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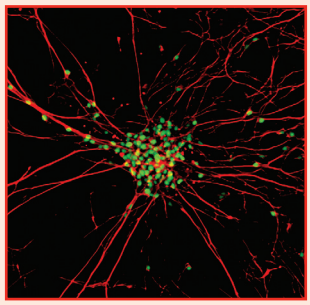

Stem-cell derived motor neurons from a patient with ALS in culture. Courtesy of Mackenzie W. Amoroso and Gist F. Croft.

SAVE THE DATE

Symposium 2014
Stroke Rehabilitation: New Insights on Motor and Cognitive Recovery

April 11-12, 2014

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BEST HOSPITALS U.S.News A WORLD REPORT NATIONAL REHABILITATION 2013-14

Broadening the Educational and Research Experience in Rehabilitation Medicine

Traditionally, the third year of medical school exposes medical students to their first major clinical experience as they rotate through a variety of services. "Generally, however, students do not rotate through the smaller, lesser known specialties such as Rehabilitation Medicine, and by their fourth year, the decision of where to specialize has already been made," says Joel Stein, MD, Physiatrist-in-Chief, NewYork-Presbyterian Hospital.

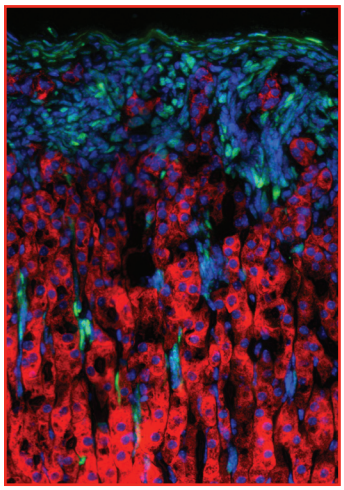
In an effort to provide medical students with earlier exposure to the field of Rehabilitation Medicine, Columbia University College of Physicians and Surgeons has introduced a weeklong "selective" into their third-year curriculum. Instituted as a pilot program last year and scheduled to begin again in January 2014, the Rehabilitation Medicine selective assigns time for students in the Hospital's inpatient unit, where patients receive intensive rehabilitation, as well as in the outpatient practice, where they see a variety of patients with sports-related problems and more severe disabilities, including spinal injuries. "We try to give the students an introduction to all aspects of the field in the short time they are with us," says Dr. Stein.

Columbia students interested in Rehabilitation Medicine also have an opportunity to spend a full month on the rehabilitation service before choosing their specialty. Students begin their fourth and final "year" (actually 16 months) of medical school in January, during what would previously have been part of their third year. "In the past, students would finish their rotations in June and then two months later they would be applying for residencies. It left very little time to explore other fields," notes Dr. Stein. "Starting their fourth year in January gives those who enjoyed the week with us to come back for a full month earlier in their elective time."

(continued on page 2)

Tapping the Potential of Stem Cells

The Department of Rehabilitation Medicine and Regenerative Medicine at NewYork-Presbyterian/Columbia University Medical Center is home to the Columbia Stem Cell Initiative (CSCI) – one of the largest stem cell operations in the world, involving some 120 different laboratories throughout Columbia. "Our conviction is that expertise across the board – ranging from basic and translational research to clinical applications and ethics – is necessary to exploit the huge promise of stem cells in a manner that is rational and safe," says Christopher E. Henderson, PhD, Chief of Regenerative Medicine and Director of the Columbia Stem Cell Initiative. "Our goal is to introduce stem cell biology into the heart of the Department of Rehabilitation and Regenerative Medicine to conduct original stem cell research, as well as to bring together members of the diverse stem cell community within Columbia under a common organization."



Multiple cell populations near the periphery of the adrenal cortex. Courtesy of Salma Begum, Daniel Stephen, Alexandra Joyner, and Ed Laufer.

A New Model for Stem Cell Research

About five years ago, Columbia University Medical Center began taking a closer look at its stem cell research programs. Although Columbia had several scientists who were clearly leaders in the field, it did not have an organized stem cell effort, and the quality of its stem cell research was not widely known internally or externally. "As these individuals

(continued on page 3)

Broadening the Educational and Research Experience in Rehabilitation Medicine

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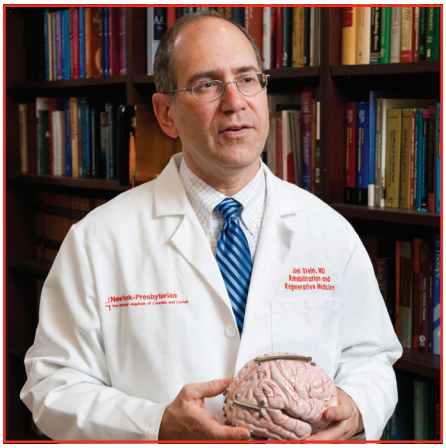

Dr. Joel Stein

> "We are excited by this team oriented approach to research projects that residents can undertake with the knowledge that the work will continue with the team even if they are personally moving on to other endeavors."
>
> — Dr. Joel Stein

Also part of the expectations for senior medical students is to undertake a scholarly project, and for many that involves research of some kind. "We currently have our first Columbia senior medical student who chose to complete his scholarly project in stroke rehabilitation research," says Dr. Stein, who is serving as faculty mentor. "The project is looking at patient priorities for rehabilitation – what are the limitations that patients are most concerned about and anxious for help with, as opposed to what physicians might think are most important."

Introducing Research: Early and Often

With medicine evolving at such a rapid pace, Dr. Stein believes that physicians cannot practice good medicine without keeping abreast of the latest research advances. "This is a longstanding challenge for physicians that has certainly accelerated," he says. "Advances in practice result from incorporating data published in biomedical journals. For physicians who have not been personally engaged in the processes of conducting research, I think their ability to evaluate the quality and relevance of that research is not as good as someone who understands the nuts and bolts and has looked inside the 'black box' of science."

To that end, Dr. Stein has enhanced research opportunities in the combined NewYork-Presbyterian Hospital Physical Medicine and Rehabilitation Residency Program. "One of the challenges with resident research is that they are here for short periods of time," says Dr. Stein. "They don't necessarily start their projects on day one, and oftentimes when they graduate, the projects aren't quite done. So we have organized the program by establishing teams consisting of a faculty mentor and residents from each of the three years to work on one or more projects."

Over time, when the most senior member of each team graduates, the two more junior residents continue those projects. "This allows for continuity and projects can actually be brought to fruition," says Dr. Stein.

"It's unreasonable to expect that residents or medical students are going to either have the time or the skill set to initiate research projects on their own," adds Michael W. O'Dell, MD, Chief of Clinical Services, Department of Rehabilitation Medicine at NewYork-Presbyterian/Weill Cornell Medical Center and Medical Director of the Inpatient Rehabilitation Medicine Center. "The far more efficient approach is to have a mechanism to identify the interests of the residents or medical students and match them up with faculty mentors who already have work ongoing in the area."

The research program consists of eight groups focusing on neurological rehabilitation, musculoskeletal disorders, and pediatric rehabilitation. Six months into their first year, the eight residents hear presentations from each group and submit a preference list of the team they would prefer to join.

"We have an ongoing database of stroke rehabilitation outcomes with some 700 variables on every stroke patient who comes through the inpatient rehabilitation unit," says Dr. O'Dell, a faculty mentor, whose own research focuses on neurological rehabilitation for stroke, multiple sclerosis, traumatic brain injury, and neurological tumors. "This database has provided the opportunity to develop a number of studies so when a resident or medical student comes on board they don't have to start from scratch."

Two residents recently completed a three-month project using the stroke database that has been submitted to the Association of Academic Physiatrists for its 2014 meeting.

New technology is helping patients to regain the ability to perform everyday tasks following a stroke.

"It is so important in Rehabilitation Medicine to foster an interest in research, especially compared to other specialties, because there is a relative lack of evidence-based data for many aspects of practice," notes Dr. O'Dell. "We are not going to be able to change that in the future unless we actively recruit and encourage medical students and residents to take an interest in research and provide mentorship during their training."

"Having physicians gain greater personal experience in the research realm, both during medical school and residency, will allow them to be better physicians ultimately because they will have greater insight into the process of research," adds Dr. Stein. "It's very important that we set out as a goal for ourselves not just to develop outstanding practitioners, but also those who will be academic leaders in the field and researchers themselves."

For More Information

Dr. Joel Stein
js1165@columbia.edu • jos7021@med.cornell.edu
Dr. Michael W. O'Dell
mio2005@med.cornell.edu

Tapping the Potential of Stem Cell Research *(continued from page 1)*

started to come together," says Dr. Henderson, "we realized that far from being a small center, Columbia actually had a major pool of stem cell researchers, including those working directly on stem cell biology, and others using stem cells to model diseases. This provided an impetus for the development of a more cohesive stem cell research program."

About the same time, Joel Stein, MD, was arriving as the new Chair of Rehabilitation Medicine, and a decision was made to change the name of the department to include regenerative medicine. "I think this was quite visionary," says Dr. Henderson. "Dr. Stein was interested in applying some of the resources of the department to foster regenerative medicine with a focus on stem cell biology. This was an opportune, slightly serendipitous, and somewhat planned convergence of the surge in stem cell biology research with the change in objectives of the department. I believe this is the only model where such a strong basic and clinical research effort is formally anchored in a department of rehabilitation and regenerative medicine."

"The Department of Rehabilitation and Regenerative Medicine is committed to the advancement of stem cell research, with an ultimate goal of creating new therapies for disabling conditions such as stroke, spinal cord injury, amyotrophic lateral sclerosis, and others," says Dr. Stein. "These therapies hold the potential to truly 'regenerate' the human body and allow for more complete and effective rehabilitation."

"In establishing the Columbia Stem Cell Initiative we organized research retreats to bring together those who do clinical research in the department and those who are doing more basic research," notes Dr. Henderson, whose own endeavors focus on amyotrophic lateral sclerosis (ALS) in which he and his colleagues are using human stem cells to model the disease in the cell culture dish. "We also created a very high level external advisory board with four outstanding leaders – two representing stem cell biology and two in the field of rehabilitation, but all with a strong interest in regenerative medicine. When they came for their first visit a few months ago, the group found the model to be very exciting and were particularly struck by the degree to which we've managed to integrate such a wide variety of different disciplines around the common theme of stem cells."

How has this been achieved in such a short period of time? "First of all, we defined 10 themes in which we felt that Columbia was particularly strong," explains Dr. Henderson. "They range from basic biology to specific diseases, such as cancer, diabetes, and brain disease, to bioengineering and neurodegeneration."

The representatives of these areas meet every month to discuss how the Columbia Stem Cell Initiative can facilitate collaborations and sharing of information. One method is a monthly series of internal seminars in which two young scientists present their work to their peers and to faculty members. In addition, a Stem Cell Biology seminar series is held monthly with invited speakers from other institutions who give a scientific talk and meet with CSCI faculty.

Perhaps the most visible event, considered "wildly successful" by those in attendance, is the annual Columbia Stem Cell Day, hosted by the Department of Rehabilitation Medicine and Regenerative Medicine. The June 2013 event attracted a standing-room-only crowd of some 200 participants who came to hear speakers on 10 of the most current topics in stem cell research. The event also featured 55 poster presentations with junior scientists providing one-on-one discussions with participants. Keynote speaker, Fred H. Gage, MD, PhD, the Vi and John Adler Chair for Research on Age-Related Neurodegenerative Disease at the Salk Institute, wrapped up the day with his talk on *Modeling Psychiatric Diseases Using iPSCs*.

ALS: How Stem Cell Biology Can Make a Difference

Dr. Christopher E. Henderson

"We are only just beginning to perceive the potential of stem cells for human health, whether for better understanding human pathologies or for treating them more efficiently and safely," says Dr. Henderson. "A particularly challenging disease is ALS, for which we have no cure. One reason is that no drug tested in the clinic has ever been pre-tested on sick human nerve cells. There simply has been no access to human neurons because you cannot go into someone's brain or spinal cord and take out a sample to culture. Because we can now make human stem cells from samples of skin, we can take those stem cells and turn them into the type of neurons that we want. In ALS, we want motor neurons."

In the Project A.L.S. Laboratory, Dr. Henderson notes, billions of human neurons are now available with the same genetic makeup as ALS patients. "We are using these to study the mechanism underlying the disease and to screen for compounds that could become drugs to prevent the nerve cells from dying," says Dr. Henderson. "We're actually looking at the neurons from the patients. That's something that has not been done before. What's exciting is that if we can find ways of protecting dying neurons or increasing their function, we will then have a therapeutic route that doesn't involve injecting potentially dangerous cells into the brain."

The Columbia Stem Cell Initiative has also brought in high-throughput screening thanks to a large grant from NYSTEM, providing the researchers with the ability to screen tens of thousands of compounds for their ability to, for example, keep a neuron alive. Adds Dr. Henderson, "Stem cells are changing the world of drug screening as well because they provide different cell types in much larger quantities then were ever possible before."

Maintaining Momentum in Stem Cell Research

Dr. Henderson and his colleagues want to ensure that there will be researchers in stem cell biology to succeed those who essentially launched the field. "Stem cell biology is a new area, and as such we feel that we must be training the next generation of stem cell biologists," says Dr. Henderson. "Through the Columbia Stem Cell Initiative undergraduate students have the opportunity to do summer internships in stem cell laboratories

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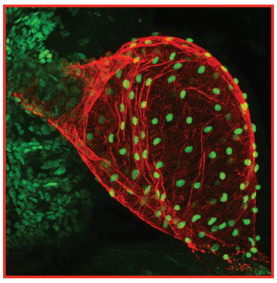
Tapping the Potential of Stem Cell Research *(continued from page 3)*

across the university and graduate students have access to stem cell biology through multiple programs, including two specifically focused on the basic and translational potential of stem cells. Medical and MD/PhD students receive training in the translational and ethical aspects of stem cell research, and can apply for training grants for clinical studies and basic research."



Zebrafish heart stem cells. Courtesy of Sophie Colombo and Kimara L. Targoff.

With funding from the Helmsley Foundation, the Columbia Stem Cell Initiative provides starter grants for new projects. Grant submissions are accepted from within and outside Columbia and are reviewed by an independent panel. To date, 14 such grants have been awarded, providing support for new projects with the potential to produce high-profile data. "The explicit aim is for the grant recipients to generate preliminary data so that they can go on to apply, convincingly, for NIH funding," says Dr. Henderson. "With each of these efforts, we are trying to provide a fertile environment for discoveries to happen."

Reference Article

Amoroso MW, Croft GF, Williams DJ, O'Keeffe S, Carrasco MA, Davis AR, Roybon L, Oakley DH, Maniatis T, Henderson CE, Wichterle H. Accelerated high-yield generation of limb-innervating motor neurons from human stem cells. *The Journal of Neuroscience.* 2013 Jan 9;33(2):574-86.

For More Information

www.columbiastemcell.org
Dr. Christopher E. Henderson • ch2331@columbia.edu