center.

The foundation of our vision for the future will quite literally take shape when we break ground on our new Medical and Graduate Education Building, a beautifully conceived structure that will provide a true unified campus "home" for our students and faculty. The cover story of this report describes the building and the people who are making it possible for our students to have state-of-the-art education facilities.

A strategic planning process, which began in October 2011 with more than 100 faculty, staff, students, and senior administrators, including hospital leaders, wrapped up work in June with a vision that will give us positive momentum for the next several years. Building on our success, we will continue to recruit top faculty

and outstanding students, strengthen our partnership with NewYork-Presbyterian Hospital, maintain community engagement, and grow philanthropic support. The planning process resulted in four primary goals for P&S: be a research pioneer and innovation engine; be the dominant tertiary/ quarternary medical center in the tri-state area; be the leading research-based medical educational center; and make the medical center a destination campus for education, patient care, and research.

Our overarching goal is for P&S to be one of the top five medical schools in the country – and arguably the best overall. By any measure, that goal is well within reach, and during the past year we made enormous progress toward achieving it. This is a testament to the vision, talents, and dedication of the entire Columbia community, from first-year medical students, to senior faculty members, to our loyal staff, and to everyone between. An organization like P&S is, in many ways, the sum of its people, and we are fortunate to have in our halls some of the finest people in their fields. Adding in the many donors, alumni, and other supporters of our missions gives us confidence in our continued commitment to our shared vision. I would personally like to thank every individual who has contributed to this year's success and who will help us build on this progress.



Lee Goldman greets families after the white coat ceremony for the Class of 2015.

Les Yelm

Lee Goldman, M.D.



# Research:

Discovery Pure and Applied

Researchers collaborate on stem cell projects, new initiatives from translational neuroscience to personalized medicine, and innovative patient screening all with a single goal: to relieve the burden of disease.



# Getting Personal Stem Cells

More Than 100 Groups Studying Stem Cells or Using Them in Patient Care Find Strength in Working Together Toward Common Goals

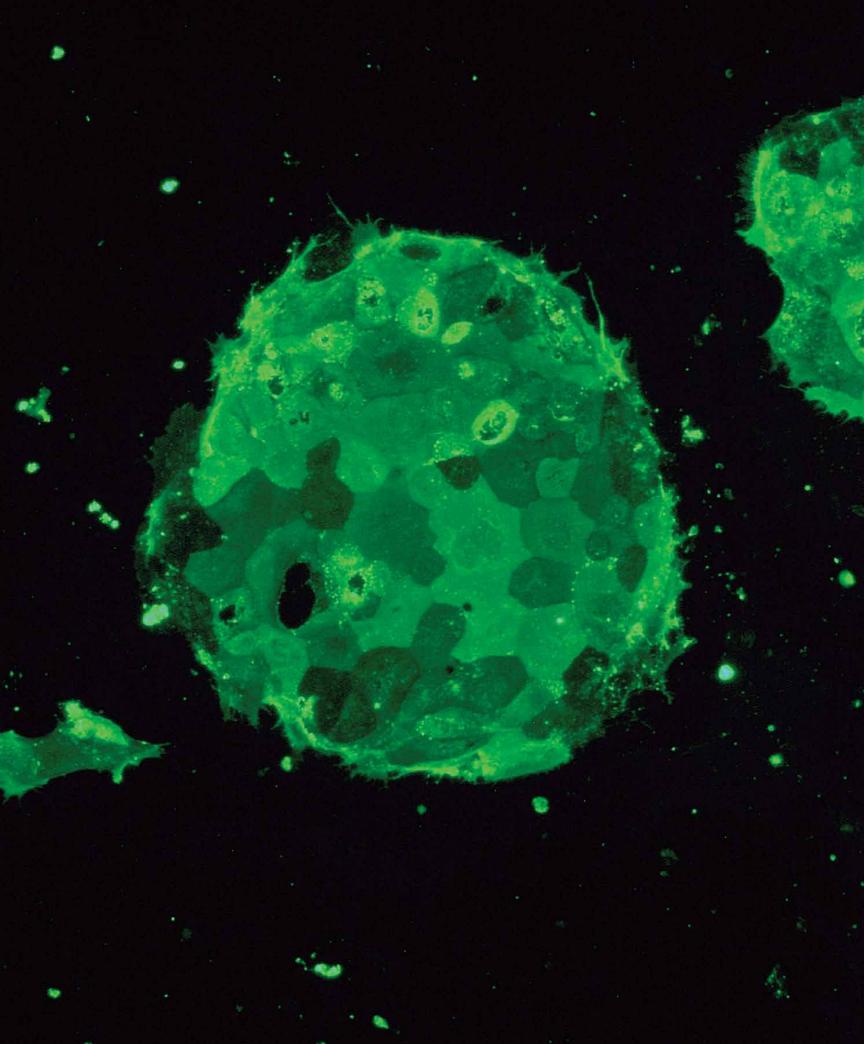
f a natural link unites virtually every scientific department at Columbia, says Christopher Henderson, Ph.D., that link is stem cell research.

"When the Columbia Stem Cell Initiative first emerged several years ago, I think our first surprise was to see what a huge critical mass of stem cell researchers we have here," says Dr. Henderson, the Gurewitsch/Vidda Professor of Rehabilitation and Regenerative Medicine and chief of the new Division of Regenerative Medicine, who this year was appointed to direct the Stem Cell Initiative. "We've counted about 120 groups both here at Columbia University Medical Center and at the Morningside Heights campus who are either stem cell experts, using stem cells in their own research, or using them as therapeutic tools."

To leverage partnerships and create more coordination within such a vast "community," the Stem Cell Initiative is organized into 10 core themes: bioengineering, blood, bone and teeth, brain, cancer,

diabetes, internal organs, neurodegeneration, skin, and stem cell biology. "These are areas of stem cell research in which we feel we're strongest," says Dr. Henderson. "Some are diseases, some are tissue types, and some are technical approaches. The point of the structure within the structure is to create 'villages within the city,' encourage people to interact more closely with other labs working on similar topics, and build bridges that go from the most basic discovery research toward the clinic."

Several major grants over the past year have helped the newly organized community get off to a running start. The New York State Stem Cell Board – NYSTEM – has provided more than 40 awards to Columbia investigators, including significant funding for a shared facility for high-throughput drug screening. The Helmsley Charitable Trust, in a joint grant to San Diego's Salk Institute, awarded \$7.5 million to Columbia toward a three-year effort to fast-track the



# Research of Note

**PARTNER Trial Tops Year's Research** Achievements. One of the most talkedabout research studies published this year was the PARTNER (Placement of Aortic Transcatheter Valve) trial, which Columbia led at 26 study sites from California to Florida to Massachusetts plus sites in Canada and Germany. Co-Pls Craig Smith, M.D., and Martin Leon, M.D., led the trial that showed that catheters can be used to replace calcified heart valves to treat aortic stenosis. Valves have long been replaced through open surgery, but nearly one in three patients about 100,000 in the United States alone are ineligible for surgery. The prognosis was grim for this group of patients until the PARTNER trial showed that surgeons could use a catheter to position a heart valve made of bovine pericardial tissue leaflets handsewn onto a metal frame inside the patient's existing valve, using a balloon to deploy the frame to hold the replacement valve in place. The 90-minute procedure does not require cardiopulmonary bypass, and recovery time is shorter, making it a good alternative for patients who cannot tolerate open surgery. (See the feature article, Page 31, for more about this research and patient care success story.)

Children, Liver Transplants, and Anti-Rejection Drugs. Many of the children who have received liver transplants from a parent may ultimately be able to stop taking anti-rejection drugs, according to a new study published by Columbia and two other leading transplant centers. Immunosuppressant drugs are associated with many serious complications, including cancer, diabetes, hypertension, and kidney failure. The pilot study, published in JAMA, enrolled 20 children and found that 12 of them were able to maintain their transplanted livers for close to three years, and sometimes more, after discontinuing immunosuppression. When the other eight children showed signs of rejection, they were placed back on medication and the transplanted livers were restored to health. The study also found predictive factors that appear to identify patients who are most likely to be able to go off anti-rejection medications successfully. "These findings bring us closer to the Holy Grail of transplant medicine, which is to give a patient an organ and then taper off use of drugs that prevent rejection," says co-author Steven J. Lobritto, M.D. A larger, 150-patient study will now be undertaken.

## Getting Personal with Stem Cells

development of novel stem cell models that can provide insight into disease mechanisms and serve as the basis for screens for novel therapeutic targets.

"Although much public interest has been focused on the use of stem cells for tissue replacement, we believe that in many clinical areas their major benefit will be to allow us to model diseases in the culture dish," says Dr. Henderson. "Such cell-based models can generate new knowledge about the disease process itself while also opening the way to high-throughput screening for test drug candidates."

Now that the community of the Stem Cell Initiative has come together, Dr. Henderson has a lofty goal for the next five years: to become one of the top five stem cell programs in the nation. "I think we're well on our way to that target, and we're working on defining parameters that will help us establish that position."

Several major achievements over the past year have raised Columbia's profile nationally as a leader in stem cell research.

When young women come to the office of Mark Sauer, M.D., to donate eggs for assisted reproduction, they probably are not thinking about curing diabetes. Their thoughts probably run more toward the compensation they will receive for the not-exactly-simple procedure and, more altruistically, toward the babies their efforts may bring into the world to help a family dealing with infertility.

But without the contribution of these women, the New York Stem Cell Foundation Laboratory research team, led by Dieter Egli, Ph.D., and Scott Noggle, Ph.D., in collaboration with Columbia researchers, would not have been able to achieve a major milestone in stem cell research this year: creating personalized stem cells that have been programmed to recapitulate the genetic code of an individual patient, meaning the cells will not be rejected as foreign tissue by the person's body but rather be recognized by the immune system as its own.

Using unfertilized oocytes donated by women at Columbia's Center for Women's Reproductive Care, the research team was able to take the nucleus of a skin cell from a patient with diabetes and transfer that cell into the oocyte without removing the oocyte's original nucleus. The result of the research was a new, reprogrammed pluripotent stem cell custom-tailored to the patient.

"For the first time, we were able to show that you could form blastocysts from somatic cell nuclear transfer, which had never before been done in humans," says Dr. Sauer, vice chair of the Department of Obstetrics & Gynecology and chief of reproductive endocrinology, of his collaboration with Dr. Egli and Dr. Noggle (both also adjunct associate research scientists in Columbia's Department of Pediatrics molecular genetics division). The resulting Nature paper on the research generated worldwide headlines.

Of course, creating cells that exactly reproduce the genetic code of an individual with diabetes also reproduces the disease itself, so they are not therapeutic, or at least not yet. They have extraordinary importance for creating models of this and many other diseases for scientists to study. "Using this technique, we've been able to make insulin-producing cells from humans who have various forms of diabetes, and those insulin-producing cells recapitulate the disease that these individuals have," says Rudolph Leibel, M.D., the Christopher J. Murphy Memorial Professor of Diabetes Research, professor of pediatrics, professor of medicine, and co-director of the Naomi Berrie Diabetes Center.

And the carefully crafted, meticulously reviewed process by which Columbia has allowed egg donors to consent to the use of their oocytes for stem cell research has jump-started this research. "World-class basic science researchers have been dying to do these projects, to try and conquer truly awful diseases, for years with no success," Dr. Sauer says. "And my patients are really excited about contributing. I'd say 95 percent of them say yes. We've had about 40 egg donors for the stem cell program in the last three years. A couple of months back, I had a woman come in to donate eggs who plans to go to medical school. When she read the Nature paper, she was so thrilled to be a part of this."

Of course, plenty of hurdles still lie ahead. Before the reprogrammed stem cells can be used therapeutically in, say, a patient with diabetes, scientists need to deal with the "small matter"



of the extra cell nucleus. When a patient's skin cell nucleus is transferred into the oocyte, that oocyte's nucleus is not removed, so the resulting personalized cell is a bit of a mutant, a "triploid" cell with an extra set of genetic material. Before these cells can be used therapeutically, researchers must find a way to transform them back to normal diploid cells.

One of the big questions in stem cell research focuses around precisely this: What is the optimum method for creating pluripotent stem cells? Somatic cell nuclear transfer is one way; another is induced pluripotency, in which adult somatic cells are artificially reprogrammed to become pluripotent stem cells, putting them on rewind in a sense.

"The iPS approach takes adult cells and moves them backward through the reproductive steps," says Robin Goland, M.D., professor of clinical medicine and pediatrics and co-director of the Berrie Center with Dr. Leibel. "Somatic cell nuclear transfer, in a way, recapitulates normal development. When we can figure out how to make SCNT stem cells with the right number of chromosomes, which I think we should be able to do within five years, we will be able to compare embryonic stem cells made through iPS to those made through SCNT."

In the meantime, scientists also continue to test the vitality of iPS cells, and another breakthrough on that front came from Columbia scientists this year. In collaboration with researchers A major milestone in stem cell research this year was the creation of personalized stem cells that will be recognized by the immune system as its own.

# Research of Note

New Prenatal Test More Powerful than Standard

Fetal Screening. Testing a developing fetus' DNA through chromosomal microarray provides more information about potential disorders than the standard method of prenatal testing, which involves visual examination of the chromosomes (karyotyping), according to a nationwide study led by Ronald Wapner, M.D. "With karyotyping, we can see only when pieces of the genome of about 5 million base pairs are missing from a chromosome. With CMA, we can see missing pieces of fewer than 100,000 base pairs. Why would anyone want to continue to use the standard method, which gives only part of the answer?" asks Dr. Wapner. He notes that it will take time and careful guidance to make this standard practice.

## A New Approach to Diabetes Treatment.

For decades, treatments for type 2 diabetes have focused on insulin, which removes glucose from the body to help maintain appropriate blood sugar levels. But a new study from P&S investigators suggests that the hormone glucagon, which adds glucose, plays an equally important role in diabetes and may offer a more attractive therapeutic target. The research team, led by Ira Tabas, M.D., Ph.D., blocked an enzyme called CaMKII, which acts to fully release glucose following glucagon binding, in obese diabetic mice. They found that blocking CaMKII reduced the animals' blood sugar with no negative side effects. "Until now, it has been difficult to block glucagon's effect on blood sugar without interfering with glucagon's other functions, but we think CaMKII is different," says Dr. Tabas.

#### **Possible New Treatment for Fatal Childhood**

Disease. According to a new study from Columbia scientists, two related enzymes, phosphoinositide-3 kinase (PI3K) gamma and delta, play a key role in the development of T-cell acute lymphoblastic leukemia, a form of childhood leukemia that is highly aggressive and difficult to treat. When these two enzymes are blocked by a dual inhibitor in a mouse model of the disease, survival is significantly prolonged, says Thomas Diacovo, M.D., who led the study. "If this treatment strategy can safely and selectively target the activity of these enzymes in T-ALL tumors, we might be able to reduce the need for conventional chemotherapies that more broadly affect proliferating cells, including those in healthy tissues. This would be a major advancement in helping to reduce drug toxicities in young patients."

## Getting Personal with Stem Cells

at Harvard, Dr. Henderson and Hynek Wichterle, Ph.D., associate professor of pathology and neuroscience, working in the Project A.L.S./Jenifer Estess Laboratory for Stem Cell Research, have been studying whether iPS cells are as robust as the "gold standard" human embryonic stem cells, a matter that has been hotly debated in the field. "We tested a panel of iPS cells against a panel of human embryonic stem cells on a wide variety of measures, including their ability to turn into motor neurons, in parallel in two different labs," says Dr. Henderson. "Although there are some variations, we found that iPS cells are just as good as human embryonic stem cells at making motor neurons, in what has been the most objective and extensive study on the subject to date."

# Why Diabetes?

Stem cells are being used to create models of dozens of different diseases in hopes that they will lead to therapies and even cures for those diseases. The nature of type 1 diabetes, the autoimmune form of the disease, makes it a uniquely well suited early front for this research. "Type 1 diabetes is a disease of one cell type," explains Dr. Goland. "It's a cell replacement problem, and what we need to replace is one cell type that makes one hormone." In type 1 diabetes, the problem is that the patients' insulin-producing cells, the beta cells, are destroyed. "It's an insulin deficiency state. If we had a way to replace those cells, there would potentially be a cure."

Researchers at the Berrie Center can now generate iPS cells and transform them into insulinproducing cells both *in vitro* and in an experimental animal model. "This holds out the promise that, in the coming decades, we will be able to create an indefinite supply of pancreatic beta cells from patients themselves and overcome immune rejections," says Dr. Goland. "Right now, the chemicals we use are not safe in patients, so we're working on getting the same outcomes with small molecules that would be safe to use in humans."

Having the model of type 1 diabetes in a dish, developed through SCNT, also gives scientists a new set of clues in their quest to find out what exactly has gone wrong in this form of diabetes. "Type 1 is caused because the patient's own immune system recognizes its beta cells as foreign," says Dr. Goland. "The ability to create beta cells *in vitro* allows us to modify them and help figure out what the patient's body didn't like about its own beta cells. Perhaps we can create 'stealth' beta cells that you could put back in that wouldn't be viewed as foreign."

If, for example, the beta cells express a protein that is viewed as a target by the immune system – but is not essential for insulin production – it might be possible to develop new beta cells that do not produce that protein.

Dr. Goland predicts that within 10 years, trials will begin to test stem cell-derived therapies for diabetes in humans. "This kind of research is exactly why the Berrie Center was established. It's an incredible collaboration between researchers, clinicians, and patients who come here to try to further the science," she says.

## **Building Diseases in a Dish**

Columbia scientists have been able to transform iPS cells into several other types of cells to recapitulate diseases and create models for future therapies. Angela Christiano, Ph.D., the Richard and Mildred Rhodebeck Professor of Dermatology and professor of genetics & development, has been able to generate iPS cells from the genetic material of patients with epidermolysis bullosa, a group of disorders in which skin blisters develop in response to minor injury, and turn them into keratinocytes, the predominant cell type found in the epidermis. "She was then able to incorporate those cells into 3-D models of skin in the culture dish," says Dr. Henderson. "Now she can use that model to study the specific individual defects that some of these patients might have."

Another type of tissue that is difficult to generate is the thymus, the gland that "teaches" the body's T-cells how to react to foreign substances by eliminating the ones that attack the body's own tissues. Hans Snoeck, M.D., trained as a clinical hematologist, joined Columbia from Mount Sinai School of Medicine this year, bringing with him the expertise that led over

the past year to generating anterior foregut endoderm cells – the precursor to the thymus – from iPS cells.

"We are also improving our understanding of stem cell differentiation through bioengineering," says Dr. Henderson. "Gordana Vunjak-Novakovic [vice chair and Mikati Foundation Professor of Biomedical Engineering and Medical Sciences] has used not iPS cells, but mesenchymal cells, to make a 3-D model of vascularized bone that's looking pretty good."

Although iPS cells have continuing promise, they are in some ways indirect avenues, says Dr. Henderson. "We turn a skin fibroblast into an iPS cell, and then that iPS cell is turned into whatever tissue one is looking for. That's normally done by adjusting the conditions in which the iPS cells are grown, putting in media supplements and known differentiation factors. But it's become apparent recently that if one takes an approach rather similar to what was done to create the iPS cells in the first place, and introduce directly into skin cells not stem cell genes but others representative of differentiated tissue, we don't need to go through that intermediate step."

That was rather dramatically illustrated this year in research published by Asa Abeliovich, M.D., Ph.D., associate professor of pathology & cell biology and neurology, who used transcription factors to induce skin fibroblasts from patients with Alzheimer's disease to develop into neurons of the forebrain. "He was able to show that these neurons had some phenotypes that seem to be linked to Alzheimer's," says Dr. Henderson. "This is an exciting new development both specifically, in terms of research models for Alzheimer's disease, and more broadly in generating differentiated cell types from a patient's skin in just one step."

Not all of the Initiative's efforts have been brought to bear on human models of disease. Insights from that classic "model" organism, the lowly fruit fly - first pioneered by Thomas Hunt Morgan at Columbia a century ago - have furthered our basic understanding of how stem cell development is regulated. In an illustration of the cross-campus synergy of the Initiative, one of this year's important drosophila papers came from Morningside Heights, while the other is from the medical center. "Daniel Kalderon, a professor of biology who works on the Morningside campus, has been working on the stem cells that make follicles in the drosophila ovary," says Dr. Henderson. "Because the eggs are constantly being laid, the follicles need to be constantly generated. He conducted a genetic screen to determine which genes are involved in the function of these follicle stem cells and came up with a whole series of different genes, including some from the PI3 kinase pathway, one widely used for cell growth and survival."

In what Dr. Henderson calls a nicely matching study, the P&S laboratory of Ben Ohlstein, M.D., Ph.D., assistant professor of genetics & development and medicine, released related insights into stem cells within the intestines of drosophila. The Ohlstein lab demonstrated that nutrition and insulin signaling regulate intestinal stem cell division by controlling the level of adhesion between stem cells and their daughters. This process known as contact inhibition is important for regulating tissue growth and preventing cancer. Thus, the drosophila midgut can serve as a model for linking the effects of diet on stem cell-driven tissue regeneration and cancer biology.

"These two scientists have identified new ways in which we can use the power of model organisms to understand how signals around stem cells allow them to proliferate and regenerate," says Dr. Henderson.

With the accumulated critical mass of the Stem Cell Initiative, advances like these should burst into full flower at Columbia over the next several years. "We will be able to build big multidisciplinary projects either across disciplines like biology, bioengineering, and chemistry, or between basic approaches and the clinic," Dr. Henderson says.

The Initiative uses internal competition to generate the best possible science. Last year NYSTEM announced plans to fund a series of consortia, but only one grant could be submitted from Columbia. "We organized a big contest to identify the single leading project we would submit. And now we're going out to look for startup funding for some of the others. These ambitious projects really build on the strength and scientific rigor of our community. I'd really like to seed a lot of large, multidisciplinary projects working together and taking parallel approaches under the same roof. There is no place in the world like Columbia to do this." ❖

Scientists have identified new ways to use the power of model organisms to understand how stem cells proliferate and regenerate.



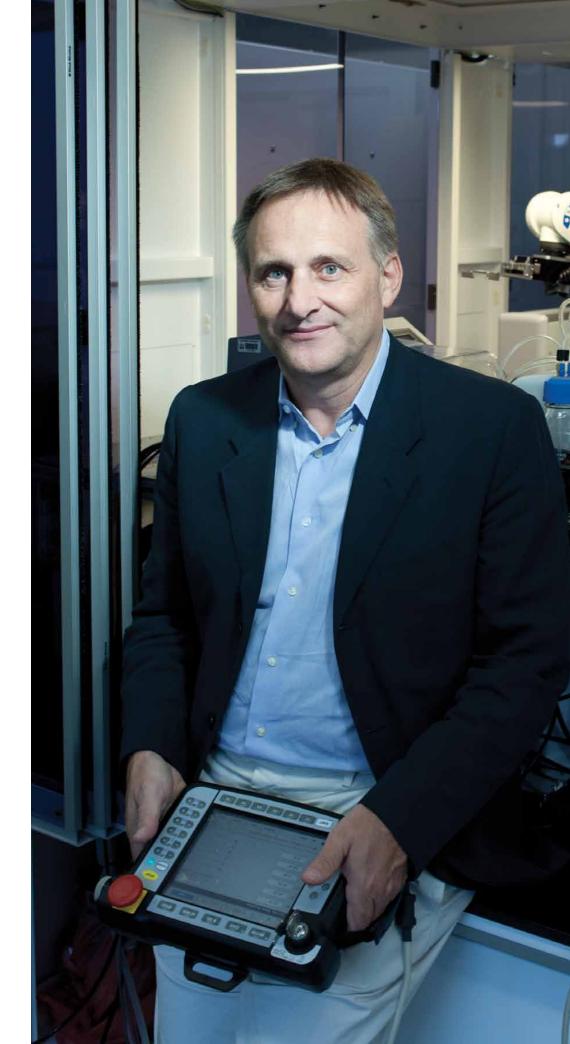
Gordana Vunjak-Novakovic, Ph.D., holds a bioreactor that can "instruct" stem cells cultured on biomaterial scaffolds to form functional 3-dimensional tissues as replacement tissue for the body.

# Research of Note

Mapping the Hippocampus. In research that made the cover of Nature Reviews Neuroscience, Columbia researchers revealed the startling finding that the hippocampus comprises molecularly and functionally distinct subregions, rather than a singular structure. Scott A. Small, M.D., used current neuroimaging studies to suggest a framework of hippocampal dysfunction in which common brain disorders differentially target distinct subregions of the hippocampal circuit. This framework should help guide future research into common brain disorders, including Alzheimer's, schizophrenia, and depression.

Folate May Prevent Stomach Cancer. Folate supplements may be able to prevent gastric cancer, especially if given early in the disease process, according to new research from Tamas Gonda, M.D. In a mouse model, folate supplements were able to prevent cancer among mice with stomach lesions induced by the bacterium Helicobacter pylori, a major risk factor for gastric cancer. "If folate also turns out to prevent stomach cancer in people, it could have an enormous impact in Asia and other parts of the world where stomach cancer is very common," says Dr. Gonda. But while folate given early could prevent tumors from developing, when given later in the disease, it could fuel the growth of existing cancers. "In a trial, we will have to screen people carefully for other cancers before giving them folate supplements."

How Alzheimer's Disease Spreads. Alzheimer's disease spreads by "jumping" from one brain region to another, according to new findings by Columbia researchers Karen E. Duff, Ph.D., and Scott A. Small, M.D. Using a novel transgenic mouse in which the gene for abnormal human tau protein, a key feature of the neurofibrillary tangles seen in the brains of people with Alzheimer's, is expressed predominantly in the entorhinal cortex, the researchers mapped the spread of the abnormal protein over 22 months. They found a pattern of spread along a linked anatomical pathway, from the entorhinal cortex to the hippocampus to the neocortex, which mimics the staging seen in early human Alzheimer's disease. Their findings also suggested that the abnormal protein was moving from neuron to neuron across synapses, which suggests that new treatments for Alzheimer's disease could possibly target tau during its extracellular phase and stop it from jumping from one synapse to the next.





# Research Initiative: Systems Biology

he new discipline of systems biology has emerged at the intersection of experimental and computational biomedical sciences to form one of the most effective frameworks for accelerating scientific discovery in both basic and translational research. Through the Initiative in Systems Biology - created in 2010 - Columbia has assembled a robust level of talent in disciplines related to systems biology, providing a home to nearly two dozen faculty members and making Columbia one of the largest centers in systems biology in the country.

An explosion of data generated by advances in biotechnology has given researchers an extensive "parts list" of the cell but little understanding of how these parts (genes, proteins, and other molecules) work together to implement specific biological processes. Thinking at the "systems level" is important to understanding how cells work normally, what happens in disease, and how diseased cells can be brought back to healthy states.

The Initiative brings together the Judith P. Sulzberger Columbia Genome Center and the Center for Computational Biology and Bioinformatics (C2B2) to combine the skills and perspectives of computer scientists, software engineers, physicists, high-throughput screening specialists, and experimental biologists. The scientific output by Initiative faculty has resulted in more than 300 publications over the past five years, about a third of those in top-tier scientific journals. NIH money has followed this expansion; NIH funds for C2B2 alone jumped from \$500,000 in 2003 to almost \$10 million today, including an NIH planning grant that made Columbia home to the Center for the Multiscale Analysis of Genomic and Cellular Networks (MAGNet), one of seven National Centers for Biomedical Computing and one of 12 interdisciplinary Centers for Cancer Systems Biology.

These funding and scholarly achievements are complemented by 30,000 square feet of modern data centers that house equipment to support systems biology work: one of the world's largest supercomputers dedicated to biological and medical research; high-content imaging equipment; a sequencing facility that has been described as the best run genomic facility in New York City; and a high-throughput discovery and microscopy facility. On the Morningside campus, a chemical probe synthesis facility helps researchers design and synthesize chemical probes of biological processes, especially those related to stem cells.

Over the past decade, Columbia has cultivated one of the most accomplished faculties and amassed a powerful infrastructure to harness our full potential in systems and computational biology as a new model for biomedical discovery in human genetics, cancer, infectious diseases, metabolic disorders, neurodegenerative and psychiatric disease, stem cells, and regenerative medicine.

Andrea Califano, Ph.D., the Clyde and Helen Wu Professor of Chemical Systems Biology, is founding director and chair of the Columbia Initiative in Systems Biology. PHOTOGRAPH BY JÖRG MEYER

# Research of Note Timothy C. Wang'83

Clues to Source of Esophageal Cancer. Esophageal adenocarcinoma is the fastest-rising solid tumor in this country. Now, P&S scientists have identified the earliest cellular and molecular changes that lead to this deadly cancer, using a new genetically engineered mouse model of esophagitis, the inflammatory disorder involved in the development of Barrett's esophagus, an asymptomic precancerous condition. For decades, it was believed that the physiological changes associated with Barrett's esophagus originate in the lower esophagus. "However, our study shows that Barrett's esophagus actually arises in the gastric cardia, a small region between the lower part of the esophagus and the upper, acid-secreting portion of the stomach," says lead investigator Timothy C. Wang, M.D. "The bile acid and inflammatory cytokines activate stem cells at this transition zone, and they begin migrating up toward the esophagus." Dr. Wang's research also suggests a possible therapeutic pathway for high-risk patients with Barrett's esophagus: the notch cell signaling system, which when inhibited blocked the proliferation and survival of premalignant cells.

#### Non-Hereditary Cases of Schizophrenia.

More than half the cases of non-hereditary, or sporadic, schizophrenia are caused by "new" protein-altering gene mutations, according to research at P&S supported by funding from the Lieber Foundation. In work published in the journal Nature Genetics, Maria Karayiorgou, M.D., and Joseph A. Gogos, M.D., Ph.D., examined the genomes of genetically isolated Afrikaner families of European descent in South Africa. The participants included patients with schizophrenia, their families, and healthy people in control groups. The researchers identified 40 mutations, all in different genes and most of them proteinaltering, that were associated with sporadic schizophrenia. The findings could point the way to finding more mutations, perhaps hundreds, that contribute to schizophrenia. "The fact that the mutations are all from different genes is particularly fascinating," says Dr. Karayiorgou. "It suggests that many more mutations than we suspected may contribute to schizophrenia."

# Research Initiative: **Translational Neuroscience**

he principal goal of the new Columbia Translational Neuroscience Initiative is to enhance translational neuroscience research and therapeutics development by coordinating existing strengths in neuroscience, neurology, neurological surgery, psychiatry, and pathology. The Initiative will provide an overarching programmatic vision to better understand and treat brain disease and trauma by connecting the clinical neuroscience departments and translational centers at the medical center with each other and with faculty on the Manhattanville and Morningside campuses.

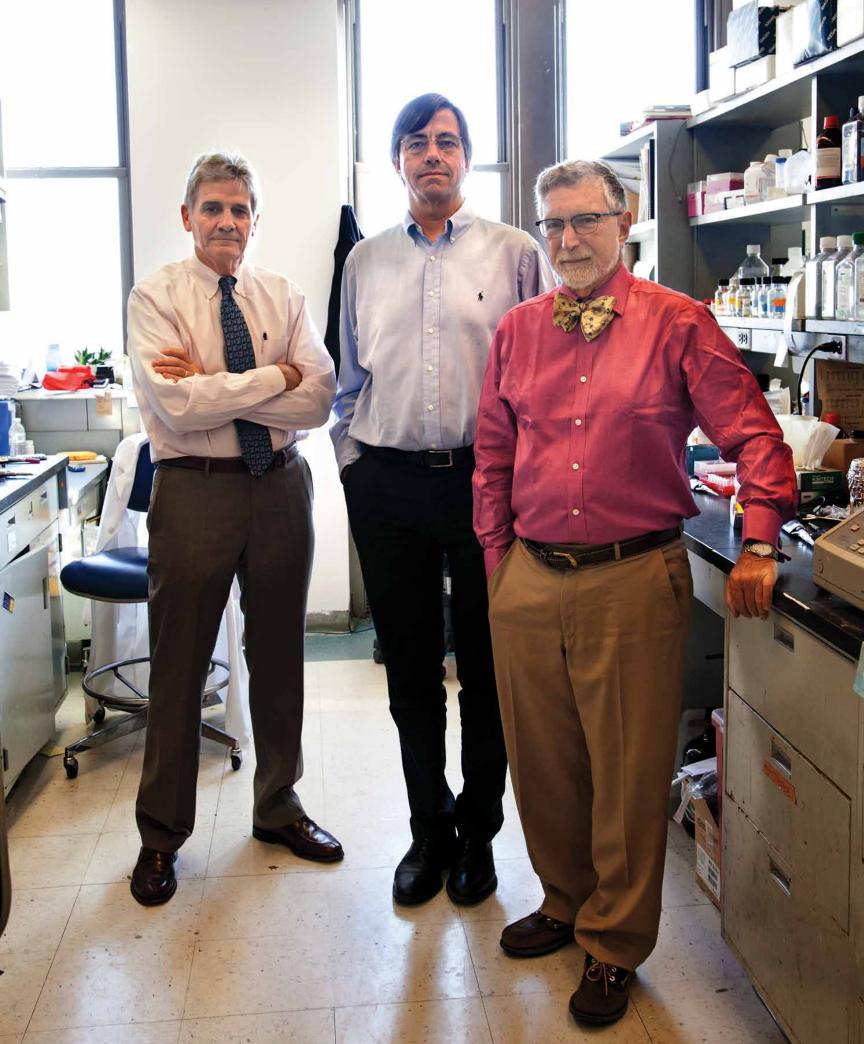
Different diseases and injuries that affect the nervous system target a specific set of brain regions and functions, and many successful translational centers and programs at Columbia have studied each condition as an individual set of scientific and therapeutic challenges. Recognizing that many pathological processes and disease mechanisms - from protein misfolding to axonal degeneration to inflammation - are common to many neurodegenerative, neurodevelopmental, and neuropsychiatric disorders suggests that studying these processes across different disease areas may generate new synergies and enhance integration.

The Translational Neuroscience Initiative will encourage scientific and clinical collaboration, oversee joint recruitment efforts, and create new shared facilities. Initial plans call for inclusion of any faculty member or translational research group whose work relates to neurological, neurodevelopmental, and neuropsychiatric disorders, from basic mechanistic and biochemical studies to novel animal and cell models to systems biology approaches to preclinical research. Full members will be faculty with significant publications and/or grants relevant to the areas of neuroscience, neuropsychiatry, neurology, and neurotrauma. Members will be drawn from departments (Neurology, Neurological Surgery, Pathology, Psychiatry, Biochemistry, and Rehabilitation & Regenerative Medicine), from centers and institutes (the Taub Institute for Research on Alzheimer's Disease and the Aging Brain, the Gertrude H. Sergievsky Center, the Motor Neuron Center, the Lieber Center for Schizophrenia Research, and the Sackler Institute for Developmental Psychobiology), and from divisions and initiatives (movement disorders and systems biology).

The move of the Department of Neuroscience to Manhattanville in 2016 emphasizes the need for intercampus collaboration among faculty and research groups dedicated to the brain. The Initiative will facilitate coordination, recruitment, training opportunities for clinicians and basic scientists, and bench-to-bedside translation of findings through clinical populations.

The historical leadership of P&S in neuroscience, neurology, neurological surgery, psychiatry, pathology, and biochemistry has provided for important contributions by individuals in basic and translational neuroscience. Combining vision, resources, and strategies through the Translational Neuroscience Initiative will strengthen the potential of the large and diverse neuroscience community at P&S to contribute in even greater ways toward understanding the mysteries of the mind and brain.

Three leaders of the new translational neuroscience initiative are, from left, Richard Mayeux, M.D., the Gertrude H. Sergievsky Professor of Neurology, Psychiatry, and Epidemiology and chair of neurology; Christopher Henderson, Ph.D., the Gurewitsch/Vidda Professor of Rehabilitation and Regenerative Medicine and chief of regenerative medicine; and Michael L. Shelanski, M.D., Ph.D., the Delafield Professor and Chair of Pathology & Cell Biology. (Not pictured: Robert Solomon, M.D., the Byron Stookey Professor of Neurological Surgery and chair of neurological surgery, and Jeffrey Lieberman, M.D., the Lieber Professor of Psychiatry, Lawrence C. Kolb Professor and Chair of Psychiatry, and director of the New York State Psychiatric Institute.) PHOTOGRAPH BY JENICA MILLER



# Research of Note

#### Kids with Head Injuries May Not Need CTs.

Many of the 450,000 children with blunt head trauma who visit U.S. emergency departments each year probably do not need head CT scans, according to research published by Peter Dayan, M.D. Although CT scans are the quickest way to identify a traumatic brain injury, they come at a price: a small increased risk of cancer later in life. Dr. Dayan's study shows that many children with minor head trauma with severe mechanisms of injury, but no worrisome symptoms or physical signs, are at low risk of clinically important TBIs and just need careful evaluation and observation by an emergency physician.

#### Columbia Researchers Find Breast Cancer Gene

Flaw. Since the BRCA1 gene was first identified in 1994, scientists have been striving to understand how mutations in the gene work to cause breast cancer. Women with a faulty BRCA1 gene are five times more likely to develop breast cancer in their lifetimes than other women. Now, in findings that upend previous theories on the matter, researchers from the Herbert Irving Comprehensive Cancer Center are one step closer to understanding that flaw. Thomas Ludwig, Ph.D., and Richard Baer, Ph.D., used a mouse model to pinpoint a discrete domain of BRCA1 that suppresses tumor formation. They found that when they generated mice with a BRCA1 mutation that ablated its ability to interact with phosphoproteins, tumors developed frequently. "These findings fundamentally reshape our understanding of BRCA1," says Dr. Baer. "If we can identify the phosphoprotein(s) that help BRCA1 suppress cancer, we may find interventions that can prevent breast cancer in women with BRCA1 mutations."

#### Finding: Two Genes that Cause Familial ALS Work

Together. Two ALS-associated genes work in tandem to support the long-term survival of motor neurons, according to new research from Columbia. The two genes, FUS/TLS and TDP-43, both recently discovered, are involved in the processing of messenger RNAs, but it was previously unclear exactly how mutations in these genes help lead to familial ALS. Using a drosophila model with mutant FUS/ TLS and TDP-43 genes, researchers led by Brian McCabe, Ph.D., found that FUS/TLS acts together with, and downstream of, TDP-43 in a common genetic pathway in motor neurons. "One could imagine that if you could develop a drug or gene therapy that could make FUS/TLS more active, it might help patients who have TDP-43 mutations," suggests Dr. McCabe. The study was funded by P2ALS and Columbia's Motor Neuron Center.





# Research Initiative: **Personalized Medicine**

ersonalized medicine is sometimes referred to as precision medicine for obvious reasons. It aims to use our best knowledge to precisely prevent and treat disease in individuals, not populations or types of patients: "the right drug for the right patient at the right dose at the right time." Personalized Medicine, Columbia's new interdisciplinary research initiative, brings genomics, biomarkers of disease stage, medical history, and risk stratification to bear on developing this precise approach to patient care.

Medicine is just beginning to reap the benefits of sequencing the human genome to understand the biological basis of uniqueness. A recent status report on personalized medicine listed dozens of personalized medicine drugs, treatments, and diagnostics available, from pharmaceutical and surgical prevention options and surveillance for women who test positive for the BRCA1 or BRCA2 genes for breast cancer to fine tuning the dose of clopidogrel, a drug prescribed to prevent heart attacks, to a targeted drug treatment for adult and pediatric patients with Philadelphia chromosome positive chronic myeloid leukemia. Technological advances in informatics and DNA sequence generation and analysis will continue to make targeted treatments more common. Burgeoning technologies such as induced pluripotential stem cells afford the opportunity to genetically re-create a living tissue from a patient in a petri dish and model how a particular patient might respond to a medication and serve as a rapid and efficient way to screen for new effective medical treatments. In addition, increased utilization of an electronic medical record offers the opportunity to build systems that will support providers by suggesting genomic tests that may be helpful in patient management and by pre-populating the electronic medical record with genomic results, such as pharmacogenomics. These results would be given to the provider to support medical decision making without the need for advanced, sophisticated knowledge of genomics. Personalized medicine will include the genome of ever mutating tumors for patients with cancer and will enable rational, targeted treatments that will attack the tumor rather than the non-specific cellular poisons often associated with the collateral damage in many forms of chemotherapy. Rather than treating all patients with diabetes in the same way, understanding the molecular basis for the diabetes will improve accuracy of prognosis and differentiate patients requiring insulin treatment from those who may be managed with diet and exercise or oral medications.

Columbia investigators will build a biobank and clinical data warehouse to create genomic tests and biomarkers that can be used clinically. Infrastructure and technological advances alone are not enough to advance personalized medicine; Columbia's large and diverse patient population will help researchers apply technological advances and develop other personalized medicine tools that can immediately help clinicians avoid adverse outcomes and improve patient outcomes.

Personalized medicine reflects the intersection of methods to target here-and-now medical issues and tools that will offer lifelong improvements in health management. The economics of genomic sequencing, new epigenetic and proteomic technologies, and increasing use of electronic health records are building momentum to make personalized medicine a powerful, transformative, even revolutionary hallmark of patient care.

Wendy Chung, M.D., Ph.D., assistant professor of pediatrics in medicine, leads the new initiative in personalized medicine. PHOTOGRAPH BY JÖRG MEYER



Personalized Immune Mouse Offers Unique Research Tool. In an advance that offers an unprecedented tool for individual analysis of abnormalities that contribute to autoimmune diseases like diabetes. P&S scientists have developed a way to re-create an individual's immune system in a mouse. The mouse model, created by a team led by Megan Sykes, M.D., is able to re-create a robust and diverse human immune system, including T cells, B cells, and myeloid cells, free of immune incompatibilities. The model is made by transplanting human bone marrow cells along with a small amount of HLA-matched immature thymus tissue into an immunodeficient mouse. Key to its success was the discovery that freezing and thawing the transplanted thymus tissue, as well as administering certain antibodies, deplete mature cells from the tissue graft, preventing rejection and graft-vs.-host disease while preserving tissue function.

Hidden Network Regulates Cancer Gene Expression. A vast, hidden network regulates gene expression in cancer, according to new findings from Columbia researchers. These findings suggest that messenger RNA in one gene can control, and be controlled by, the mRNA of other genes via a large pool of microRNA molecules, with dozens to hundreds of genes working together in complex self-regulating sub-networks, a stunningly powerful role for mRNA, which for years was underestimated as a relatively unimportant genetic delivery boy, simply shuttling information from the DNA to the ribosomes, where proteins are synthesized. The newly identified regulatory network, dubbed the mPR network, allows mRNAs to communicate through small bits of RNAs called microRNAs. The new studies reveal that mRNAs use microRNAs to influence the expression of other genes. "The discovery of this regulatory network fills in a missing piece in the puzzle of cell regulation and allows us to identify genes never before associated with a particular type of tumor or disease," says Andrea Califano, Ph.D.

# Research Initiative: I-4

he Initiative in Infection, Immunity, and Inflammation, or "I-4," aims to achieve significant advances in age-old areas of medicine and science that still have many unanswered questions. Gathering those questions under one umbrella will help researchers harness interconnected strengths to find answers.

Infection remains a major medical problem in all parts of the world. Pandemics, including zoonotic influenza strains and HIV, spread rapidly through intercontinental travel. Longstanding targets of global public health initiatives - malaria, tuberculosis, salmonellosis, cholera, and many others - remain alarmingly prevalent. In the developed world, multi-drug resistant pathogens and nosocomial infections are increasingly significant causes of morbidity and mortality. A three-pronged approach - prevention, treatment, and eradication - will require fundamental advances in understanding microbial biology and host responses. Although advances in the genomics of microbes, structural information about microbial enzymes, now allow the development of novel antibiotics, vaccination remains the No. 1 weapon against infectious disease. I-4's strong synergistic programs in immunology, microbiology, genetics, structural biology, and genomics will make way for progress in the area of novel vaccines and vaccination approaches.

Advances in genomic technologies, gene targeting, and humanized mouse models have opened up new possibilities to answer fundamental, but previously unanswerable, questions about the immune response. From the identification of Toll-like receptors to our increasing understanding of the functional specialization of lymphocyte subsets, we have witnessed an explosion in our knowledge about how the immune response is orchestrated. I-4 will leverage this rapidly expanding knowledge base along with advances in vaccinology, immunotherapy, and transplantation science (through Columbia's Center for Translational Immunology), achievements that depend on insights into basic immunological mechanisms.

The third "I" - inflammation - is normally associated with the innate immune responses to infection or irritants. However, it is now appreciated that dysregulated inflammation is a key factor in the pathophysiology of numerous diseases including cardiovascular disease, cancer, and neurodegenerative diseases. Understanding basic principles underlying aberrant inflammation is a prerequisite to the development of targeted therapies against numerous chronic diseases such as diabetes, atherosclerosis, arthritis, and asthma.

The influence of the microbiome on the immune system and the inflammatory state illustrates the rapid convergence of multiple disciplines on these areas of study. I-4 cuts across different disciplines, taps the greatest minds in the individual fields, provides a unifying structure for the common pursuit of answers, and holds promise to move us from the cusp of fundamental breakthroughs into revolutionizing science and medicine through the application of new knowledge.

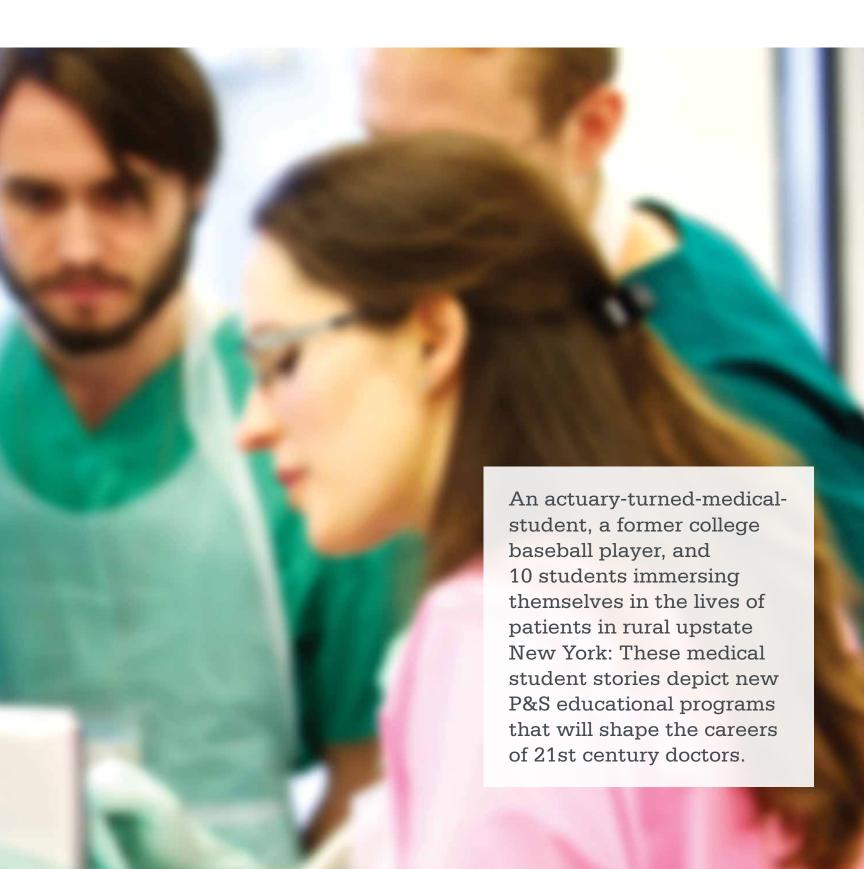
> Leader of the new "I-4" initiative is Sankar Ghosh, Ph.D., the Silverstein and Hutt Family Professor and Chair of Microbiology & Immunology. PHOTOGRAPH BY JÖRG MEYER

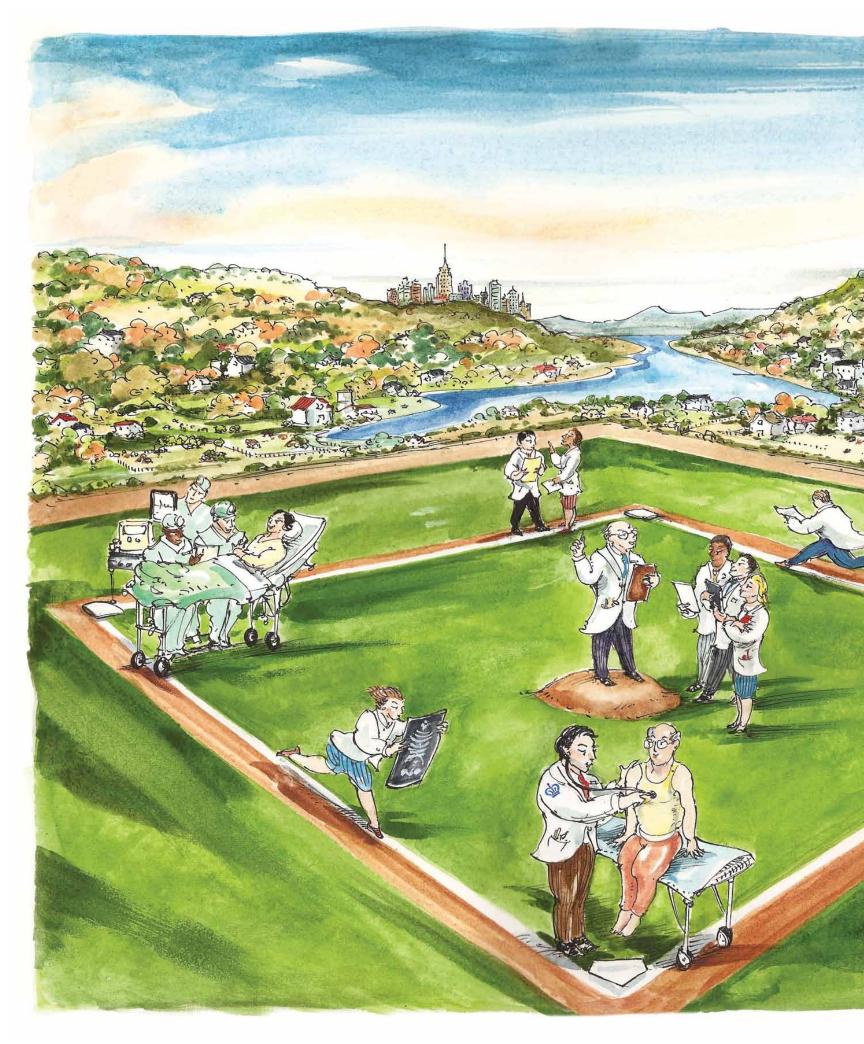


# **Education:**

A New Generation of Doctors









# AHYBRID Medical Education

Pioneering Columbia-Bassett Students Try a Different Glove on for Size

the Bassett Healthcare System campus in the quaint and historic upstate New York village of Cooperstown – best known as the home of the Basseball Hall of Fame – for the second half of their undergraduate medical education.

Having grown up on a farm in Michigan, Mr. Chapel says that his roots instilled in him a passion for rural medicine, so the Bassett track intrigued him when it came up in a Google search of medical school programs offering options in that field. In November of 2010 he drove from Ann Arbor, Mich., where he was finishing his undergraduate studies at the University of Michigan, and interviewed in Cooperstown. The next day, he came to Columbia's northern Manhattan campus for a second interview.

"By Christmastime, I was notified that I had been accepted into the program," he says. "But by that point I had also been accepted at several other schools, including Washington University, the University of Chicago, and the University of Michigan. Those three were the most tempting geographically and financially, and Bassett was still so new that there wasn't much information about it."

But Walter Franck'64, Columbia's senior associate dean at Bassett, was persistent. He spoke with Mr. Chapel a few times on the phone throughout that spring and, finally, Mr. Chapel decided he needed to visit Cooperstown again to make a final decision. "I got back in the car and did a marathon drive back," he says.

Illustration by Mark Steele

# **Education Highlights**

The Class of 2012. During the course of their time at P&S, 35 percent of the Class of 2012's graduates took an extra year for research and 24 percent spent time abroad. In this year's residency match, 22 percent of the Class of 2012 matched to a residency program at Columbia, part of the 42 percent staying in New York state for residencies. Members of the Class of 2012 also had busy lives beyond medical school: 19 students got married, 17 babies were born, and 35 triathlons and marathons were completed.



#### New Master's Degree in Biomedical Informatics.

A new master's degree program in biomedical informatics is available at P&S for health care professionals and medical center students. The Office of the National Coordinator for Health Information Technology within the Department of Health and Human Services, which oversees several programs to train health IT workers, provides tuition assistance for eligible students in the program, which can be completed in as little as 12 months.

**Summer Public Health Scholars Program** Funded by CDC. The Summer Public Health Scholars program, a partnership among P&S, the Mailman School of Public Health, the College of Dental Medicine, and the School of Nursing, aims to foster an interest in public health and biomedical science among minority undergraduates. The program received five-year startup funding from the Centers for Disease Control and Prevention for an intensive 10-week program that includes three days a week of fieldwork in public health alongside professional mentors. The program will recruit and train 50 students a year who are undecided about

"I got to talk in more detail about whether or not the fundamental clinical model of the program, the longitudinal clinical year, had been verified in other realms, which it had. I made sure that the Columbia administration was fully supportive of the program. And I saw how happy the students were and how warm the work environment was."

Just a month before, Mr. Chapel had been fairly certain that he would stay at Michigan for medical school. But within 10 days after his second trip to Cooperstown, he knew that he would accept Columbia-Bassett's offer.

In August 2011, he and his fellow Columbia-Bassett students, just the second class of medical students to be accepted into the program, spent a week in Cooperstown to get to know the campus and the faculty before heading to Washington Heights to spend the first 18 months of medical school with the rest of the Class of 2015. In January 2013, they will return to Cooperstown for the remainder of their medical education.

## **Heavy Competition for Few Positions**

With just two classes of students accepted so far, the Columbia-Bassett program has already proved to be extraordinarily popular and competitive. Dr. Franck and Henry Weil'86, assistant dean for medical education at Bassett, recently completed reviewing applications for the Columbia-Bassett class of 2016 (the program has an application process separate from the other P&S admission process).

"We had 758 applicants for 10 positions the first year, 698 the second year, and this year, we received 971 applications," Dr. Franck says. "We believe we have a higher ratio of applicants to spots available than any other program in the country. We interview 100, and we only have to accept 14 of those to retain 10. Last year, we actually only had one student offered a place turn us down."

Columbia-Bassett draws applicants from across the country, including a distribution of colleges and regions that have not traditionally sent applicants to P&S. "Our first class has students from South Dakota and Arizona, and we receive applicants from states like Nebraska and Wyoming as well," Dr. Franck notes. "We get applications from many small liberal arts colleges."

What do these students find so compelling? Besides the focus on rural medicine, many of them are drawn to the longitudinal integrated curriculum, that unique aspect of the program that Mr. Chapel wanted to make sure had been vetted.

During the 40-week longitudinal integrated block, Columbia-Bassett students follow their own panel of patients, getting to know them and their families as people and seeing their medical situation as a process, not simply a snapshot of one point in time.

That's certainly what attracted Katherine Schwartz'14, a member of the inaugural Columbia-Bassett class, who started her clinical block in Cooperstown in January 2012. A graduate of the State University of New York at Geneseo who decided on medical school relatively late - during her junior year of college - Ms. Schwartz fell in love with the idea of Columbia-Bassett the minute Drs. Weil and Franck made a presentation at her school.

"The thing that first caught me was the longitudinal curriculum for patient care, and Bassett's focus on good interpersonal relationships in medicine," she says. "I think relationships among patients, doctors, medical students, and other health care professionals are the key to good medicine, and I just couldn't be happier here."

At the beginning of their time in Cooperstown, students launch their Major Clinical Year in a 10-week series of "rapid inpatient blocks," which Dr. Weil says incorporate rotations that are very similar to what a regular P&S student does in Manhattan, only much shorter. "The long inpatient blocks [in Manhattan] that total up to 52 weeks in the disciplines of medicine, surgery, obstetrics and gynecology, pediatrics, psychiatry, primary care, and neurology, we do in 10 weeks. Students are assigned to two disciplines for two weeks at a time, with the exception of pediatrics and neurology, which are one week each."

Ms. Schwartz says she enjoyed the rapid inpatient blocks, even though the long hours and frequent changes were stressful. "Being on the OB rotation and getting to deliver babies was the

their career choices.

coolest thing that has happened to me ever!" she says. "And we had responsibility for our own patients. We really did get immersed in that specialty, even if just for a week, and then we'll go back throughout the year and see these things over and over again."

The unique opportunities afforded by such a small program stood out to Ms. Schwartz during her two-week surgical rotation. "There's not that large a volume of students and residents here, so in surgery, there were occasions where we'd go in on surgical cases and it would just be the surgeon, the scrub team, and the medical student," she says. "There just aren't the same kind of barriers between medical students and attendings that there are in other programs."

While working with the same surgeon and resident team for three consecutive inguinal hernia repairs, Ms. Schwartz was afforded an exciting educational opportunity. "The first time, the attending was quizzing me and the resident," she says. "And for the second two, which were very straightforward cases, the attending just stood back and let the resident do the surgery and teach me. That was a phenomenal, powerful experience."

In late March, Columbia-Bassett students rejoined their counterparts in Manhattan to participate in Mechanisms & Practice weeks, three one-week rotations. "Then," Dr. Weil says, "they started the meat and potatoes of the Major Clinical Year at Bassett, the longitudinal program, which is different from every medical school in the country except for a small group of students at the University of California-San Francisco and another small group at Harvard."

#### **Two Threads**

The longitudinal curriculum has two major threads. The first is a series of clinics within the rapid inpatient blocks disciplines, spread throughout the year with consistent preceptors. "This allows for long and authentic relationships with preceptors, allowing the students to develop a better sense of what they want to do in medicine as a career. It's a huge challenge to pick from all the career opportunities in medicine in a fairly short time," notes Dr. Weil.

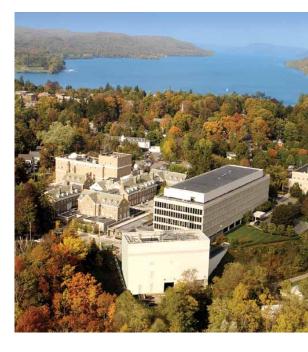
The second thread is the patient panel. When a student meets a patient who might be interesting for any number of reasons - the nature of the patient's disease, family situation, or personality the student asks if the patient is willing to be added to the student's panel. "Our patients virtually always say yes," says Dr. Weil.

By the end of March 2012, just two months into her Major Clinical Year, Ms. Schwartz had a panel of 10 patients she would follow throughout the coming year. She met the first patient on her panel on her first day in the hospital. "I was working with a woman who was awaiting a kidney transplant, writing notes on her, and reporting to my team, and we formed a very good bond," she says. "I asked if I could follow her throughout the year, and she was agreeable. I ended up seeing her as an inpatient, and then went with her to an outpatient appointment, and in February I was invited to go up to Rochester to observe her kidney transplant! It was a remarkable experience and a very early example for me of how well this longitudinal curriculum can work."

Each day, students review a computer summary of their patient panels using a specially created computer program (temporarily called Portfolio) to see if any of their patients is scheduled to visit Bassett. "Say you have a general medicine clinic in the morning, but your panel view shows that Mr. Jones is getting a cardiac catheterization at that time," says Dr. Weil. "It's very important to your relationship with Mr. Jones, and to your learning, that you be there. So you let your preceptor know that you'll be skipping that clinic to go to the cardiac catheterization, be with your patient, and see how the procedure is done."

Ms. Schwartz learned about the value of that versatility almost immediately. "We started our outpatient curriculum on a Tuesday. I was in a clinic in the morning, and in the afternoon, one of my clinics was rescheduled. So drawing on the relationship I had already established with one of the ob-gyn attendings, I went to the birthing center and got to see more patients and attend another delivery."

While learning about typical medical school staples such as differential diagnoses and surgical procedures, Dr. Weil says, Columbia-Bassett students also are learning "...what it means to be a



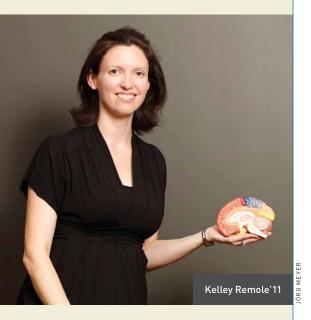
"Being on the OB rotation and getting to deliver babies was the coolest thing that has happened to me ever!"

— Katherine Schwartz'14

# **Education Highlights**

**Neuroscience Outreach Program Reaches** 

Record. Columbia's Neuroscience Outreach program reached a milestone in 2011, contacting more than 1,000 New York City students at schools in Manhattan, Brooklyn, and the Bronx to engage them with classroom presentations involving hands-on activities designed to spark their interest in neuroscience. Launched in 2006 by Kelley Remole'11 Ph.D., the program sends up to three dozen graduate student volunteers into the classroom. "We make the brain fun and accessible rather than mysterious and distant," says Cate Jensen, a Ph.D. student in neuroscience. The program also partnered with the Dana Foundation, a non-profit that promotes brain research and education, to prepare New York City high school students for the International Brain Bee.



Academic Careers in Neurology, Neurosurgery

Popular Choice. Columbia's medical school produces more academic neurologists and neurosurgeons than any other medical school in the United States, reported two studies from a group of physicians from other universities. The studies counted 79 P&S graduates working as academic neurologists and another 40 as academic neurosurgeons. Columbia's residency programs in neurology and neurosurgery also produce high numbers of academics. The neurology residency program ranks No. 1, with 134 alumni working in academia; the neurosurgery residency program ranks third, with 31 graduates following careers in academia. Faculty credit the strong clerkships in neurology and neurosurgery that all P&S students take and the research component in both residency programs.

human being passing through a complex, scary health system. If your patient has heart failure, you learn what heart failure looks like not just in a moment such as a surgical procedure, but as an ongoing process in a patient's life."

Most students will accumulate some 200 patients in their panels, although they will follow only about 50 with great regularity. "The software program that we've created for them allows them to look at their P&S course objectives every day, see which ones they've satisfied and which ones they haven't," Dr. Weil explains. "As they see a patient that manifests that course objective, the computer asks them questions that help them feel confident that they have achieved those objectives."

The course objectives - which include the course objectives for all P&S students - must be completed by the end of the 52 weeks that make up the Major Clinical Year. "At the end of this very important year, we will have a good sense of what are the strengths and areas of opportunity for each student," says Dr. Weil.

#### **Real-World Problems**

The longitudinal curriculum is the centerpiece of the Columbia-Bassett program, but it is not the program's only unique feature. Columbia-Bassett weaves its students into life in Cooperstown from the start of medical school in a way that goes beyond what even the most communityoriented medical schools achieve.

On the first day of a one-week orientation in Cooperstown in August before the academic year starts in New York City, students go in pairs to businesses in the Cooperstown community. "Their whole first day is with people," says Dr. Weil. "We want them to understand that of first and foremost importance is the human being before you. We want them to see the complexity of the lives of these people."

This year, two students spent time with an organic dairy farmer, two with a carpenter building a barn, two at a health food store, two at a restaurant, and two at a leather goods company.

"In the leather goods place, two of the students ended up talking to a worker there who's in her 50s. She can't afford health insurance, even with the 40 percent of the expenses that are paid by her employer," Dr. Weil says. "She explained to them that she fell down in the kitchen a couple of weeks previously, lacerated her forehead, and had to sew it up herself."

The students also heard from the owners of the company, who struggle each year to continue paying that 40 percent of their employees' health insurance premiums. "Every year, the costs are going up 12 to 14 percent and it's eating into their profits," says Dr. Weil. "They told the students that they feel morally obligated to offer it, but that they constantly pray that their employees will marry someone with a better health plan or just feel that they can't afford the 60 percent of the premiums so they'll drop the coverage. It's destroying their sustainability. The students got to see this microcosm of American commerce."

At the organic dairy, two students met a farmer with a wife and two small children who are barely scraping by. They cannot afford health insurance and never go to the doctor unless they have to. "If he gets hurt, his whole family suffers," says Dr. Weil. He believes that these deeply personal experiences will inform the kind of doctors that Columbia-Bassett graduates become. "You can give someone a bunch of prescriptions, but if you haven't found out what their situation really is, you're not helping. We're bringing the future managers of health care in touch with the realities of medicine that our profession has to begin improving."

And that's just the first day. On their second day, the new Columbia-Bassett students meet with Columbia professors of health and business to get acquainted with another unique aspect of the program: the "SLIM" - Systems Leadership Integration and Management - curriculum, which focuses on concepts of ethics, evidence-based medicine, systems, leadership, integration, and management.

"SLIM goes across the entirety of a student's medical education," Dr. Weil says. "It takes up a total of 5 percent or less of their time, but it's meant to address the great irony of medical education: that although health care is the largest industry in the world, and physicians are managers of health care, they get almost no training in management. We know, for example, that between 20 and 25 percent of Medicare overspending is due to overtreatment and overutilization, but almost nowhere are physicians being trained to improve this."

Over the course of their medical education, Columbia-Bassett students attend "SLIM lunches" introducing the real-world situations of stakeholders ranging from individuals who cannot afford health insurance, to employers, to insurers, to politicians, to public health officials. They participate in a monthly Journal Club focused on the spectrum of American health care compared with other systems around the world, the disparity in expenses, and the impact of cost on people, companies, taxes, governments, and outcomes.

They also participate in Bassett Functional Teams, working with management and leadership to observe how the health system addresses non-clinical challenges, everything from how to effectuate better hand hygiene, to how to organize a revenue cycle, to how to systematize risk/ quality/safety.

"One week, two teachers from the business school and the school of public health talked with our students about the famous Dana-Farber case," says Dr. Weil, referring to the 1994 case in which one patient died and another suffered irreversible heart damage when they were accidentally prescribed four times their normal chemotherapy dosage. "How did a problem like that happen and what did they do? They discussed how it led to a host of systems management and performance improvement practices. A week later, Robert Kocher, former special assistant to President Obama for health care, talked to our students about the policy process."

When they complete their Major Clinical Year, just like their counterparts at the P&S campus, Columbia-Bassett students will take eight weeks to study for their boards before beginning their scholarly projects. Most of their projects will likely focus on some element of the SLIM curriculum.

Mr. Chapel is already preparing for that. "Even though we're not required to visit Cooperstown between orientation and next January, I spent my spring break up there doing a research project and will be living up there this summer doing clinical research," he says.

He is working on two projects. One is an investigation of health outcomes in aging farmers, a longitudinal study that is part of the broader health census done in the Bassett network catchment area. "The data we're working with were first collected in 1989, the year I was born," he says. "The survey was readministered in 1999 and 2009, so now we're analyzing data to compare occupation with outcomes in people with significant agricultural exposure. It's a good embodiment of the things I find most appealing about the program: It emphasizes community responsibility, along with the rural and agricultural environment I find important."

The second research project is a smaller, but perhaps more complex, survey in the SLIM wheelhouse: an effort to gauge physician awareness of and response to different reimbursement models. "Substantial research indicates that our current fee-for-service model increases health care costs," Mr. Chapel says. "We're trying to survey physicians to assess how they respond to other approaches to reimbursement."

At the conclusion of their medical school years, Columbia-Bassett students will be burdened with less debt than the average medical student: Each one receives \$30,000 in annual grant funding. That will, Dr. Weil says, enable them to begin their residencies with less debt. "That allows those students interested in health policy or primary care or rural medicine, which are typically less lucrative, to make their choice without undue pressure from economic factors."

Dr. Weil says that he thinks some of the program's graduates may choose ultimately to practice in Cooperstown. Ms. Schwartz could well be one of them. "It's a very different type of atmosphere. Just within the first 10 weeks, we already knew so many of the doctors and nurses and had established great relationships," she says. "We get so much more hands-on experience and so much more personal attention. This has been driven home when we talked to our classmates back at the main campus. Overall, people are happy, but it's the typical medical school complaints: all the work and the hierarchical environment. The environment here at Bassett is so universally welcoming, and everyone is so enthusiastic about teaching us. It's like the ideal for medical education and health care that doesn't always show up in practice." ❖

"You learn what heart failure looks like not just in a moment such as a surgical procedure, but as an ongoing process in a patient's life."

- Henry Weil'86



P&S Dean Lee Goldman, center, during a July 2012 visit to Cooperstown, photographed with Bassett deans Henry Weil, left, and Walter Franck, right, members of the inaugural Columbia-Bassett class, and one member of the second class. Students from left are Andrew Gomez, David Chapel (a member of the second Columbia-Bassett class), Freda Ready, Krista Suojanen, Daewoong Lee, Mark Harris, Haley Masterson, and Katherine Schwartz. Class of 2014 Columbia-Bassett students not shown: Blake Alberts, Allan Guiney, and Monika Laszkowska.



t 30, Deirdre Brazil'13 is six years older than most of her P&S classmates. Before applying to medical school, she had been an actuary. But when Ms. Brazil's beloved younger sister, Eileen, died at the age of 20 from the bone cancer she had battled since age 14, it rocked her world.

"It was a long, long battle where she never really had a remission, and we were constantly in the hospital," Ms. Brazil recalls. "The doctors there were so busy and so excited that it really made me reconsider what I was doing with my life."

The fourth of eight children, Ms. Brazil was born in the part of Ireland they call "the bog" – "Pretty, but you can't grow anything." Her parents moved to New York after having their fifth child. Although Ms. Brazil's mother is a nurse, she recalls that her parents were suspicious of education, particularly the English degree that she originally wanted to pursue.

"I was always a big fan of reading and writing, and I never got to pursue either of those skills," she says. "Once I convinced them I could go to college and have a career, they couldn't wrap their head around an English degree, so I absolutely couldn't do English."

And then she came to Columbia and found the narrative medicine program. "I realized it wasn't a choice of being a doctor *or* writing; you could have the best of both worlds."

As a member of the Class of 2013, Ms. Brazil is one of the first cadre of P&S students to be able to explore such passions in greater depth through the scholarly projects program, which gives students four months of protected time following their Major Clinical Year to pursue, under the guidance of a faculty mentor, an area of medical practice or research with the aim of creating new knowledge.

In structuring their research, students may choose from six available tracks: basic science, clinical research, global health, medical education, narrative and social medicine, and population health. "In the six tracks, we can find a home for any student who has an idea of what they want to do," says Jonathan Amiel'07, assistant dean for curricular affairs, who oversees the Scholarly Projects Program. "About half of the students are doing their projects in clinical research, a fifth are doing them in global health, and the remainder are divided among the other four tracks."

Senior faculty members direct each of the tracks and are bringing together wide-ranging, multidisciplinary cohorts of individual faculty mentors to provide close supervision and guidance as students pursue their projects.

"Our faculty has a long tradition of mentoring students doing research," says Dr. Amiel. "In the Scholarly Projects Program, we are helping students pair with faculty known for their prolific work in basic and clinical research and we're also reaching even more broadly into the academic community, to people who have interests in areas like population health or the humanities. So, for example, this year a student is working with an NIH-funded translational scientist studying the ways in which cells can transfer organelles to one another while one of his classmates is working with an emergency department psychiatrist who used to be a classics professor to undertake a critical analysis of the way mood disorders have been represented in the arts."

Within the narrative and social medicine track, Ms. Brazil plans to write a memoir to tell her sister's story in conjunction with her own. "It's almost like Russian dolls, the way it all nests together. Telling my sister's story will help me to better understand and tell my patients' stories," she says.

For example, she still regrets her family's decision not to pursue palliative care for Eileen. "Ultimately she died not from cancer, but from graft-vs.-host disease as the result of a bone marrow transplant," she recalls. "I think the doctors felt that if they had just gotten her to turn around a little bit, she would have gotten better. But she actually asked to stop taking the steroids, which would have killed her very quickly. We didn't recognize or understand that question as the cry for palliative care that it was. She went through a lot, she was very tired, she was ready for a different type of care, and it wasn't recognized. It's what doctors feel in ourselves, sometimes, that makes the patient not get what they want."

That's part of the story that Ms. Brazil wants to tell in her scholarly project, and it forms the key thread of another in the first group of scholarly projects.

Eric Bank'13 began thinking about his project by considering what he would like to learn more about as a medical student. He kept coming back to the difficulties of having conversations about end-of-life care. "I began my project by meeting with Dr. Craig Blinderman [director of adult palliative medicine at Columbia] and other faculty members who are known as being great communicators with their patients."



Columbia's First Scholarly Projects Range from Clinical Research on Postpartum Diabetes to a Global Health Project in Nicaragua

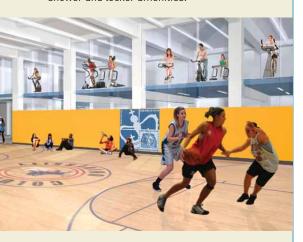
# **Education Highlights**

Narrative Medicine Techniques Taught to Improve Care for Wounded Vets. In an effort to increase the satisfaction of veterans and their families with the care they receive at VA hospitals and clinics, Columbia's program in narrative medicine hosted a first-of-its-kind three-day workshop, "Challenges in VA Health Care: A Narrative Response," held in March 2012. The workshop aimed to equip the 40 VA doctors, nurses, social workers, and therapists in attendance with the narrative techniques needed to form therapeutic alliances with veterans and their families and improve communication and respect among members of the VA health care team. Participants learned narrative approaches to clinical interviewing and reading and writing interventions to enable them to better hear and understand patient experiences.

#### First Narrative Medicine P&S Graduate.

Sneha Mantri'12 became the first medical student to graduate with a master of science degree in narrative medicine. The first degree program of its kind, the narrative medicine master's degree instills the skills of narrative competence and leadership required to develop and implement narrative-based learning and practice in clinical settings. Dr. Mantri, who served as an adviser for the Lang Youth Medical Program during medical school, matched to a neurology residency at the University of Virginia.

Bard Hall Gym Gets Makeover. The Bard Athletic Center within Bard Hall is slated for an upgrade. In response to a user survey, the center will be renovated to include two levels of exercise equipment overlooking the basketball court. Other upgrades will include central air conditioning and ADA-compliant shower and locker amenities.



Physician Memoir, End-of-Life Care, and Pitching Injuries

Dr. Blinderman will mentor Mr. Bank as he researches the best ways to educate medical students about good communications skills around end-of-life conversations and to work with the curricular heads of the "Foundations of Clinical Medicine" course to develop possible ways to introduce improved educational models for these conversations into the P&S curriculum. "The faculty members I'm working with are very excited about this," he says. "They acknowledge that there's always room for improvement in anything, and this is a particularly challenging area."

Ms. Brazil and Mr. Bank are two of about a dozen students that Rita Charon, M.D., Ph.D., professor of clinical medicine and director of Columbia's Program in Narrative Medicine, oversees in the Scholarly Projects Program's narrative and social medicine track.

"I'm having a great deal of pleasure as I meet with the students who are interested in devoting time to my domain," says Dr. Charon. "They are imaginative, creative students who are going out on an intellectual limb, because they see clearly how medicine - and the practice of medicine – is not restricted to care for the malfunctioning organ, but it's rather really addressing our health, wellness, and living in the world."

Ms. Brazil, for example, will not only contemplate her sister's illness and her own journey into medicine, but also, more broadly, consider both how having a sick sibling affects the healthy children in the family and how the autobiography of the individual doctor influences that person's formation of professional identity. Dr. Charon has connected Ms. Brazil with child psychiatrist Jonathan Slater'85 as an additional mentor to help explore these complex questions.

Within the clinical research track, students are exploring topics as diverse as laparoscopic banding for obesity in children, exercise in anorexia nervosa, improving results of glioblastoma multiforme resection, postpartum diabetes, hyponatremia prevalence in the United States, predicting results of cataract surgery, and effects of fatigue on injury in baseball pitchers.

"It's their best early opportunity to do something that may be publishable in medical research, so they're very wound up about it," says Henry Spotnitz'66, the George H. Humphreys II Professor of Surgery, who co-directs the clinical research track this year with Daniel Wang, M.D., assistant professor of clinical medicine. "They recognize it as a very important opportunity to be creative and to work with established investigators in their area of interest, to make an important research contribution."

The fact that they're the first P&S class to engage in the scholarly project program isn't lost on the Class of 2013, Dr. Spotnitz says. "There's definitely a sense of the historical importance of it. But they're probably also a little apprehensive, because it hasn't been done before and they don't have anything to look back at for guidance."

About a dozen of the approximately 70 students pursuing the clinical research track for scholarly projects have chosen to focus on orthopedics, says Dr. Spotnitz. One of these is



Jeff Grantham'13, who has channeled his college baseball career and lifelong love of the sport into research on pitching mechanics.

While playing shortstop at the Queens campus of St. John's University, Mr. Grantham made connections that eventually allowed him to meet the team physician for the New York Yankees, Christopher Ahmad, M.D., associate professor of clinical orthopedic surgery at P&S. Even before his Major Clinical Year, Mr. Grantham was eager to begin his research.

"I started three projects in the summer after my first year," he says. "One was a project looking at the baseball community's perception of 'Tommy John' surgery and its indications. Another project is looking at the use of platelet-rich plasma injections in the treatment of ligament injuries in the elbow." The third, which Mr. Grantham wrote the IRB application for that summer, became his scholarly project, under Dr. Ahmad's mentorship: a study of the kinematics of the baseball throwing motion. "Everyone postulates that pitch count is directly related to injury in young pitchers, and even competitive pitchers. We want to see if fatigue has any impact on the throwing motion and possibly increasing the pitcher's risk of injury."

Mr. Grantham plans to videotape players in game situations to see if their throwing motion changes over the course of the game. Videotaping players throughout the season will assess if their pitching motion changes over the long term and whether the mechanics change in a way that predisposes them to injury. Mr. Grantham is videotaping players at the Little League, high school, and college levels.

"I know orthopedics is my route," he says. "I'm not sure if it's sports medicine necessarily, but these projects are fun and interesting and they give me a good jump start on the future. I've been very impressed by how encouraging everyone has been, and how everyone seems to be interested in helping medical students do research."

The scholarly projects have had a ripple effect on the rest of the curriculum. For example, developing the first set of projects for the global health track has also spurred a more cohesive approach to global health studies at P&S in general. "Once we got into the process of trying to line students up with a mentor here in New York and a mentor in a foreign country, we realized the global health track, without any doubt, is far more complicated than any of the others," says Stephen Nicholas, M.D., professor of clinical pediatrics at P&S and of clinical population & family health at Mailman School of Public Health, who directs the global health track. "Indeed, we discovered that we need to strengthen our preclinical curriculum and add content so that we are doing a better job of educating students about global health as an entity - all students, not just those who will do their scholarly projects in this track."

About 15 students in the Class of 2013 have chosen global health projects that include clinical competency training for cardiac life support for physicians in Nicaragua, a study of the effect of temperature variations on complication rates in cleft lip and palate repairs in India, and a retrospective survey of the impact of global health experiences on the careers of medical school graduates who have done programs in the Dominican Republic.

"One thing we saw early on was that a significant number of students began thinking about what they might do for a scholarly project as they began planning their summer between their first and second years," says Dr. Nicholas, who also is associate dean for admissions. "We realized that we didn't have that much of a preparatory process for them."

That changed with the presentation of Columbia's first Global Experience Pre-departure Symposium, a full-day session held in April 2012 to brief students on everything from safety and insurance to cultural and ethical concerns. Students had the opportunity to get first-hand information from other students who had traveled abroad.

"Making the experience more high profile in this way will allow us to attract students to the global health track that I don't think we otherwise could have gotten," says Dr. Nicholas, who predicts a larger cohort for this track in the future. "Our first-year class is now completely fired up and involved with international health."

Students exploring scholarly projects are not limited to finding mentors at P&S; they have the entire Columbia University faculty at their disposal. "Students pay a lot of tuition to come to Columbia, and a down side of this place is that it's a big, cumbersome university in which the



"We want to see if fatigue has any impact on the throwing motion and possibly increasing the pitcher's risk of injury."

Jeff Grantham'13

# **Education Highlights**

International Residency Program. Surgical residents at Columbia have the opportunity to gain valuable surgical experience in underserved countries through a program that sends them on six- to eight-week surgical rotations in foreign hospitals that are generally not equipped with the kind of technology used in American hospitals. Run by Mark Hardy, M.D., the program allows residents and faculty to teach foreign residents and staff the newest surgical techniques developed in the United States. A new program allows the exchange of NYP/Columbia and Korean Hallym University surgical faculty with local senior surgeons in underserved nations. The American Board of Surgery and the Resident Review Committee have also agreed to selectively approve some of the resident foreign country rotations and even provide accreditation for some appropriately supervised cases performed by fourth-year and fifth-year residents at foreign institutions.

#### **Musicians' Guild Presents First P&S**

Messiah Sing. In December 2011, members of the student-run P&S Musicians' Guild presented the campus' first official performance of George F. Handel's well-known oratorio, "Messiah," with instrumental musicians and vocalists. Vocalists Michael Ayers' 14 and Jennifer Russo' 15 were among the singers who led an audience composed of students from all medical center schools, faculty and administrators, pre-medical applicants, and community members.



Physician Memoir, End-of-Life Care, and Pitching Injuries

medical student is not a very powerful figure," says Dr. Charon. The scholarly projects program demonstrates the positive side of being a small medical student in a big institution. "They have an open door to all this brilliance. There's the law school, the journalism school, the school of the arts, the Millennium Villages, and the Earth Institute."

For example, another student Dr. Charon mentors is interested in the economics of health care, specifically the role that private investors, drug companies, and device manufacturers might play in questions of equity in health care, health care disparities, and the agenda of medical research. That is a topic that could engage not just P&S faculty, but also faculty in public health, business, economics, and biomedical engineering.

"I have one student who had been a Spanish literature major in college, who was a real reader and missed it terribly," says Dr. Charon. "One of the things I said to her in planning her scholarly project was that she could take the time to enroll in a course on the main campus, in the English department or in writing. She came back to me with the dazzling news that she had gotten into a writing seminar taught during the spring by novelist Colm Toibin, whom Columbia somehow managed to recruit away from Princeton. She was only one of eight students accepted, but it conflicted with one of the seminars in my March elective. We were happy to make arrangements for her to be able to be in that writing seminar."

Scholarly projects have some inherent limitations, admits Dr. Spotnitz. "Even with a lead time of close to two years, it's difficult for a student and a mentor to come up with a specific, fully developed research project and achieve IRB approval in that time frame. So, for the most part, the majority of these projects must be some sort of compromise between the student's interest and drive and what can practically be achieved in the space that's available."

Other medical schools have developed programs like P&S's Scholarly Projects Program, but Dr. Amiel notes that the P&S program is notable in that it encourages a wide scope of study that allows students to immerse themselves in projects according to their intellectual passion. "Here, we want to think very broadly about scholarship and allow students the maximum flexibility. Many will want to do clinical, basic, and translational research. Others will want to work in the community or to travel abroad and learn about health systems overseas. Still others will want to think critically about medical education, either in our own curriculum or elsewhere. And some will want to reflect and write about the experience of being a health care provider, or pursue areas like bioethics, the business of finance and medicine, intellectual property and intellectual history, within the narrative medicine track. In our program, we want to encourage our students to find their scholarly voice as they integrate the core qualities of medicine they learned at the beginning of their time at P&S and differentiate into the doctors they want to be."

Dr. Amiel says it is enlightening to see how the scholarly projects are taking shape in this first year. "We've known that our students are adept at joining a clinical research or wet lab project, but here we're seeing them broaden their view to access the breadth and depth of the faculty in an unprecedented block of protected time within the curriculum."

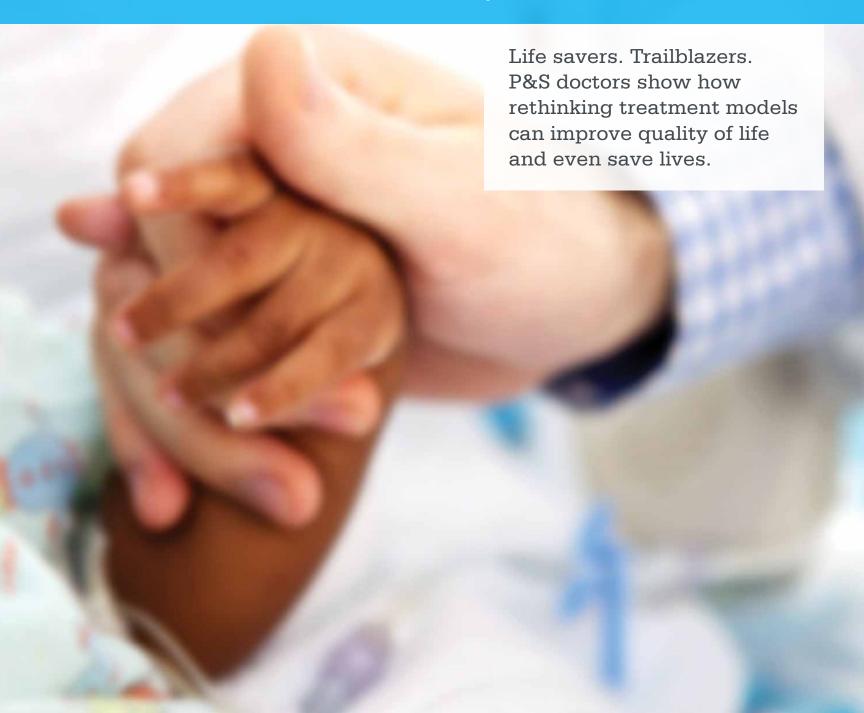
The program has plenty of room to grow. "We want to get smarter about this and develop a faculty development program for student-centered mentoring," says Dr. Amiel. Such a program would teach mentors how to be responsive to students' needs and talents and help scholarly projects develop around the student's trajectory rather than the mentor's, or, at least, find a synergy between the two.

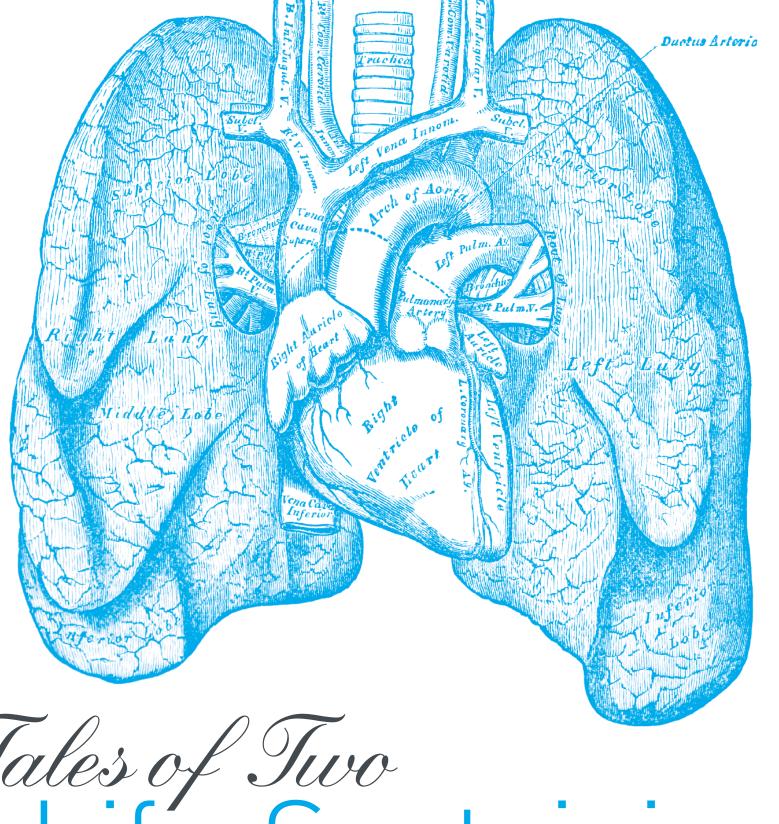
"We don't want a student to simply join a project and do work that would otherwise have been done by a research assistant," Dr. Amiel says. "We want to provide cohesion, a thread that will allow the student to develop and grow so that by the time they're applying to residency, they have a sense of what their passion is and what they bring to the table, so that they not only have the clinical skills to prepare them for residency but are also ready to engage academic medicine in a real way." •

Other track directors are Richard Kessin, Ph.D., professor of pathology & cell biology (basic science track); Marc Dickstein'87, professor of clinical anesthesiology (medical education track); and Neil Schluger, M.D., professor of medicine at P&S and professor of epidemiology and environmental health sciences at Mailman (population health track).

# Clinical Care:

Patients Benefit from the Best that Today's Medicine and Science Offer





Tales of Two Life-Sustaining

he heart beats, the chest rises and falls with each breath. From the earliest days of medicine, long before physicians mapped the inner workings of the brain, we have understood that these two functions – heartbeat and breathing – are essential to sustaining life.

Advances in cardiac and pulmonary care at Columbia this year have made it possible to sustain life for people who, just a few years ago, at even the most advanced medical centers, would likely have been told, "We're sorry. There's nothing more we can do."

#### Second Chance at a Second Lung

Patricia Kingsbury knew she should not smoke, a habit she developed in her teens. She had struggled since childhood with asthma, a condition that seemed to run in her family. By the time she was in her early 40s, she found herself frequently struggling to breathe, and her job as a crisis counselor for the New York State Office of Mental Health was increasingly taxing. The albuterol inhalers her doctors gave her did not seem to help.

In 1996, at the age of 46, a chest X-ray and a pulmonary function test showed that she had severe chronic obstructive pulmonary disease. For the next several years, Ms. Kingsbury tried different medication regimens, but every respiratory infection triggered an exacerbation of her COPD. At work, she switched to a desk job and tried to hide her symptoms but in 2000, with her lung function at 17 percent, was forced to go on disability. "The bathroom was probably about 100 feet away from my office, and I could barely get there," she recalls.

After leaving her job, a round of hospitalizations started. She finally quit smoking for good in January 2003, which should have helped, but a trip to Florida the following spring triggered a flare-up of her pollen allergies and a three-week stay on a respirator in the hospital. She would experience periods of improvement with pulmonary rehabilitation, but after a particularly tough hospitalization in 2007, "Things just went south," she says.

By 2010, Ms. Kingsbury was on the list at Columbia for a lung transplant. She got called several times, eagerly setting out for the hospital only to learn that the lungs that had been donated were not viable.

After a trip to the emergency room in 2011 with a headache and vomiting, she was erroneously given morphine. "That's something that most people with respiratory problems don't get unless they're on a vent," she says. "I went into respiratory arrest, my heart stopped working, and I had to be resuscitated. I was put on a respirator again, and, of course every time that happens, it does more damage." During the summer of 2011, she spent several months in a rehabilitation hospital. In September, she was sent home to Albany to await a transfer to a nursing home.

She never made it to the nursing home. The call from Columbia came after she had been home for only one day. It was another set of lungs. Ms. Kingsbury was second on the list for new lungs, so she would be backup for another patient ahead of her in line on the list that averages about 50 people and a six-month wait. She and her grown daughter made the trip to Manhattan yet again, but it turned out that these lungs, too, were not viable. However, another option was available this time. Months earlier, Ms. Kingsbury had agreed to participate in Columbia's clinical trial of a new method for increasing the availability of lungs for transplant, the NOVEL (for Normothermic Ex Vivo Lung Perfusion as an Assessment of Extended/Marginal Donor Lungs) trial.

Developed by surgeons at Lund University in Sweden and by surgeons at the University of Toronto, ex vivo lung perfusion allows transplant surgeons to maintain donor lungs outside the body to test their suitability for transplant. Using this method, lungs that might otherwise have been discarded as too poor for transplant can sometimes be better assessed and reconditioned.

"So far, within the trial, we have tested eight lungs, and three of those were suitable for transplant," says Frank D'Ovidio, M.D., Ph.D., assistant professor of surgery and associate surgical director of the lung transplant program. "That is a very favorable thing: Three lungs that we otherwise would have discarded have been transplanted, with great results. On an average, only one in five organ donors ends up being a lung donor, so there are not a lot of donors right now. Even if we are only able to increase the number of donors by 10 percent, that will mean everything to the patients who are able to receive those lungs."

Organs

Advances in Surgery, Organ "Reconditioning" Give Second Chances to Patients

# Tales of Two Life-Sustaining Organs

It certainly meant everything to Patricia Kingsbury. As it turned out, the patient ahead of her in line turned down the ex vivo lungs, so she was able to get a double lung transplant rather than a single. A month later, she left the hospital.

"I don't think I would have made it through another hospitalization and intubation," she says. "Now, I'm amazed with what I can do. There's so much that I haven't done since I was 42. Now I can walk outside in front of my apartment. I've lived here for three years and had never walked on the sidewalk before! I've started taking my own garbage out and I volunteer to help my neighbors. I can go grocery shopping, I cook, clean, vacuum. I play with my grandchildren! I can do all the things I love to do."

The other patients who have received lungs tested and reconditioned by the ex vivo method also are doing well. Stephen Davis, a 60-year-old Connecticut landscape designer who had to sell his business due to COPD and spent two years on the transplant list, looked forward to waterskiing this summer.

"When you hear that you have end-stage COPD, it's very frightening," he says. "My doctor explained that the disease would keep flaring up and it would take more and more oxygen to keep me alive, and I'd have less and less ability to do things. I would have lived the rest of my life the way I spent last winter: on the couch hooked up to an oxygen tank. Eventually, I would have suffocated. That's how you die from emphysema."

Instead, he received his transplant in March 2012 and returned home from the hospital just a week later. Today, he says, "I can breathe fantastically. I can breathe forever."

## Minimally Invasive Valve Replacement

More than 1.5 million people every year are diagnosed with aortic stenosis, a progressive narrowing of the aortic valve. Affecting approximately 5 percent of older Americans, it is the most common valve disease among the elderly. Open-heart surgery to replace the aortic valve is effective, but at least 30 percent of older people with aortic stenosis are not healthy enough for such an invasive procedure.

But now thousands of people who previously had few options to treat their rapidly deteriorating cardiac condition have a new option, thanks to the successful trial of a non-invasive approach to treat aortic stenosis, led by pioneering cardiac interventionalists at Columbia.

The Food and Drug Administration, in two decisions over the past year, approved the SAPIEN Transcatheter Aortic Valve, based on the results of the landmark PARTNER trial led by Martin Leon, M.D., director of Columbia's Center for Interventional Vascular Therapy, and Craig Smith, M.D., chair of surgery at P&S.

The non-invasive procedure replaces the diseased valve with a biologic valve made of bovine pericardium. The valve is sewn onto a metal frame affixed to a balloon catheter then placed in the femoral artery, advanced to the heart, and deployed to replace the diseased native valve. "It's much like the way we treat coronary atherosclerosis with a stent," says Dr. Leon. "The old valve is pressed against the aortic wall and becomes non-functional."

Performing a procedure of this magnitude – transplanting a heart valve without opening the chest – was long thought impossible, Dr. Leon says. "Despite early skepticism, we now have a predictable, less invasive procedure to replace the aortic valve in high-risk patients. To successfully

implement this therapy requires a multidisciplinary heart valve team that assesses, treats, and follows patients with advanced valvular disease."

The team at Columbia has performed more of these procedures than any other group in the United States, more than 500 by early July 2012. For 2012 alone, Dr. Leon expects that the group will perform more than 300 cases. "Within the past 18 months, the PARTNER trial has had four manuscripts accepted by the New England Journal of Medicine," he says. "No other study has ever led to four publications in the New England Journal. That speaks to the rigor of the study and the importance of the results."

The procedure was approved originally for patients too sick for openheart surgery. "Patients in this category who do not receive a valve replacement have a 50 percent mortality in the first year and close to 70 percent mortality by the end of the second year," Dr. Leon says. "The valve procedure leads to an absolute reduction in mortality of 20 percent during the first year. In other words, the number needed to treat to save a life in the first year is five patients. This procedure has mortality benefits to patients which are similar to heart transplantation and LVADs."

But patients too sick for surgery are not the only ones Dr. Leon believes will benefit from the SAPIEN valve. "The second cohort randomized in the PARTNER trial were patients who could tolerate an operation but were in the upper decile of risk," he says. Study results showed that the valve procedure is equivalent to open-heart surgery, in terms of mortality, after the first two years. "Patients tend to recover much more quickly with the non-invasive procedure, ICU days are reduced by 40 percent, and overall hospital length of stay is reduced as well. All the metrics for quality of life show an early recovery benefit with the SAPIEN valve, which is important for frail, elderly patients." The most recent FDA decision extends the approval of this new procedure to this group of patients.

Is there a down side to the SAPIEIN valve? No procedure comes without risk, Dr. Leon says. "The risk of stroke and vascular complications within the first several days is higher than with surgery, but the risk of bleeding complications and arrhythmias is higher with surgery."

The research team is now proceeding to the PARTNER 2 trial, which will study a new version of the device that is 40 percent smaller and believed to be more durable. "We have confidence that this will lead to fewer vascular complications and overall better outcomes."

The therapy may have other important areas of application. Surgically implanted valves do not last forever and when they fail, a re-operation is needed. "Repeat surgery for a failed surgical valve can be problematic in some patients," says Dr. Leon. "So far, we have tested 15 patients at Columbia using the SAPIEN valve to treat a surgical valve failure, and the results are very promising."

In January 2012, the Heart Valve Center at NewYork-Presbyterian/ Columbia University Medical Center opened. Co-directed by Susheel Kodali, M.D., assistant professor of clinical medicine, and Mathew Williams, M.D., assistant professor of surgery and medicine, the center brings the expertise of clinical cardiology, echocardiography, valvular disease specialists, cardiac surgeons, and a host of disciplines together in the comprehensive management of patients with valvular disease. The center also acts as a training program; approximately 40 percent of physicians performing the procedure in the United States have learned their skills from Columbia experts.

"Prolonging life is an important goal of this new therapy, but as important is the improvement in quality of life," says Dr. Leon. "Elderly patients want to feel better. They don't want to be in and out of the hospital. And this procedure leaves people dramatically improved in terms of how much better they feel."

#### **Keeping the Beat**

Columbia's Mechanical Circulatory Support program, founded in 1990, is one of the nation's top centers for patients with advanced heart failure. This year, it became one of the first programs in the nation, and the first in the New York City area, to transplant the SynCardia Total Artificial Heart.

The SynCardia Heart is a temporary device designed to completely replace the dying heart of a severely ill cardiac patient, replacing both failing heart ventricles and all four heart valves. Once implanted, the device provides immediate blood flow of up to 9.5 liters per minute. This high volume of blood flow helps speed the recovery of vital organs and helps to make the patient a better transplant candidate.

"The artificial heart does more than improve a patient's chances of surviving to transplant. It reduces some of the risks of the transplant surgery itself. When we implant the device, we are already preparing for transplant," says Yoshifumi Naka, M.D., Ph.D., professor of surgery and director of the cardiac transplantation and mechanical circulatory support programs.

Surgeons at Columbia have implanted two artificial hearts. One severely ill patient later died, but the other recovered sufficiently to be a candidate for a heart transplant. Her January transplant surgery was successful, and she returned home and is doing well.

The artificial heart will be used for only a limited number of patients, but for those, it is literally a lifesaver. "There are some patients whom we otherwise would have very limited options to help," says Ulrich

Jorde, M.D., associate professor of medicine and medical director of the mechanical circulatory support program. "Usually you can get away with just maintaining the left side of the heart, using a left ventricular assist device, and the right side can manage as a bystander. But, for example, people with conditions such as amyloidosis or restrictive cardiomyopathies, or patients with heart transplants that have failed, the patient will not do well unless you take out the entire heart. This is very exciting, because at least we have something to offer these patients."

Equally exciting, says Dr. Naka, have been recent advances in the more common forms of device therapy. "We are expanding the mechanical circulatory support program very rapidly: This year, we project about a 25 percent increase in cases."

He and his team are participating in clinical trials for a new left ventricular assist device called the HVAD, a miniaturized heart pump designed to be implanted next to the heart. "This device is likely to be approved as a bridge to transplant therapy this year," says Dr. Naka.

Columbia is also one of the nation's leading centers in implanting the current generation of LVADs, which for many patients have become destination therapy rather than simply a bridge to transplant. In April 2012, Dr. Jorde helped to present the latest results from a study of these devices for that indication at the International Society for Heart and Lung Transplantation meeting. "It turns out that with the learning curve that has happened, the real-world results with these devices as destination therapy are actually better than those seen in the clinical trial that led to FDA approval," he says. "The one-year survival rate for these patients on medical therapy would have been about 25 percent; on the pump, their one-year survival rate is about 75 percent. That's a huge jump. Assist device therapy has now become mainstream. Assist device therapy and percutaneous valve replacement are going to drive cardiology over the next 10 years, and Columbia is a global leader in both." \*

# Other Highlights in Patient Care

Another Year at the Top. Once again, P&S partner hospital NewYork-Presbyterian is the No. 1 hospital in New York City and the New York metro area as ranked by U.S. News & World Report, which reviewed data for nearly 5,000 hospitals. NYP was one of only 148 hospitals nationally ranked in one or more of 16 adult specialties. This is the 12th consecutive year that the hospital has been among the elite hospitals - 17 this year - that made the magazine's honor roll by scoring near the top in at least six specialties. NYP is nationally ranked in 14 of the 16 specialties the report rates: cancer, cardiology/heart surgery, diabetes/endocrinology, ENT, gastroenterology, geriatrics, gynecology, nephrology, neurology/neurosurgery, orthopedics, psychiatry, pulmonology, rheumatology, and urology.

Life-saving First. A 10-hour operation in February was the first reported emergency pediatric surgery of its kind. A 5-year-old New York girl with an otherwise inoperable tumor benefited from the operation, which involved the removal and partial reimplantation of her liver and her right kidney plus open heart surgery to resect the tumor. The surgery was led by Tomoaki Kato, M.D., chief of abdominal organ transplantation and a pioneer in multiple-organ transplantation, and Emile Bacha, M.D., chief of cardiothoracic surgery, director of congenital and pediatric cardiac surgery, and a pioneer in novel heart surgery for children.

**Robotic Surgery Brings Sweet Dreams to Apnea** Sufferers. Many patients with chronic sleep apnea cannot tolerate one of the most common treatments for the condition, continuous positive airway pressure, or CPAP. Approximately half of patients who try it eventually give up. But now, apnea patients are finding relief from a new robotic surgical



procedure designed to remove blockages from one of the most troubling areas of the airway to become obstructed during sleep: the base of the tongue. Jeffrey Ahn, M.D., director of sleep disorders and robotic surgery, specializes in the robotic treatment of obstructive sleep apnea.

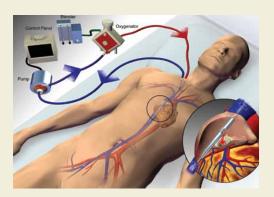
# Other Highlights in Patient Care

Preparing for Breast Surgery at Home. Women preparing for breast reconstruction surgery at Columbia can now use an at-home method to create the space within their chest wall for a breast implant. Columbia is the first location in the United States to offer this option, in which patients use a remote control to activate an implanted expander device to release a small amount of compressed carbon dioxide. The process is much quicker and more convenient than the traditional means of implant preparation, which involves several months of physician visits for saline injections. Jeffrey Ascherman, M.D., is principal investigator in an ongoing clinical trial comparing this procedure with traditional tissue expansion. Simplifying the reconstructive surgery process may encourage more breast cancer survivors to consider breast reconstruction.

#### Columbia and NYP Launch Integrated Medical Record. Columbia and NewYork-Presbyterian Hospital have created a jointly managed electronic health record for the Columbia faculty practice organization, Columbia Doctors, which is one of the largest multi-specialty practices in the nation. The system is installed in 150 of the FPO's outpatient

practices, with more than 1,000 Columbia physicians and their staffs actively using it.

New Center for Acute Respiratory Failure. Already one of the largest centers in the world for respiratory and cardiac failure in adults, Columbia this year dramatically expanded its services with the opening of the Center for Acute Respiratory Failure, which includes among its areas of expertise the use of lung bypass technology called ECMO, for extracorporeal membrane oxygenation. ECMO can take over the function of the lungs in adults with acute respiratory distress syndrome, allowing severely damaged lungs the time they need to rest and heal. Columbia treats about 100 ECMO patients a year, putting it among the leaders worldwide in using this technology. The new center, directed by pulmonary critical care specialist Daniel Brodie, M.D., and thoracic surgeon Matthew





Eastside Practice to Relocate. Columbia Doctors, the P&S faculty medical practice, will move to new facilities adjacent to Rockefeller Center in early 2013. The practice signed a 25-year lease for 120,000 square feet at 51 W. 51st St. The new location will replace the existing ColumbiaDoctors Eastside practice on East 60th Street. The new space will allow the practice room for expansion.

Bacchetta, M.D., also offers other lifesaving procedures for lung failure patients, including embolectomy, a surgery that directly removes clots from the lungs of patients with severe pulmonary embolism. "We are one of the few centers in the U.S. that does this procedure," Dr. Bacchetta says.

**Berrie Center Launches First National Type 1** Diabetes Exchange. The Naomi Berrie Diabetes Center has announced the creation of the first national "T1D Exchange," a unique program that will allow patients around the country to share information in a national registry. Coordinated by Berrie Center lead research coordinator Ellen Greenberg and directed by Berrie Center co-director Robin Goland, M.D., the registry asks participants to fill out a 20-minute questionnaire involving such topics as medical history, treatment, and other health problems or complications. Ms. Greenberg and Dr. Goland say they hope to enroll 100,000 participants nationwide, including more than 3,500 people the Berrie Center treats for type 1 diabetes. The project is sponsored by the Leona M. and Harry B. Helmsley Charitable Trust.

**New Treatment for Deadliest Brain Tumors** in Children. A new treatment method has now been used to successfully treat two children with the deadliest type of brain tumor, diffuse intrinsic brainstem glioma. A fast-growing, difficult-to-treat tumor located deep within the most vital structures of the brain, this tumor now accounts for the majority of brain tumor-related deaths in children. Neurosurgeons Jeffrey Bruce, M.D., and Richard Anderson, M.D., were able to use convection enhanced delivery to get a chemotherapy agent directly to the tumors of the two patients, using stereotactic brain imaging to correctly place ultra-thin catheters deep within the brain with minimal disturbance to the surrounding tissue. This allows doctors to target a higher dose of the drug exactly where it is needed, avoiding the intolerably high toxicity that would result from the doses needed to kill cancer cells if chemotherapy were delivered in the standard way.

#### Chief Named for New Neuro-Oncology Program.

Andrew B. Lassman, M.D., has joined the P&S faculty as chief of neuro-oncology, a new program focusing on caring for people with brain tumors and metastases. Dr. Lassman has designed and led clinical trials to evaluate new drugs, novel combinations of existing drugs, and regimens that combine chemotherapy and radiation therapy. He is the national study chair of a phase 2 trial of the drug dasatinib for recurrent progressive glioblastoma. Dr. Lassman's ambitious plans for a multidisciplinary, pre-eminent facility for primary and metastatic brain tumor care, research. and education will establish Columbia as the leading center for neuro-oncology, says neurology chair Richard Mayeux, M.D.

# Esnews

P&S Reports Unprecedented Growth. On many fronts, 2011-2012 was a record-setting year at P&S. The percentage of accepted students choosing to attend P&S reached the highest level in 35 years and the third highest yield among the nation's top private medical schools. This achievement is attributed in part to the new curriculum, which will enter its fourth year in the fall of 2012. Meanwhile, clinical revenue grew by 8 percent and NIH grants increased by 5 percent. New donations to P&S have broken all records.

Columbia's CTSA Renewed for Five Years. The Irving Institute for Clinical and Translational Research has received \$38.9 million in renewed funding from the NIH for the Clinical and Translational Science Awards program. "The renewal of CUMC's CTSA," says Lee Goldman, M.D., dean, "reflects our commitment to interdisciplinary research that translates our discoveries into improved patient care, both in our community and around the world."

New Community Health Advisers. Rafael Lantigua, M.D., and Dennis Mitchell, D.D.S., were appointed Dean's Special Advisers for Community Health Affairs to counsel all medical center deans on community health issues and facilitate new collaborative initiatives with community and academic stakeholders. They also will provide a faculty voice in efforts to engage community health organizations and optimize academic-community partnerships.

New York Genome Center. Columbia has joined 10 other world-class academic medical centers and research universities in the New York area in an unprecedented collaborative venture to create one of the largest genomic facilities in North America: the New York Genome Center. NYGC ultimately aims to open a genome sequencing facility in Manhattan that will be one of the largest such facilities in North America. Through this collaboration, scientists and physicians from member institutions will share diverse clinical and genomic data on a massive scale to discover the molecular underpinnings of disease, identify and validate biomarkers, and accelerate development of novel diagnostics and targeted therapies.





Extraordinary New Donation for the Cancer Center. Herbert and Florence Irving, the medical center's leading benefactors, have given an additional \$40 million to support the Herbert Irving Comprehensive Cancer Center. With this new gift, Mr. and Mrs. Irving have generously committed nearly \$200 million to CUMC and the hospital, of which \$177 million has supported the cancer center and other cancer-related programs. The new grant will be used by cancer center director Stephen G. Emerson, M.D., Ph.D., to recruit and retain new cancer investigators, support current investigators, and fund center operations.

Legacy Challenge Raises Nearly \$20 Million. A program to match new planned estate gifts at one-third their value raised nearly \$20 million for P&S by the time it concluded in December 2011. The brainchild of P. Roy Vagelos'54, chair of CUMC's Board of Visitors and the medical center's capital campaign, the Legacy Challenge used the matching funds to help support student scholarships immediately. "By helping students fulfill their dreams of becoming leading physicians and scientists, alumni leave a legacy that will truly resonate for generations to come," Dr. Vagelos says.

Prestigious Biomedical Engineering Partnership. Columbia has been selected to join the highly competitive Coulter Translational Partnership program, sponsored by the Wallace H. Coulter Foundation. These partnerships are designed to accelerate faculty innovations toward clinical use. Deploying \$5 million of funding over five years (two-thirds from the Foundation and one-third from Columbia) the program will identify projects with the highest chance of a successful outcome, that is, licensure to a commercial partner with the ability to bring the product to market. The program will be led by the Department of Biomedical Engineering, in close collaboration with Columbia Technology Ventures and the Departments of Surgery, Orthopedic Surgery, and Radiology.





# Gifts Large and Small Prepare for the Campus of the Future

State-of-the-Art "Sculpture in the Sky" Will Transform the Skyline, Student Learning, Campus Life

ittle girls do not usually raid their piggy banks to invest in real estate, even if it has a knock-out view of the George Washington Bridge.

But when 7-year-old Elizabeth Lee found out about her father's role in helping raise support for the campus revitalization project at Columbia University Medical Center, the first thing she did was run up to her room and come back downstairs with her bank, asking to make a donation.

Elizabeth's parents, James Lee'99 and Gretchen Crist'99, met while students at P&S, and Dr. Lee is assistant director of the new advanced simulation center, the centerpiece of the new Medical and Graduate Education Building that is the heart of the campus revitalization project. Ground is expected to be broken within the next year on the building: 100,000 square feet of state-of-the-art architecture and design that will give students and faculty a modern, unified home for living and learning.

The project will cost \$151 million and several contributions have already reduced that lofty goal by \$93 million. A transformational gift of \$50 million from Roy Vagelos'54, chair of the CUMC Board of Visitors and chair of the Defining the Future campaign, and his wife, Diana, launched the campaign with additional leadership gifts from Philip Milstein, a member of the CUMC Board of Visitors and vice chair of the Columbia University Board of Trustees, and his wife, Cheryl; Clyde Wu'56, former Columbia Trustee and currently a Board of Visitors member, and his wife, Helen; Karen Kennedy, a 1991 P&S graduate and also a member of the Board of Visitors, and her husband, Kevin; and an anonymous gift from a Board of Visitors member.

Elizabeth Lee's contribution to the effort is much smaller, but equally heartfelt. "She asked to make a donation of \$2, which is a lot for her," says Dr. Lee. "She was so excited to know it would go to help teach new doctors."

#### A State-of-the-Art Student Home

Dr. Vagelos came to Columbia when many of the buildings on today's storied campus, where much of the history of medicine and medical education has been made, were still somewhat new. "Naturally, over time some of them have aged, and new technologies and teaching resources are now required to provide the best modern education opportunities. It is important that the educational facilities for the doctors who will deliver medical care, the scientists who will perform groundbreaking scientific research, and the teachers who will help train the future generation of physicians and scientists are as exciting as medical science is today."

Located at 104 Haven Avenue between the two P&S residential towers, the 14-story education building will include high-tech classrooms and innovative learning facilities, a state-of-the-art two-story auditorium overlooking the George Washington Bridge, and plenty of warm, welcoming social spaces for students to study, relax, and connect with each other.

Architect Liz Diller of Diller Scofidio + Renfro, the MacArthur genius award winner who designed the High Line park on an elevated rail line on Manhattan's West Side and who recently completed the redesign of the Lincoln Center for the Performing Arts, has envisioned a space that takes maximum advantage of the area's breathtaking vantage point overlooking

# Gifts Large and Small Prepare for the Campus of the Future

the Hudson River, with plenty of green spaces and extraordinary views of the famous George Washington Bridge and the cliffs of the Palisades.

Perhaps the most striking feature of the building at first glance is the transparent walls with views in all directions. The conceptual drawings of the building show not only how the building will look, with a strikingly modern design that seems to bring exterior space indoors, but also how it will function.

The entire south side of the building will be the "study cascade," designed to foster social interaction. This network of spaces, located off the main stairwell, will give busy students and faculty comfortable places to pause, breathe, and connect. "The building will be less technical and more about social space," says Ms. Diller. "We're mixing up social space and learning space. It will really be a second home to these students."

"P&S has a long tradition of attracting students who combine the study of medicine with ambitious extracurricular activities through the uniquely Columbia P&S Club," says Lee Goldman, M.D., dean of the faculties of health sciences and medicine at the medical center and executive vice president for health and biomedical sciences at Columbia University. "This new building will provide a remarkable venue for this blend of formal and informal learning and development."



The new building has been shaped with the input of faculty and P&S medical and graduate students, a number of whom serve on the advisory group planning the project. "All of our schools are growing and developing and doing great things, and they need space for a million different activities and classes," says Hayley Born'14, a member of the Dean's Advisory Council and a student adviser to the building project. "The competition for space has been crazy. I'm so excited about space that will be reserved specifically for medical and graduate students."

Ms. Born also sees the new building as a forum to build bridges between medical and other graduate students at the medical center. "Dr. Vagelos has put a lot of importance on this," she says. "A new building that provides a central location for us to mingle, collaborate, participate in extracurriculars, and share resources will be great to bring us closer together."

"This is a really powerful effect of the architecture, where we have medical students, dental students, graduate students all coming together to feel like we're a part of the community," says Ph.D. student Kally Pan, also a member of the student advisory committee.

"Medicine is practiced in a team environment, so providing a space in which people come together, where they share ideas and learn from each other, is going to enhance the experience for our students," says Ron Drusin, M.D., vice dean for education.

#### Simulation Second to None

The centerpiece of the building is a simulation center that is poised to become the most advanced center of its kind in the nation. Four floors will be dedicated to the center, to be directed by Dennis Fowler, M.D., the Gerald and Janet Carrus Professor of Clinical Surgery. The center will allow students to immerse themselves in the world of medical practice before they interact with real patients. Residents, fellows, and faculty also will have access to the simulation center.

In many ways, the 13,000-square-foot simulation facility will feel like a hospital in miniature, featuring standardized patient exam rooms plus mock emergency rooms and surgical suites.

It will boast the most advanced equipment and software, designed to help students maximize their learning and performance in a controlled setting where they can receive immediate feedback. Here, students will hone clinical skills, including diagnosis and patient communication, while learning to be compassionate caregivers.

"The new center will dramatically improve what we are doing in patient simulation," says Dr. Fowler. "We have been as resourceful as we can in providing students with robust simulation experiences, but having a dedicated space will vastly improve the student simulation experience."

All rooms in the simulation center will feature video recording from several angles. "You can see someone do a procedure or take a history from multiple perspectives and hear it clearly. The clinical spaces will often have one-way mirrors so that a group of educators or students can observe what's going on in real time, and one person at a bank of video monitors can stand outside and observe what's going on in real time," says Deepu Gowda, M.D., assistant clinical professor of medicine and co-director of the "Foundations of Clinical Medicine" course for medical students.

Some simulated patient interviews now take place in non-clinical spaces, such as the library. "That's not quite the same environment," says





Ms. Born. "The new simulation rooms will look, feel, and smell the same as real exam rooms. If you don't pull out the footrest, for example, the actor will know."

#### Growing Green

As befits a campus of the 21st century, the Medical and Graduate Education Building has been designed to fit responsibly and sustainably into the surrounding community. Columbia has made an ambitious commitment to cut greenhouse gases and the new building promises to meet or exceed that pledge.

The University is planning the building to meet LEED-Gold standards, the Leadership in Energy and Environmental Design national design standard for green buildings and sustainability. The building's design will use passive radiant heating, involving solar water heaters, in interior and exterior gathering spaces and will respond to the changing seasons and time of day to maximize the use of light and preserve or eliminate heat naturally rather than artificially whenever possible. It will make optimum use of building materials that are local, sustainable, and recycled.

Students have been surprised and delighted by the addition of new green space to their community as well. "They are turning the space between Tower 2 and Tower 3 into a beautiful garden," says Samantha Shapiro'14. "We hadn't even thought about the potential uses of that lot, so we're very excited about being able to have Columbia events on the Washington Heights campus in this beautiful new landscaped space. The amazing view of the GW Bridge will be an added plus."

"The medical and graduate students have probably needed a building like this for at least a decade, but it has taken the leadership of Dr. Roy Vagelos and Dean Lee Goldman to get us to this point," says Mr. Milstein. "I think it will be transformative, something that everyone will appreciate for generations to come."

#### A New Front Door

The campus revitalization project also includes development of a new front door to the medical center through the P&S and William Black Medical Research buildings, allowing natural light in through an atrium

and mezzanine. Renovation of the P&S/Black auditorium will improve acoustics and sightlines and provide for digital connectivity.

Together, the new building and the Black and P&S renovations will renew and reinvigorate the medical center campus, where the education infrastructure has not undergone significant updates in more than 50 years. "We go to this venerable institution that's been here for years and years and has such a rich history, but you can get a little jealous of other schools with shiny brand-new facilities," notes Ms. Born.

Historic elements of the campus, such as the iconic P&S entrance on West 168th Street, will merge seamlessly with more modern ones, including a glass-enclosed promenade extending across the front of the Black Building.

The campus revitalization project also will benefit patients. "The medical center's new 'front door' will reassure patients, from the moment they set foot on campus, that they have arrived at a world-class institution and have chosen well by entrusting us with their care," says Dr. Goldman. "The new building provides upgraded education facilities that reflect the eminence of one of the top medical schools in the world. Both the building and the newly created green space that will surround it will also revitalize our campus in ways that will benefit both our medical center and the entire community."

"The physical aspects of the new building and the new auditorium will enable us to have a tangible link where students have a sense of a campus," says Mr. Milstein, chair of the capital planning committee of the Board of Visitors.

The education building's youngest supporter – 7-year-old Elizabeth Lee – has been invited to return in a few years to see how her piggy bank donation was put to use to give students that new sense of campus. And perhaps a few years beyond that, she will be one of those students who directly benefit in a way current students will not. Howard Park'13 has been a student adviser on the revitalization project even though he expects to graduate before the building opens in 2016. "The campus revitalization project is an incredible opportunity for the school," says Mr. Park. "The excitement that surrounds it comes from a place of need and, also, hope for the future." \*

For more information, visit www.educationbldg.cumc.columbia.edu

## Graduate School Life: 2012 in Review

#### By Richard Robinson, Ph.D. Associate Dean for Graduate Affairs

The Coordinated Biomedical Doctoral Programs encompass five program groups that together represent the breadth and depth of basic science research conducted within the College of Physicians & Surgeons. At the start of the 2011-2012 academic year, 351 students in these programs were working toward their Ph.D. degree, and by the end of the year 50 had completed their research and successfully defended dissertations.

Almost all Ph.D. graduates (80 percent) have embarked on postdoctoral research at an academic or research institution. Students in the M.D./Ph.D. program who completed their Ph.D. have returned to medical school studies to finish their M.D. degree.

During doctoral training, our students are supported by a variety of sources, including direct institutional support, research grants of mentors, and national training grants. The graduate programs continue to be highly successful in obtaining national training grants: Currently, 83 students are being supported by 16 NIH-funded training grants. An additional three students are funded through an HHMI training grant devoted to advancing translational biology. Our students also have been successful in obtaining support through individual fellowships from NIH, NSF, HHMI, and other sources (see list below).

Our programs continue to excel in attracting and recruiting the most outstanding graduate school candidates. For the fall 2012 incoming class we

Columbia Univ.

Award-winning Ph.D. graduates, from left, Jeremiah Osteen, Qiangfeng Cliff Zhang, and Pallav Kosuri with Richard Robinson, associate dean for graduate affairs.

received more than 1,100 applications, allowing us to be highly selective in those offered admission. We issued offers to 13 percent of applicants, and 43 percent of these accepted our offers, resulting in an incoming class of 60.

The Office of Graduate Affairs has continued its aggressive recruiting efforts among minority populations. A record 17 percent of the incoming class in 2012 is from groups historically underrepresented in the sciences. Each year we send faculty and student representatives to several national meetings that are forums for minority education. In keeping with the NIH mandate to extend diversity initiatives to the disabled population, this past year we also established a relationship with the National Technical Institute for the Deaf - Rochester Institute of Technology. As a result, the first undergraduate from that program is working in a CUMC laboratory during the summer of 2012.

#### Awards, fellowships, and honors received by graduate students during the 2011-2012 year:

(student name in italics; mentors noted by parentheses)

Dean's Award for Excellence in Research: Jeremiah D. Osteen, "Characterization of Cardiac IKs Channel Gating Using Voltage Clamp Fluorometry" (Robert Kass); Qiangfeng Cliff Zhang, "Towards the Integration of Structural and Systems Biology: Structure-based Studies of Protein-protein Interactions on a Genome-wide Scale" (Barry Honig)

Titus M. Coan Prize for Excellence in Research in Basic Cell & Molecular Biology: Pallav Kosuri, "Methods for Detection of Single Biochemical Reactions and Applications to Protein Thiol Chemistry" (Julio Fernandez)

Titus M. Coan Prize for Excellence in Research in Translational Biology: Dara L. Sosulski, "Wired for Smell: Structure and Function in the Mouse Olfactory System" (Richard Axel)

#### Integrated Program in Cellular, Molecular and Biomedical Stud-

ies: El-ad David Amir, HHMI International Student Research Fellowship, "Mapping Development through Mass Cytometry" (Dana Pe'er); Joshua Levine, NIH-NIDDK Fellowship, "Nkx2.2 In Pancreatic Development: The Role of the NK2-SD Domain" (Lori Sussel); Vanessa Hill, NSF Graduate Research Fellowship Honorable Mention, "Mitochondrial Motility, Fusion, Anchorage, and Mitophagy: A Mitochondrial Quality Control System in Budding Yeast"; Chandler Walker, NSF Graduate Research Fellowship Honorable Mention, "p53 SUMOylation and NEDDylation Regulation of LTD via Bax/Bad Cascade in Hippocampal Neurons and Astrocytes"

Program in Neurobiology and Behavior: Scott Bolkan, NSF Graduate Research Fellowship Award, "The Role of Mediodorsal Thalamic Activity on the Development of Prefrontal Cortex Circuitry" (Joshua Gordon/Christoph Kellendonk); Ana Calabrese, HHMI International Student Research Fellowship, "The Structure and Dynamics of Functional Interactions in Neuronal Populations and Implications for Optimal Cod-



ing" (Sarah Woolley/Liam Paninski); Nalini Colaco, Dean's Day Award for Research, "Specific Connectivity and Molecular Diversity of Mouse Rubrospinal Neurons" (Christopher Henderson); Heather El-Amamy, NIH-NIMH Fellowship, "Developmental Role of Neuregulin-1 in Subventricular Zone Stem Cell Fate" (Jay Gingrich); Zvi Fishman, NSF Graduate Research Fellowship Award, "Could the Superior Colliculus Be Directly Involved in Visual Awareness?"; Leora Fox, NSF Graduate Research Fellowship Award, "Investigating a Role for Macroautophagy in Clearance of Nuclear Protein" (Ai Yamamoto); Bethany Johnson-Kerner, NIH-NINDS Fellowship, "Dysfunction of Neurofilaments in Disease: An iPS Model of Giant Axonal Neuropathy," and the Dean's Day Award for Research, "Mapping Biochemical Pathways Underlying the Pathology of Giant Axonal Neuropathy Using iPS Cells" (Christopher Henderson); Derek Oakley, the Brunie Prize in Neural Stem Cell Research (Christopher Henderson); Ali Raza, NSF Graduate Research Fellowship Award, "Computational Modeling of Intraretinal Axon Guidance with Physiological Bounds" (Donald Hood); Timothy Requarth, NIH-NINDS Fellowship, "Neural Mechanisms for Sensory Prediction in a Cerebellum-like Structure" (Nathaniel Sawtell); Priyamvada Rajasethupathy, Kavli Graduate Thesis Award, "Novel Small-RNA Mediated Gene-Regulatory Mechanisms for Long-Term Memory," and the Harold M. Weintraub Graduate Student Award (Eric Kandel); Martin Vignovich, NSF Graduate Research Fellowship Honorable Mention, "Tuning in Taste: How Inhibition Shapes Perception" (Charles Zuker) Programs in Basic Cell and Molecular Biology: Elena Abarinov, NSF Graduate Research Award, "Decisions, Decisions: Role of Nkx2.2 Domains in CNS Cell-fate Specification" (Lori Sussel); Bridget Huang, NSF Graduate Research Award, "Characterizing the Dynamics of Translation Termination Using Single-Molecule Fluorescence Resonance Energy Transfer (smFRET)" (Ruben Gonzalez); Angela Pring-Mill, NSF Graduate Research Fellowship Honorable Mention, "Groucho-mediated Repression in Pancreatic Differentiation"; Carmen Taveras, Jonas E. Salk Scholarship CUNY; Christal Vitiello, Richard C. Parker Graduate Student Award (Max Gottesman)

Programs in Molecular Basis of Health and Disease: Douglas Barrows, Brian F. Hoffman Award for Academic Excellence (Ramon Parsons); Roxanne Dutia, First Place in Poster Competition, New York Academy of Sciences and PepsiCo Journey through Science Day, "Melanocortin Regulation of Energy Balance and Metabolism" (Sharon Wardlaw); Celia Keim, Richard C. Parker Graduate Student Award (Uttiya Basu); Gregory Minevich, NIH-NINDS Fellowship, "Identifying Genes That Turn Skin Cells Into Neurons" (Oliver Hobert); Kyrie Pappas, NSF Graduate Research Fellowship Honorable Mention, "Investigating the Molecular Mechanism of Downregulation of PTEN in Human Cells" (Ramon Parsons); Lindsay Tannenholz, Brian F. Hoffman Award for Outstanding Service (Rene Hen)

# **Alumni Profiles in Giving**

P&S alumni are among the most committed and generous graduates of any major medical school in the country. During 2011-2012 alumni contributed a total of \$3.9 million, with gifts from anniversary classes up significantly over last year. These gifts demonstrate the ongoing commitment of alumni who exceeded the original capital campaign goal and have now contributed more than \$100 million to the campaign.

Every group has its leaders, individuals whose exceptional philanthropy stands out, and their generosity is worth saluting. The following describes a few people whose recent gifts have made a major difference.



#### Diana and P. Roy Vagelos'54

Diana and P. Roy Vagelos'54 have long been mainstays of support for P&S. In 2010 they made philanthropic history by donating \$50 million toward the new Medical and Graduate Education Building. Their gift is the largest received during Columbia University Medical Center's capital campaign, Defining the Future, which Dr. Vagelos chairs. Dr. Vagelos also initiated a successful matching gift scholarship fund. Retired president and CEO of Merck & Co., a company he helped lead to record success in drug discovery, and current chairman of the board of Regeneron Pharmaceuticals Inc., Dr. Vagelos and his wife exemplify continuing support of academic excellence and the quality of life and learning at P&S.



#### Judith P. Sulzberger'49

A visionary physician-philanthropist who applied her medical knowledge to advance medical research at P&S, Judith P. Sulzberger'49, who died of pancreatic cancer Feb. 21, 2011, was best known at P&S as the driving force behind the creation of the Columbia Genome Center that bears her name. She topped off her giving with a \$20 million bequest that includes generous provisions to support several endowed professorships and a scholarship fund.



#### Helen and Clyde Y.C. Wu'56

In addition to establishing a fifth endowed professorship at P&S, Columbia University Trustee Emeritus Clyde Y.C. Wu'56, the longest serving P&S trustee, and his wife, Helen, made a commitment of \$10 million for the new education building, the centerpiece of the medical center's campus revitalization program. The Wus previously committed \$10 million to a molecular cardiology center and \$5 million toward the recruitment of the dean. Their wide-ranging support of P&S also has included the funding of scholarships, loan funds, research in osteoporosis, a historic educational exchange program with major academic institutions in China, the Wu Music Room in Bard Hall, and restoration of a piano once used by virtuoso composer and pianist Sergei Rachmaninoff.



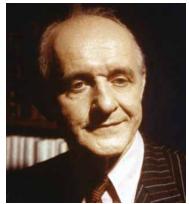
#### Thomas P. Sculco'69

With a recent commitment of \$500,000, orthopedic surgeon Thomas P. Sculco'69 built up his named P&S scholarship fund to \$1.5 million. Dr. Sculco, professor and chair of the Department of Orthopedic Surgery at Weill Cornell Medical College and surgeonin-chief at the Hospital for Special Surgery, is an internationally recognized expert in joint replacement surgery of the hip and knee. Through a family foundation, he and his wife, Cynthia, have made medical school financial aid one of their top philanthropic priorities.



#### Marc D. Grodman'77

The Pam and Marc Grodman'77 Dual Degree Fund is a philanthropic trailblazer at P&S. Intended to support student programs, including lectures and seminars, for students interested in exploring interdisciplinary career options, the fund is a first step toward creating a home for dual degree students. The first part of this new program concentrates on the MD/MBA program at P&S and the Columbia Graduate School of Business, Dr. Grodman is the founder, chairman of the board, president, and CEO of Bio-Reference Laboratories, the largest independent regional clinical facility of its kind in the Northeast and the fourth largest clinical laboratory in the country.



#### Madge and Paul J. Bilka'43D

"Education has to be the salvation of our society," reflects retired rheumatologist and American College of Rheumatology Master Paul J. Bilka'43D. Giving to scholarships, he says, "isn't so much a duty, in the sense of an onerous task, as rather a strong heartfelt desire to play a part and do what I can to help." The charitable gift annuities and charitable remainder annuity trust he set up to endow the Paul J. and Madge M. Bilka Scholarship Fund at P&S, as a testament to his commitment and in memory of his late wife, have surpassed \$1 million. Dr. Bilka has contributed to P&S every year since 1966.

#### P&S Alumni Legacy Challenge Attracts Nearly \$20 Million

The P&S Alumni Legacy Challenge that came to a close on Dec. 31, 2011, brought in planned gifts totaling \$14.6 million and matching funds of \$4.8 million from an anonymous group of P&S alumni. Numerous alumni took advantage of this unique opportunity to create a medical legacy in their lifetime.

Notable among these benefactors is Ephraim Engleman'37, a pioneering rheumatologist who at age 101 still strokes the strings of his Stradivarius violin and advises selected patients. Dr. Engleman has made a generous provision in his will for a scholarship in his name at P&S.

Family bonds and debts of gratitude run deep for Shearwood J. McClelland'74, director of orthopedic surgery at Harlem Hospital, and his wife, Yvonne Thornton'73, former vice chair of obstetrics & gynecology at Jamaica Hospital Medical Center, former professor of clinical obstetrics & gynecology at Weill Cornell Medical College, and author of a bestselling memoir. Dr. McClelland paid tribute to his mother, the late Zenobia Pruitt McClelland, with a bequest agreement to support a scholarship in her name. And Dr. Thornton honored in like manner the memory of her parents, Donald E. and Itasker F. Thornton.

In a letter accompanying her pledge to P&S, Muriel Kowlessar'51, a retired pediatrician and professor emeritus of pediatrics at the Medical College of Pennsylvania, paid tribute to the late Dr. Aura E. Severinghaus, former dean of admissions, whom she called "a pioneer in recruiting members of underrepresented minorities. I will forever be grateful to him and to P&S." Dr. Kowlessar has left a bequest to fund a scholarship in her name.

Radiation oncologist Karen Fu'67 honored her late mother, Lien-Sun Ho, who had a profound influence on her, with a sizable bequest assigned to a scholarship in her mother's name, thereby extending that influence to benefit future generations of students.

Other alumni who signed generous bequest agreements in support of named scholarship funds: Lyndon M. King Jr.'43, Ralph N. Wharton'57, John R. Johnson'60, William H. Fleming'61, Lucy Waskell'67, Brooke Milton Barton'79, Ellise Delphin-Rose'75 and Eric A. Rose'75, and Jerry I. Gliklich'75 and Jane E. Salmon'78.

#### Alumni Estates and Bequests, 2012

A few of the P&S alumni beguests:

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The late Mrs. Cora Marks, widow of the late Jerome Marks'25, a distinguished gastroenterologist who taught on the faculty of NYU medical school, has bequeathed more than \$1 million to P&S. Dr. Marks was a former president of the New York Gastroenterological Association and the New York Academy of Gastroenterology.

"We were the group," said the late **Helen Ranney'47**, "who were there in medicine when medicine became a science." A pioneering hematologist, she was the first woman in the United States to be named to chair a department of medicine. In her will Dr. Ranney included a vote of confidence for the scientific enterprise at P&S, bequeathing a sizable sum to be used at the dean's discretion.

The late Samuel Dvoskin'45 M.D., Ph.D., a retired internist and avid botanist, left more than \$3 million toward a scholarship fund, the Samuel Dvoskin, M.D.'45 and Leila Dvoskin Endowed Scholarship Fund, in memory of his wife, Leila. "My wife and I both felt an obligation to return to society what society had given us," he once said. "Here was a poor boy born with nothing who ended up studying medicine at one of America's finest schools. I'll never forget the privilege P&S gave me. What a wonderful profession medicine is. You can not only learn the secrets of life, but also help people in the process."

## About P&S

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# FACTS & STATISTICS, FY 12

MEDICAL SCHOOL ENROLLMENT			APPLICATIONS (ENTERING CLASS 2011)		
Total medical school enrollment			Number of applicants		6,907
Total enrollment of underrepresented minorities			Number of applications considered		
Total enrollment of minorities			Number of applicants interviewed		
Total enrollment of international/non-resident27			Number of acceptance letters issued304		
Total enrollment of in-state residents			Number of new entrants	169	
Total enrollment of men		343	Bassett Program applications		698
Total enrollment of women		320	Number of new entrants		10
ENROLLMENT BY YEAR			FACULTY DURING 2011-2012 ACADEMIC YEAR		
	MALE	FEMALE		FULL TIME	PART TIME
First-Year Class	85	84	Number of faculty in basic sciences	211	64
Second-Year Class	85	81	Number of faculty in clinical program	1,600	2,597
Third-Year Class	85	81	Total medical school faculty	1,811	2,661
Fourth-Year Class	88	74			
Total Enrollment	343	320	FACULTY HONORS		
			Nobel Prize in Medicine2		
DEGREES GRANTED, JULY 2011 TO JUNE 2012			National Academy of Sciences		
M.D		Institute of Medicine of the National Academy of Sciences 30			
Ph.D		44	Howard Hughes Medical Institute		13
Doctor of physical therapy		53			
M.S. in occupational therapy		48	FINANCIALS		
Certificate in psychoanalysis		5	Budget (FY 2012)		\$1.4 billion
			Endowment		\$1.5 billion
ETHNIC BREAKDOWN			Endowed chairs/professorships		
Non-resident aliens		26	Research support (FY 2011)		\$440 million
Hispanic/Latino51			NIH research support (FY 2011)\$316 million		
Black or African American, non-Hispanic/Latino					
White, non-Hispanic/Latino363					
American Indian or Alaskan Native, non-Hispanic/Latino1					
Asian, non-Hispanic/Latino114					

Two or more races, non-Hispanic/Latino......21  College of Physicians and Surgeons

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# Tales of Two Life-Sustaining Organs

Patricia Kingsbury, who lived in an apartment for three years but had never walked on the building's sidewalks because of illness, can now walk, go grocery shopping, and help her neighbors. Stephen Davis, who last winter was a couch potato hooked up to oxygen, spent the spring making plans to go waterskiing. Both are alive because of clinical innovations pioneered by P&S doctors.



# Physician Memoir, End-of-Life Care, and Pitching Injuries

Jeff Grantham played shortstop on his college baseball team. After starting medical school, he met New York Yankees team physician Christopher Ahmad, a Columbia orthopedic surgeon, and was inspired to channel his love for baseball into his scholarly project. The new requirement in the P&S curriculum allows students to explore their passions in depth.

## Getting Personal With Stem Cells

Type 1 diabetes is a form of the disease in which the patient's immune system recognizes its insulin-producing beta cells as the enemy. Stem cell research at Columbia may shed light on why the cells are recognized as foreign while at the same time identify ways to modify the cells to overcome immune rejections.

