Columbia Launches Stem Cell Initiative

NEW RESOURCES FOR RESEARCHERS; NEW DIRECTION FOR REHABILITATION MEDICINE

It’s not every day that a discovery made by tissue engineers working to improve dental implants piques the interest of diabetes researchers, but it happened at a Columbia stem cell symposium held earlier this year.

It’s the type of interaction that the new Stem Cell Initiative at CUMC is designed to encourage, says the Initiative’s interim director, James Goldman, MD, PhD, professor of pathology and cell biology. “There are common themes shared among different types of stem cells, so advances made in one cellular or tissue system can help investigators working in other systems,” Dr. Goldman says. “We already have more than 70 stem cell labs, representing virtually every organ system in the body and a multitude of different diseases, so having an organization that ensures rapid communication of advances is critical to make the research more efficient and productive.”

The Initiative, announced in November, will increase resources and attention on fundamental and translational stem cell research at CUMC, seeking to promote interactions among many different scientists and departments. Several new scientists are expected to be recruited over the next 18 months. Two of these scientists will be recruited to new endowed professorships in the Department of Rehabilitation Medicine, soon to be renamed the Department of Rehabilitation and Regenerative Medicine, pending University Senate and Trustees approval.

Joel Stein, MD, the new chair of rehabilitation medicine, who will oversee these new recruitments, says the new researchers and name change reflect the department’s new mission. “From a conceptual perspective, rehabilitation medicine is about restoring function,” Dr. Stein says. “The challenge is that existing treatments only take us so far. We can partially improve patient abilities, but the outcomes are not what we want them to be. If there is a way to utilize one’s own stem cells, or to add new stem cells, to repair damage, there’s...
Renewing Our Commitment

A new year brings a new opportunity to renew our commitment to excellence in education and research. The past year has been filled with numerous achievements that have solidified our position as a leading institution in our field.

**Teaching**

We are proud to announce the recipients of the 2009 Presidential Awards for Outstanding Teaching. These awards recognize the exceptional contributions of our faculty members in the classroom and beyond.

- **Awards for Outstanding Teaching**
  - Three awards will be presented to graduate students.
  - Nominations should include a detailed description of the candidate's teaching accomplishments.

**Recruitments**

We have been actively recruiting new faculty members to fill department chairs from universities around the country as well as from within our ranks. We are committed to attracting top talent to our institution.

**New academic programs and initiatives**

- **New Ph.D. degree in Nursing**
- **New academic program in Climate and Health**
- **Dental Education Track**

**Research**

- **New faculty discoveries**
- **New research breakthroughs**

**In Memoriam**

We mourn the recent passing of three outstanding leaders: Robert Weiss, MD, Robert Weiss, MD, and Bernard Weinstein, MD, DSci (Hon).

- **Dr. Bob Weiss**
- **Dr. Robert Weiss**

**Correction**

The number published in the Oct 2008 issue was incorrect. The number published in the Oct 2009 issue is 722-326-8889.
The Department of Medicine aspires to preeminence and national leadership in... Department during my comparatively brief... lessons taught to me by previous chairs... enterprise. In terms of change, I envision... insights into the wider... the broadest possible range of self-overlapping... P&S and to each other....... by reports that it may... not just prevent its loss... and sleep, also controls... bone. After age 20, the balance... of its size and scope, the obligation... for patients... the body's serotonin is produced. It... to provide leadership as we face the chal...ued their talents... clinical medicine, biomedical research, and... me that the role of this officer is to serve... in NIH funding, and an aggregate budget... to provide leadership as we face the chal...... than a calcified bone... fragility and risk... even maxillofacial transplantation... by NIH... is produced. It was... and national leadership in... are the leading causes of death... thus, there is a need... with severe osteoporosis... bone formation and bone... and a hundred enthusiastic allies in the depart-... that serotonin is produced in the gut, and... for osteoporosis, Dr. Karsenty says he has new respect for the... to identify new structures that encourage cooperation... the fact that serotonin is produced in the gut... and innovative research efforts... such as... far from being inert, bone constantly undergoes... into removing old material and... bone, but because of reports that it may... include bone cancer, it is restricted for short-term use in women... bone growth that released from the gut, according to a new discovery by CUMC scientists. The discovery will likely stun researchers in the field, who have thought for years that the skeleton itself controls bone mass. Instead, the new research found that serotonin released by the gut tells cells in the skeleton to slow production of new bone. The new insight could transform how osteoporosis is treated by giving doctors a way to increase bone mass, not just slow its loss. The findings were reported by Gerard Karsenty, MD, PhD, chair of genetics and de-... osteoporosis in mice. The treatment had no effect on the brain's serotonin. "The brain's serotonin and the gut's serotonin are separated by a barrier more hermetic than the Berlin wall was," Dr. Karsenty says. "They do not talk to each other." Like most other bone researchers, Dr. Karsenty and his lab were searching for new ways to build bone by trying to under-... bone formation because some mutations in the... that it may increase the risk of bone cancer, it is restricted for short-term use in women with severe osteoporosis. "The lack of safe bone-promoting drugs is a major concern because osteoporosis is often diagnosed when the damage to bone is already significant and fracture risk is already too high," Dr. Karsenty says. "We need something to build bone, not just prevent its loss." Shutting off the intestine's serotonin production could be an effective way to increase bone formation, and, indeed, the team was able to use this strategy to pre-... with various clinical and research programs, and divisions. Clinical programs of great strength such as cardiology and organ transplantation are poised for great strides as we build research programs to complement them. In the weeks and months ahead I will elaborate on the research areas for recruit-... postdoctoral fellowships and other research and educational initiatives for implemen-... and medical education – is essential. While our national reputation will hinge largely on our research, clinical medicine is our reason for being, and medical education provides the pipeline of interns, residents, fellows and junior facul-...ty who are our future. What have you learned from past P&S Medicine chairs, and how will that affect how you do your job? The lessons taught to me by previous chairs include prominence among them the notion that the role of this office is to serve... to collaborate with other programs, and divisions. The Department of Medicine is the largest department and interacts pervasively with... are gifted, enthusiastic, and committed to... annual meeting of the American Medical Association in June. He was also on the advisory commit-...e special role for the Department of Medicine in CUMC at large? What is that role, and how do you see this changing during your leadership? The Department of Medicine is the largest department and interacts pervasively with... costs to our medical school to our students... are the leading causes of death... the task is to rid... the top 10 and many in the top 5. The Department has the opportunity, and, by virtue of its size and scope, the obligation to provide leadership as we face the chal-...concentration of medical centers in the United States... of the medical school you graduated from? It does feel a bit strange to have almost continuous recollections of the institution going all the way back to my medical school interview with Dr. Andrew Franza and the fourth-year research I did with Dr. Quis Al-Awqati. The office that I now occupu-...cated from? the P&S class of '83 and I would surely be humbled were I among our students today. I have been on the P&S Committee on Admissions for 16 years and the intellectual quality of our students has only risen over time with no decrement in their scope of interests or concern for humanity. Perennially, the students of P&S are gifted, enthusiastic, and committed to P&S and to each other.
Stem Cells Find Niche in Brain

When Fiona Doetsch, PhD, peers at brain stem cells through a microscope, it’s always magical. “There’s something amazing about seeing unexpected patterns of glowing cells deep inside the brain that reveal insights into how the brain works,” says Dr. Doetsch, assistant professor of pathology and cell biology, neurology, and neuroscience.

That stem cells even exist in the brain is a recent revelation. For a long time scientists believed that people were born with a finite number of neurons in the brain that died off over time. But about 10 years ago, a new era in neuroscience began when scientists discovered that two parts of the brain, the hippocampal formation and the subventricular zone (SVZ), continue to generate neurons throughout life.

“The discovery of these new neurons was fascinating. If neurons are born throughout life, then there should be stem cells creating these new neurons,” Dr. Doetsch says. “And if these stem cells can be precisely targeted in vivo, it may be possible to direct them to make new replacements for people who have lost brain cells, as in stroke, Parkinson’s disease, multiple sclerosis, or other neurodegenerative diseases.”

But first the stem cells had to be identified. The brain has both neurons and glial cells, and scientists initially thought that there were progenitor cells restricted to creating neurons and different progenitors restricted to producing glia. “Surprisingly, we discovered that the stem cells that produce new neurons in the adult brain are actually glial cells called astrocytes,” she says. “That astrocytes give rise to neurons revealed an unexpected role for glia, which had long been considered simply support cells in the brain.”

Neural stem cells are special, but so is the brain region in which they reside. Astrocytes are spread throughout the brain, but new neurons are generated only in the SVZ and hippocampus. Are astrocytes in other parts of the brain prevented from generating neurons because they are in a different environment? Or are neural stem cells special types of astrocytes? Dr. Doetsch’s findings suggest the environment plays a big part. Her team recently found that the SVZ’s vasculature is a key component controlling the lives of stem cells. Stem cells are often found in direct contact with blood vessels at specialized sites and divide most frequently at these sites. Combined with an unusual blood brain barrier the team discovered in these regions, Dr. Doetsch speculates that the arrangement may make the stem cells more accessible to drugs and facilitate the stimulation of the brain’s own stem cells for repair.

“In the past decade we have learned that the brain has an unexpected ability to change and respond dynamically to its environment,” Dr. Doetsch says. “That gives me hope that we will soon have a new understanding of brain function and, eventually, new treatments.”

Stem Cell Exploration: Scientists

In a search for clinical treatments that will defeat the advancement of many chronic and untreated diseases, scientists at Columbia are actively investigating embryonic stem cells and adult stem cells from nearly every organ in the body. The three researchers profiled provide pre- and postdoctoral research stipends. Several groups are pursuing translational research, with the goal of using stem or progenitor cells to intervene in pathological conditions.

Dr. Goldman and Stein say that now is a good time to begin the Initiative, since President-elect Barack Obama promised to lift President Bush’s restrictions on human embryonic stem cell research. Funding is also now available from the Empire State Stem Cell Trust Fund, which will provide up to $600 million over 11 years for stem cell research in New York. The fund has already delivered more than $1 million to CUMC for stem cell research in the past year.

Starting an initiative now also makes
Cardiologists also are investigating the use of stem cells for other cardiovascular diseases, including myocardial infarction (which often leads to heart failure) and refractory angina. “Patients with the last condition have advanced coronary disease but without having sustained serious heart attacks or developed heart failure. Their burden is quite different: chronic chest pain that limits the simple, daily activities and impacts the quality of their lives. Most have undergone numerous stent procedures and bypass surgeries without lasting relief and have only medications to allay their symptoms,” Dr. Sherman explains.

Dr. Sherman is optimistic that stem cell therapies will help such patients soon. “What we are seeing now is a remarkable expansion of scientific investigation in the field, at every level, with so much of it centered here at Columbia. It has taken many decades for cardiovascular disease to achieve the unfortunate distinction of being the nation’s No. 1 cause of suffering and death. It has taken scientists less than one decade to demonstrate the positive potential of stem cells. If we continue along the path of careful, collaborative research, it would not be extreme to suggest that the first approved stem cell-based therapy will be available to patients with cardiac disease in two to five years. When taken in perspective, it’s quite an extraordinary timeline.”

A second recent advance – the transformation of a patient’s skin cells into embryonic-like stem cells, accomplished by a team of Harvard and Columbia researchers – has huge potential to help researchers understand the genesis of complex disease like ALS and develop better treatments. “This use of stem cells may, in fact, have just as big a clinical impact on treatment as the use of stem cells for regeneration,” Dr. Goldman says.

The news media’s coverage of the potential of stem cells for regeneration has, unfortunately, given the impression that cures will come next week, adds Dr. Stein. “That’s not feasible, but the field is clearly moving forward. The potential in the long term is great.”

“Investigate Brain, Heart, Skin below – who study stems cells in the brain, heart and skin – represent just a few of the scientists in more than 70 labs at Columbia whose research has the potential to revolutionize the practice of medicine.”

---All stories by Pat Olsen

“Our hope is that identifying genes unique to these stem cells will lead to new treatments for skin diseases, cancer, or wound repair.”

DAVID OWENS

Photo: Derrick Biskos

Stem cells in the skin’s hair follicles, recently discovered by David Owens, may give rise to certain types of skin cancer or new ways to treat skin diseases. (photo courtesy of David Owens)
Columbia University awarded the 2008 Louis Gross Horwitz Prize to Ulrich Hartl, MD, and Arthur Horwich, MD, for work that helped elucidate how proteins fold into their final shapes and how mistakes in folding can lead to diseases such as Alzheimer’s. Before their breakthrough, it was thought that proteins, which initially resemble a line of beads on a string, spontaneously fold themselves into their final three-dimensional structures. Drs. Hartl and Horwich discovered, however, that proteins need assistance to ensure they fold into the proper shape. When the protein-folding pathway is imperfect, the researchers discovered, proteins can accumulate in cells and lead to disease.

The Horwitz prize was established by Columbia University in 1967 to recognize outstanding contributions to basic research in the fields of biology and biochemistry. Dr. Hartl, professor and director of biochemistry at the Max Planck Institute of Biochemistry in Germany, and Dr. Horwich, the Eugene Higgins Professor of Genetics, professor of pediatrics, and Howard Hughes Medical Institute investigator at Yale, received their prizes at a dinner in November.

An honorary 2008 Horwitz Prize was awarded posthumously to Rosalind Franklin, PhD, for her seminal contributions to the discovery of the structure of DNA. Using X-ray crystallography, Dr. Franklin obtained the data that Nobel laureates James Watson and Francis Crick used to develop the double helix model of DNA. Physiology chair Andrew Marks, MD, a member of the selection committee, said: “Rosalind Franklin’s scientific contributions were achieved despite social barriers, many of which persist to this day. In awarding the prize to Dr. Franklin we say to the world that the doors of science are open to those committed to a life of discovery, regardless of gender, color, religion or nationality, and that in this time and place, it is the force of one’s ideas that matter.”

Trio of Cardiologists Wins Katz Prizes

Columbia awarded the 2008 Katz Prizes in Cardiovascular Research to the research team of Christine E. Seidman, MD, and Jonathan G. Seidman, PhD, of Harvard University. The young investigator award went to Andrew J. Einstein, MD, PhD, assistant professor of clinical medicine in P&S.

The Seidman team has detected the genetic causes of many heart diseases, including hypertrophic cardiomyopathy. Their discovery has enabled early and accurate gene-based diagnosis of the disease and the identification of individuals at risk for sudden death.

Dr. Einstein was recognized for his advances in the area of cardiac imaging research. His work on the estimation of cancer risks from cardiac CT imaging procedures led to findings that women and younger patients have a greater lifetime risk of cancer associated with radiation exposure from the scans. Dr. Einstein now is researching strategies to minimize the risk.

The Katz Prizes were established in 2006 by Lewis Katz, entrepreneur and philanthropist, to recognize outstanding contributions in cardiovascular research by senior scientists and young investigators working on pertinent questions related to cardiovascular health.

New AAAS Fellows Elected

The American Association for the Advancement of Science (AAAS) has awarded the distinction of Fellow to five P&S faculty members: LAURENCE F. ABBOTT, PHD, the William Bloor Professor of Theoretical Neuroscience, professor of physiology & cellular biology, and co-director of the Center for Theoretical Neuroscience; GERALD FISCHBACH, MD, the John E. Borne Professor of Medical and Surgical Research; MICHAEL E. GOLDBERG, MD, the David Mahoney Professor of Brain & Behavior, Neurosciences, Neurology, Psychiatry and Ophthalmology, and director, Mahoney-Keck Center for Brain and Behavior Research; RODNEY ROTHSTEIN, PHD, professor of genetics & development; and HOWARD A. SHUMAN, PHD, professor of microbiology.

Gene Linked to Cognitive Deficits in Down Syndrome

A single gene on chromosome 21 may be implicated in some of the learning and cognitive disabilities characteristic of Down syndrome, Columbia researchers have found. The finding raises the prospects that a drug targeting the gene could improve memory abilities.

The idea of treating Down-related mental retardation with therapeutics has been all but considered impossible until recently. Down was considered too complex to treat because it is caused by an extra, third copy of chromosome 21, and numerous genes on the chromosome were believed to contribute to the disorder. Recent research, however, has suggested that learning and cognitive disabilities in Down syndrome may stem from only one handful of genes.

The new study, led by Gilbert Di Paolo, PhD, assistant professor of pathology, shows that one gene in particular – SYNU1 – causes subtle biochemical changes in the brain’s neurons and learning deficits in mice with three copies of the gene.

“We’ve now come to a point where therapeutics for Down are seriously discussed at scientific conferences,” Dr. Di Paolo says. “That’s a huge change from the past and an encouraging sign for the future.”

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Funders include NIH, Foundation Jerome Lejeune, National Down Syndrome Society, and the McIntosh Foundation.

Cardiac Stents Impeded by Leptin

Clogged stents are twice as common in diabetic patients as in the general population, and a hormone released from fat, called leptin, may be partly responsible, according to new research led by Andrew Marks, MD, chair of physiology & cellular biology and Clyde and Helen Wu Professor of Molecular Cardiology, and Steven Marx, MD, associate professor of medicine and pharmacology.

The study found that leptin – at the elevated concentrations frequently found in patients with diabetes – stimulates the growth of cells responsible for clogging the stents, even in the presence of sirolimus, a drug used in many stents to prevent cell growth.

The same mouse study also identified a drug that counters the effect of leptin on cell growth. If added to current drug-eluting stents, such a drug may further reduce redocking rates in patients with diabetes to the single digit rates seen in other patients.

About 250,000 Americans with diabetes receive drug-eluting stents every year. An improved stent would significantly reduce reclogging rates in patients with diabetes to the single digit rates seen in other patients.

The research was supported by the NIH and the American Heart Association.

Single Protein Can Initiate Stomach Cancer

A single inflammatory protein is enough to trigger the development of stomach cancer, a finding that shows inflammation has a more leading role in cancer formation than previously believed.

“For many years, inflammation was considered to promote the growth of tumors that already existed,” says the study’s senior author, Timothy Wang, MD, chief of digestive and liver diseases and Dorothy L. and Daniel H. Silberberg Professor of Medicine. “But now we show that inflammation alone can initiate stomach cancer and that just one inflammatory molecule is sufficient.”

The study shows that excess amounts of an immune system protein called interleukin-1 beta (IL-1B) – when present in the stomachs of mice – can start the inflammatory processes that ultimately lead to stomach cancer. IL-1B, or the inflammatory cells it recruits, has more leading role in cancer formation than previously believed.

The study was supported by the NIH.
Sixty Years Later, Genome Retains Sign of Famine

Dutch men and women conceived during the Dutch Hunger Winter of 1944-1945 still bear an imprint on their genomes of their mother’s undernourishment, according to a team of researchers from the Mailman School of Public Health and Leiden University in the Netherlands.

The marks may explain how famine during pregnancy could be linked to diseases like cardiovascular and neuropsychiatric disorders that develop decades later in adulthood, says one of the study’s senior authors, L.H. Lumey, MD, PhD, associate professor of clinical epidemiology.

The idea that many adult diseases have roots in the prenatal environment has become increasingly widespread in the last 10 to 15 years. Studies in animals have shown that health in adulthood can be influenced by marks acquired by the genome before birth, and that these marks are related to the mother’s nutrition.

The Dutch Hunger Winter, caused by a German embargo imposed on the Netherlands during World War II, provided the researchers with a unique natural experiment to see if such changes also occur in the human genome in response to the prenatal environment.

Dr. Lumey and his colleagues found that the genomes of 60-year-old men and women who were conceived during the famine had fewer marks on a gene called IGF2 than their unexposed siblings. Such “epigenetic” alterations do not mutate a gene’s DNA but can cause life-long changes in the activity of certain genes by adding or subtracting chemical compounds to the DNA strand.

It is the first time that environmental conditions during early development have been found to cause life-long epigenetic changes to the human genome.

Because IGF2 plays a major role in growth, the researchers speculate that the epigenetic changes may have altered the activity of IGF2, leading to an adult metabolism more suited for a time of starvation than for the time of abundance following the end of World War II. The epigenetic changes to IGF2 also may play a role in schizophrenia, which was first linked to prenatal famine exposure by Ezra Susser, MD, DrPH, professor of epidemiology and psychiatry and a co-author of the current study. “Epigenetic changes to IGF2 have been recently hypothesized to contribute to schizophrenia,” Dr. Susser says, “and these new findings provide another piece of evidence to bolster that hypothesis.”

Dr. Lumey and his colleagues are now examining the relationship between changes in IGF2 activity and adult health. “That’s the missing link. If we make that connection, then we’ll have a mechanism that links famine exposure to adult health,” Dr. Lumey says. “And ultimately that may suggest new ways to prevent human disease.”

The study was supported by the NIH, Netherlands Heart Foundation, Netherlands Organization for Scientific Research, and the European Union.

Applications to the School of Nursing’s accelerated Entry to Practice (ETP) program have risen 50 percent over last year, the biggest increase in applications since the program opened in 1988.

“The increased interest and competitiveness of the program are clearly a multi-year reflection of Columbia’s reputation,” says Mary O’Neil Mundinger, DrPH, dean of the Columbia University School of Nursing.

The ETP program prepares college graduates with no prior experience in nursing for a career as an advanced practice nurse. Students earn a BSN in nursing in the first year of study before proceeding to a master’s program in advanced practice specialties such as anesthesia or oncology. The ETP program was the first curriculum of its kind in the country and currently enrolls about 170 students a year. The school plans to increase class size in the future.
Microbe Hunters Dedicated to Preventing the Next Pandemic

New lethal infectious diseases like AIDS, SARS, and bird flu emerge every year, and now internet giant Google is looking to CUMC microbe hunters to help prevent the next pandemic. The philanthropic arm of Google has awarded $2.5 million multi-year grant to W. Ian Lipkin, MD, the John Snow Professor of Epidemiology in the Mailman School of Public Health and professor of neurology and pathology in P&S, and colleagues Thomas Briese, PhD, and Gustavo Palacios, PhD, both associate professors of clinical epidemiology in Mailman.

The new Google award will allow these microbe hunters to pursue pathogen discovery in hot spots of infectious disease emergence in Asia, Africa, and South America and build laboratory capacity needed for rapid containment of new diseases at the source.

The effort is part of Google’s “Predict and Prevent” initiative, which awarded $14 million in October to six research centers to identify hot spots where diseases may emerge, discover new pathogens circulating in animal and human populations, and respond to outbreaks before they become global crises.

Dr. Lipkin and colleagues at Mailman’s Center for Infection and Immunity have already helped to pioneer a new era of rapid pathogen discovery. They have developed a technology to scan the “entire tree of life” – bacteria, viruses, fungi, and parasites — in a matter of days to help identify new pathogens. With such techniques, the team has discovered more than 75 viruses; has been instrumental in efforts to identify, and prevent the spread of, SARS and the West Nile, Ebola and Marburg viruses; and has solved outbreaks that threatened the safety of transplantation, the food supply, and wildlife.

Dr. Lipkin also directs the World Health Organization Collaborating Center for Diagnostics in Zoonotic and Emerging Infectious Diseases (zoontic diseases start in animals and jump to humans; they account for 75 percent of all new infectious diseases). The Center for Infection and Immunity is dedicated to global research and training programs focused on pathogen surveillance and discovery and on biodefense. More than 35 scientists from around the world have been trained at the Center in state-of-the-art diagnostic techniques. Dr. Lipkin also directs the Northeast Biodfense Center (NBC), a Regional Center of Excellence in Biodefense and Emerging Infectious Diseases, comprised of 28 private and public academic and public health institutions in New York, New Jersey, and Connecticut. The NBC addresses the challenges of hemorrhagic fevers, unexplained febrile illnesses, pneumonias, and meningococcalpneumoniaealss as basic and translational research focused on pathogen biology, diagnostics, innate and adaptive immunity, drugs, and vaccines.