Dean's Newsletter May 2, 2005

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NAS Issues Guidelines for Stem Cell Research and the CIRM

On April 26th the National Academy of Sciences and its Institute of Medicine jointly issued the highly anticipated "*Guidelines for Embryonic Stem Cell Research*" (see http://www.iom.edu/report.asp?id=26661). Prior to this report, there were no clearly defined national guidelines for embryonic stem cell research, in part because the NIH has not been engaged in human embryonic stem cell research with the exception of the restricted stem cell lines allowed under the ruling imposed by President Bush in April , 2001. Even so, the NAS guidelines are timely because of ongoing stem cell research being funded by private philanthropy and publicly, at the state level. Perhaps the most notable source of public support is the California Institute for Regenerative Medicine (CIRM) created by the passage of Proposition 71, which will award nearly \$3 billion over ten years for stem cell and regenerative medicine research in California.

The NAS Guidelines offer 23 recommendations including the establishment of institutional Embryonic Stem Cell Oversight (ESCRO) Committees. These committees would work with Institutional Review Boards to provide the additional review and scrutiny warranted by the complexity of Human Embryonic Stem (hES) cell research. The ESCRO would assure that procurement processes were reviewed and approved in tandem with adherence to ethical and legal principles of informed consent and protection of confidentiality. The guidelines address the types of research that are acceptable (which include somatic cell nuclear transfer [SCNT]) and also address research that should not be permitted (i.e., in vitro culture of intact human embryos longer than 14 days or until the formation of the primitive streak; research in which hES cells are introduced into nonhuman primate blastocysts or in which ES cells are introduced into human blastocysts; and the committee notes that "no animal in which hES cells have been introduced at any stage of development should be allowed to breed"). The Committee

also offers recommendations on the procurement of gametes, blastocysts and somatic cells "for the purpose of generating new hES cell lines" and also addresses the informed consent of donors, adherence to standards of clinical care, compliance with HIPPA and guidelines governing other related areas of research (e.g., recombinant DNA research, animal care, gene therapy, etc). In addition, the Committee addresses the banking of hES cell lines and recommends the establishment of a National Policy Review Board.

The decision about how these guidelines will impact the work supported by the California Institute for Regenerative Medicine will be determined in the near future. There is every reason to believe that the NAS guidelines will underpin the CIRM standards, which are currently being developed by a Standards Committee. CIRM guidelines should be available in the next couple of months.

Also of note, the CIRM is making progress in getting its research management infrastructure in place. This past week, the committee assigned to select scientific grant reviewers met to consider potential reviewers, who had been distilled from a list that initially exceeded well over 1,000 names. The committee, on which I serve, vetted the list and selected as finalists the most promising and experienced individuals. All of the potential reviewers are from outside California, and some are even from outside the USA. Each of the finalists, who will be presented at the May 6th meeting of the ICOC (Independent Citizen's Oversight Committee), was interviewed by committee members and the Acting President and was discussed extensively by the search committee. I have been enormously pleased and impressed by the quality of the scientific credentials of the scholars who have agreed to serve if selected. Clearly, proposals to the ICOC will benefit from extremely experienced and high quality scientific reviews.

In addition, progress is also being made on the selection of the President of the CIRM. I also serve on this committee, which has identified some wonderful candidates. We will be interviewing finalists in the weeks ahead. These discussions are occurring in executive sessions so I can only report my enthusiasm for the process at this point. Of course I don't need to offer an update on the selection of the site where the CIRM will be located in California. I am not serving on that committee but the debate around this topic is being extensively covered in the press. Lots of progress is being made.

Faculty Counts and Challenges

At the Academic Senate on April 27th, Dr. Patricia Jones, Professor of Biological Sciences and Vice Provost for Faculty Development, presented the annual report on faculty "Gains and Losses". The data presented included annual trends as well as 5 and 10-year comparisons. In the aggregate, the overall number of full-time faculty throughout the university increased from 1,431 on September 1, 1994 to 1,785 on September 1, 2004. Included in these numbers are tenure line faculty, non-tenure line (e.g., research and education) and medical center line faculty (The School of Medicine's Clinician-Educator faculty are not counted in this survey).

As of September 1, 2004, medical school faculty comprised 42% of the Stanford faculty. Further, medical center faculty accounted for 66% of the overall increment in faculty size during the past decade. To provide some additional perspective and context, I made several comments regarding our faculty size and composition. First, while the size of the medical school faculty (i.e., 750 as of 9/1/04) is larger than any other school at Stanford (e.g. Earth Sciences (47), Education (46), Engineering (227), Graduate School of Business (94), Humanities & Sciences (530), Law (43) and SLAC/Research (48) as of 9/1/04), I made it clear that the Stanford School of Medicine is still among the smallest in full-time faculty size for peer research-intensive medical schools in the nation. In fact, we are only approximately 60% the size of UCSF, a third as large as Johns Hopkins and less than 10% the size of Harvard Medical School, our size does pose some challenges. I have previously pointed out how it negatively impacts our ranking by magazines like US News & World Reports and also challenges us in developing or providing a critical mass of expertise in various programmatic areas of research, education or patient care.

As you likely know, while there has been faculty growth during the past decade, we have been carefully regulating and, where possible, prioritizing our growth in light of the overall faculty cap of 900 that was determined by the Provost in 2003. Indeed, in a number of areas the historic incremental growth of approximately 30 faculty per year has slowed somewhat and is being carefully monitored by the Offices of Academic Affairs and Institutional Planning. For example, the faculty number as of 4/27/05 was actually lower (739) compared to the 750 recorded on 9/1/04.

In addition to supporting important departmental needs, our goals are to assure the optimal balance of faculty (including basic and clinical) and, in addition, to allow our Stanford Institutes of Medicine, related clinical centers of excellence and strategic centers to help define and regulate the areas of faculty growth. However, a number of drivers impact this. For example, clinical program development can necessitate growth in certain areas. I would argue that our investments in clinical faculty during the past several years have contributed significantly to enabling both Stanford Hospital & Clinics (SHC) and the Lucile Packard Children's Hospital (LPCH) to achieve their programmatic and financial successes during the past several years. While additional programmatic growth in clinical programs will surely occur in the years ahead, it is also imperative that we support necessary and appropriate growth in our basic and clinical research programs. One of the major rate-limiting steps we now face is laboratory space for new faculty. While our long-term facilities plans will address this over time, the current limitations are stifling. I hope that our plans to lease research space off-site will help alleviate some of the bottleneck. However, I think the only realistic solution will come from the construction of our Stanford Institutes of Medicine research buildings on campus, which will hopefully take place over the next several years.

While there has been an increase in the overall number of women faculty at the University (from 17.1% in 1994 to 23% in 2004), the percentage increases in minority faculty has been less than desired (for men the change was from 9.8% of the faculty in 1994 to 12.3% in 2004 and for women it was from 3.3% in 1994 to 4.9% in 2004).

Within the School of Medicine, the percentage of women faculty grew from 19.2% in 1994 to 25.2% in 2004. The overall percentage of minority faculty in the medical school rose from 13.3% in 1994 to 19.6% in 2004. However, we still have much to do in this area – especially among Black, Native American and Hispanic faculty. We are committed to making improvements in this important area since we believe it will enrich our school and community. Clearly there will be reports on our progress in the years ahead.

Enhancing Career Development for Women

As noted above, one of our continuing and most important goals is enhancing the career development for women and minority students, staff and faculty. In discussions following our most recent Strategic Leadership Retreat in January 2005 (see the coverage in the Stanford Report: <u>http://news-service.stanford.edu/news/2005/february2/med-retreat-020205.html</u>), I have focused on the challenges we face and underscored the importance of a serious commitment to improving our recruitment and retention of talented individuals who can further expand diversity within the School. A process to address this is being led by our recently appointed Senior Associate Dean for Diversity and Leadership, Dr. Hannah Valantine, and reports of the progress of her initiatives will be presented in future Dean's Newsletters.

While our local efforts are essential, various national organizations are also committed to leadership training. On April 20-21 I attended the annual meeting of ELAM (Executive Leadership in Academic Medicine), which focuses on leadership development of women faculty. I was impressed by the high quality of this program and do believe that it can play an important role in nurturing, developing, and networking future women leaders in academic medicine. Dr. Julie Barr, Associate Professor of Anesthesia, was in this year's ELAM class, and she shares some of her observations and experiences below.

Comments by Juliana Barr, MD, Staff Intensivist and Anesthesiologist, VAPAHCS and Associate Professor of Anesthesia, Stanford University

Good leadership is hard to come by these days, particularly in Academic Medicine. Few individuals applying for and promoted to positions of responsibility, be it a Department Chair, Institute Director, Senior Associate Dean or even a Medical School Dean have had any formal leadership training. Traditionally, the criteria for promotion to these positions in academic health care have been primarily based upon seniority and research productivity in terms of peer reviewed funding and publications. In the past, if you could "run a successful and productive lab", you could run a Department, an Institute, or even a Medical School. Today's leaders in Academic Medicine face many new challenges that call for a broader set of leadership skills. Having a fundamental understanding of accounting principles, development and fund raising, strategic planning, interpersonal and communication skills, curriculum development, and understanding organizational systems, dynamics, and the influence of change are all necessary in order to be a successful leader these days in an Academic Health Center. Leaders must also reflect their constituencies. Over half of the students entering medical school, including Stanford, are now women. Yet women currently make up only 10% of the Deans of US Medical Schools, with even fewer minorities being represented. Most female physicians, who initially pursue an academic career in medicine, leave before being ever being promoted above the rank of Assistant Professor, with the attrition continuing exponentially above that level. For many years, the American Association of Medical Colleges (AAMC) has offered several multi-day seminars focusing on leadership training and professional development for women (www.aamc.org) at various stages in their academic career, but the numbers of women promoted to the top positions in Academic Health Centers continues to be small.

In 1995, the Hedwig van Ameringen Executive Leadership in Academic Medicine (ELAM) Program for Women was established as the first in-depth national program that prepares senior women faculty for leadership positions at Academic Health Centers. The year-long ELAM curriculum combines traditional MBA training oriented toward issues and strategies pertinent to academic health management, with personal and professional development focused on leadership, career advancement, communication, and the use of new information and learning technologies. Moreover, ELAM provides a unique learning experience for 45 senior women at either the Associate or full Professor level from academic medicine, dentistry, and the basic sciences. Most of the course curriculum is in the distance learning format, utilizing WebCT, conference calls, and email list serves to complete course assignments and readings. There are also 3 separate week-long residency sessions that ELAM Fellows are expected to attend: one in the fall and one again in the spring at a suburban setting in Bryn Mawr, Pennsylvania, and one session is held in November to coincide with the annual AAMC meeting, which ELAM Fellows are also expected to attend. Now in its tenth year, ELAM has matriculated over 400 women from its fellowship program, and the majority of these women have subsequently been promoted to leadership positions within academic health centers. Of the 13 women Deans of US Medical Schools, 4 of them are ELAM graduates (31%), and many other ELAM graduates now hold Vice Dean, Senior Associate Dean, Executive Vice President, Provost, Executive Director, and Department Chair positions at their institutions.

As a recent graduate of the ELAM fellowship, this has been an extraordinary year for me. My experiences as an ELAM fellow have fundamentally changed the way that I view Stanford Medical School, the VA Health Care System, and Academic Medicine in general. For me, the end of ELAM marks a new beginning. I am forever grateful for the opportunity to have spent this year developing my leadership skills and getting to know such a remarkable group of women, whose relationships I will continue to nurture and cherish throughout my career. And I look forward to the opportunity to share my ELAM leadership experiences with the students and faculty at Stanford and the VA as a way of "giving back" to my academic community.

Stanford in Chicago

As part of our continuing discussions with Stanford alumni, we traveled with the President, members of the Board of Trustees and faculty to Chicago for another Stanford Day. As we did in New York City a couple of weeks ago, Drs. Paul Berg, Irv Weissman Hank Greeley, and I joined together to conduct an interactive panel on stem cell research and biology. As with our past presentations, this topic has been of considerable interest to the public and our alumni, who are eager to hear more of the facts as well as the challenges this new area of research poses. This event ends this year's nationwide city visit. I am pleased that the medical school has able to participate in these events and to provide expertise that is of general and timely interest.

Admit Weekend

On April $20 - 22^{nd}$ the School hosted 77 outstanding students who have been admitted to the School of Medicine Class entering this August. This is the highest number in the past three years, since the school has been having combined Admit Weekends, rather than two separate events. Based on the reports from the Admissions Committee the students who have been admitted to date are truly outstanding. Special attention has been paid this year in assuring that applicants are cognizant of our new curriculum emphasizing scholarship and research in addition to excellence in clinical training and that they are committed to the goal of becoming both clinicians and scholars/investigators.

Biosciences Ph.D. Admissions

Next Autumn there are 83 students who will begin studies toward their Ph.D. degrees in the twelve Home Programs in the Biosciences (Biochemistry, Biological Sciences, Biophysics, Cancer Biology, Developmental Biology, Genetics, Immunology, Microbiology & Immunology, Molecular and Cellular Physiology, Molecular Pharmacology, Neurosciences, Structural Biology.) The accepted students were drawn from more than 1,000 applicants. Each student was interviewed by 5-6 members of the Biosciences faculty. More than half of those students who were accepted to Stanford Biosciences decided to matriculate here.

This is the smallest class of Ph.D. candidates we have admitted in many years and it includes 15 students from under-represented minority groups. The students who will join the Biosciences community next Autumn include scientists from 12 countries: China, Venezuela, Japan, Trinidad and Tobago, Taiwan, Korea, India, Canada, Singapore, Croatia, Romania and of course, the United States.

We look forward to welcoming these highly qualified young scientists to the Stanford Community.

Update on Funds Flow

In the February 22nd issue of Dean's Newsletter I presented some of the governing principles that are guiding the plans to change the "funds flow" between Stanford Hospital & Clinics (SHC) and the School of Medicine (SoM). Establishing the further validation of these principles and the developing the new funds flow methodology have been an enormous undertaking. The committee that has worked on this effort (from the SoM Marcia Cohen, Mike Hindery and Norm Rizk and from SHC Gerry Shefrin and David Keane) has put in countless hours of effort to keep this process on its very ambitious schedule. I am pleased to say that the Joint SoM/SHC Funds Flow Committee has been able to meet its aggressive timelines, and it delivered an interim report at the SHC Finance Committee on Tuesday April 25th.

The Committee is further testing the model in order to determine what accommodations might be needed to make it most successful and also to develop a transition plan that will allow the new model to be instituted in the FY06 budget planning process, which is already underway. While I know that no new model is perfect and that there will be some adjustments necessary in this one, it bears underscoring that the new funds flow model is extraordinarily more rational that any that has existed to date. Accordingly I firmly believe that once fully implemented we will have a much improved funds flow – and equally if not more importantly, a significant diminution of the usual contention that has routinely surrounded the annual negotiations on funds flow.

Medicine and the Muse

Because I was out of town and thus unfortunately missed this year's Medicine and the Muse event, I asked Dr. Audrey Shafer, Associate Professor of Anesthesia, to provide a summary of her observations. According to Dr. Shafer "Stanford's annual arts, humanities and medicine symposium, packed well over 100 attendees into the Cantor Arts Center auditorium on April 21, 2005 for an exciting celebration of interdisciplinary work and creativity. Medical student committee members James Andrews, Sarah Bein, Tina Allee, Sarah Hilgenberg, Sarah Langley, Byran Maxwell, Cindy Mong, Jason Moss, Peter van Roessel and Joanna Wrede, as well as faculty sponsor Audrey Shafer, organized the event. Hosted by James Andrews, the evening featured keynote speaker David Morris, University Professor at University of Virginia and a cultural studies specialist on pain; project presentations by Jessica Goldman, Emmanuel Osei-Kuffour Jr., Joyce Pan and Erin Butler (Anatomy of Movement), and Hetty Eisenberg, Chris Adams, Cheri Blauwet and Lori Rutman (medical scholars and concentration projects); poetry readings by Tina Allee and Candace Pau; and musical performances by Cindy Mong, Prasanna Ananth, Jason Moss, Jonathan Riboh and Matt Siedhoff. The art and poster exhibit included sculpture, literature, painting and photography by 19 students. The event was sponsored by the Biomedical Ethics and Medical Humanities Scholarly Concentration, the Stanford Center for Biomedical Ethics and the Cantor Arts Center, and supported by grants from the Osher Foundation, The Wall Center, and Helen and Peter Bing.

I am so very pleased that the artistic talents of our students are valued by the School and that there is an opportunity for them to share their many contributions with our community at the annual Medicine and the Muse event. I also want to thank Dr. Shafer for her wonderful leadership.

Practice of Medicine (POM) Projects in the News

I was pleased to see the recent media coverage on two projects completed by some of our first year medical students, under the direction of Dr. Clarence H. Braddock, Associate Professor of Medicine, as part of the Practice of Medicine course.

One project, a proposal to let unused medicine be dispensed to the needy, was aired on April 27 before the State Senate Health Committee. State Senator Joe Simitian submitted the proposal, which calls for the State to establish a program allowing pharmacies to dispense previously sold, unexpired and unopened prescriptions medications to patients, especially those with low incomes or severe disabilities. The students who worked on this project were Josemaria Paterno, Emiley Chang, Michael Mancuso, Joe Peraza, and Sheila Ravi. The second project, launched on April 5th, is a state-wide online organ donation registry. More than 87,000 Americans, including about 18,000 Californians are waiting for an organ transplant, and 17 patients on the waitlist die every day. The goal of the online registry is to help organize a database, so that, in case someone doesn't have a donor card on them, this can now serve as the backup method. The students involved with this project were Liz Oosterhuis (a first year law student), Meghan Ramsey, Frederick Dewey, Emily Curran, Sudeb Dalai and Monique Barakat.

The Practice of Medicine is one of the new courses in the curriculum revision that began in the fall of 2003. Its goal is to provide students with the skills and perspective necessary to begin their entry into medical practice. In addition, the course has embraced our collective goal that Stanford Medical School graduates become excellent clinicians and future leaders in medicine. It is this latter emphasis that led to the "POM Project."

At the beginning of the first year of medical school, Stanford medical students form groups that select a contemporary topic in public health or community medicine. Over the course of the year, they conduct background research on the topic, including becoming informed about ethical, health policy, and community health implications of the issue. They also attend sessions in which they are introduced to the community perspective, both in concept and in practice, as they are hear from people in communities about how they have turned their passion for change into actual change.

As the students become more informed about their chosen topic, they are teamed with a community partner, someone working in the area of their interest who can mentor them into turning their interest and passion into action. Each student group develops an advocacy plan, in which they will take some concrete action to make an impact on the health of the community. The POM Project embraces a larger role for the physician in society – not just a healer and advisor, but also a community advocate and effective agent for change. This perspective on the physician's role in contemporary practice puts Stanford at the forefront of preparing future physician leaders. Stanford students will indeed be future leaders, as they enter practice equipped with skills and perspectives that to date few physicians have ever possessed.

History of Social Work Exhibit at Lane Library

There is a new exhibit at Lane Library that I want to bring to your attention. It is entitled *From the Fruit and Flower Mission To the McGann Lectures: An Historical Record of Social Work at Stanford University*. The exhibit was inspired by the recent publication by Leona M. McGann and Flora M. Finney, emeritae members of the Department of Family, Community and Preventive Medicine, of their *History of Social Work in the Leland Stanford Jr. University School of Medicine, 1913-1981.* Lane Library has combined photographs and documents from Lane's Special Collections and Archives with original correspondence and memorabilia provided by McGann and Finney to tell the story of the history of social work at Stanford. The exhibit is located in two cases on the courtyard level of Lane Library.

In the early years, the Stanford Department of Family, Community and Preventive Medicine collaborated with the small town of Livingston in the Central Valley (18 miles north of Modesto) and established a student volunteer clinic, primarily serving migrant workers. When McGann joined Stanford, she assumed responsibility for recruiting volunteer medical faculty. A similar clinic, called the Farm Worker Clinic, was later set up in the Salinas-Watsonville area. After their full day in Stanford Clinics, which ended at 5pm, a social worker and volunteer physician traveled to these remote clinics to treat patients the medical students had screened earlier in the day. Students were responsible for follow up patient care. Below are some links to early photos in other clinics in San Francisco:

Waiting Room, Stanford Hospital Clinics, 1920

Cardiac Clinic, Stanford Hospital Clinics, 1955

After the Stanford School of Medicine moved to Palo Alto in 1959, the Medical School Social Work program continued to make lasting contributions. This well-established clinical program was inherited by the Stanford Hospital in 1981 and continues to grow. It is complemented by the Department of Social Work in Lucile Packard Children's Hospital (LPCH).

The legacy of Stanford's Clinical Social Work program is alive and well in programs that include:

If you are interested in a copy of *History of Social Work in the Leland Stanford Jr*. *University School of Medicine, 1913-1981*, contact Lane Library. Thanks to Leona McGann and Flora Finney for their valuable efforts to ensure that this important part of the School's history is preserved and to Heidi Heilemann for her work in putting together the exhibit. I hope you will stop by Lane Library to view the exhibit, which will be up through the summer.

Thanking Those Contributing to Financial Aid

Stanford is unique in a number of important ways. One perhaps not as well known as others is the remarkably low debt burden that our MD students incur upon graduation, even though many do 5 or more years of matriculation. Indeed, whereas the average national debt burden for students graduating from four years of medical school is approximately \$131,000, Stanford students graduate with about \$61,000 of debt – the lowest in the nation for private or public medical schools. Not only is this low debt level an enormous benefit to young people beginning their lives and careers, it also permits our students to feel free to engage in research during medical school and to pursue career pathways that are most consonant with the goals and values of Stanford School of Medicine. Of course this doesn't happen by accident. The low debt burden is the result of a robust financial aid program that is made possible by the remarkable gifts and donations of alumni and members of our community on behalf of medical education.

It is nearly impossible to thank enough those have had contributed so much to the financial aid of our students. One lovely event that helps us to express a portion of our gratitude is the annual "Financial Aid Dinner" that unites donors with the students to whom they have provided support. Allowing students and their sponsors to meet, share their stories and get to know each other provides a remarkable bond as well as a human face that each can value and celebrate. Thus it should not be a surprise that both donors and students love to attend this dinner event and find it emotionally exhilarating.

The Financial Aid Dinner we held on April 26th was no exception. Donors and students met, some for the first time, while others re-acquainted past relationships. We also had the opportunity to hear personal life stories from Sepideh Gholami, Lance Okeke and Joshua Spanogle, three of our students. They talked about how they came to Stanford and about the positive impact the financial aid they are receiving will have on their lives and careers. While there was only time to hear from three students I know that the personal stories from virtually every student would be compelling and meaningful.

I too want to thank our very generous donors for their wonderful and enduring contributions to our students and the School. They are one more reason why the Stanford School of Medicine is so special.

Upcoming Events

Cinco de Mayo - Celebrate Cinco de Mayo at a Happy Hour hosted by the Office of Diversity and Leadership, Thursday, May 5, 5-6 p.m., at the Alumni Green (by Fairchild Auditorium)

Diversity in Action: The Changing Face of Stanford University School of Medicine, presented by the Stanford Medical Alumni Association, Friday, May 6, 9:30 a.m. -2 p.m., Fairchild Auditorium

Stanford University School of Medicine recognizes the importance of diversity. The number of women and minorities among the student population and faculty is growing, and work continues to increase their numbers. A diverse group of participants will share their Stanford experiences from medical school, postgraduate training, and faculty life. The panel exemplifies the positive role diversity plays in the practice of medicine in the 21st century.

Discussion concludes at noon and is followed by a luncheon on Alumni Green Panelists include Dr. Fernando Mendoza (moderator), Dr. Bonnie Maldonado, Dr. Roger Peeks, Dr. Estaban Burchard, Dr. Iris Gibbs, Melissa Enriquez (student) and Cheri Ann Blauwet (student).

Information and registration about this event and other Stanford Medical School Reunion 2005 programs can be found at: <u>http://med.stanford.edu/alumni/reunion2005.html</u>

Community Lecture Series - Fifty Years of Computational Biology, by Michael Levitt, PhD,

Professor of Structural Biology. May 4, 7:00 p.m., Clark Center Auditorium. Free and open to the public.

The lecture will survey the field of theoretical structural biology as it has developed since the prediction of the alpha-helix structure by Linus Pauling in 1951 and DNA by Crick and Watson in 1952. Topics will include: predictive modeling and simulation of molecules as 3-D objects; protein molding—the process of self-assembly in which protein molecules organize into precise nano-machines; and bio-informatics with attention to classification of protein structures.

Appointments and Promotions

• *Jayanta Bhattacharya* has been appointed Assistant Professor of Medicine (Primary Care and Outcomes Research), effective 11/01/2005.

- *Mildred Cho* has been appointed to Associate Professor (Research) of Pediatrics, effective 5/01/2005.
- *Thomas Clandinin* has been appointed to Assistant Professor of Neurobiology, effective 2/01/2006.