

Dean's Newsletter

June 30, 2005

Table of Contents

- Shared Responsibility, Individual Integrity
- Comparing Notes on Translating Discoveries
- Getting Ready for a Review by the Association for the Accreditation of Human Research Protection Programs (AAHRPP)
- Differentiating the Cancer/Stem Cell Institute and the Comprehensive Cancer Center
- California Health Care Institute Advocacy in Sacramento
- Honors and Awards
- Appointments and Promotions

Shared Responsibility, Individual Integrity

On Wednesday June 15th I participated in a panel discussion sponsored by the Executive Leadership group of the Federation of American Societies of Experimental Biology (FASEB) to address “Shared Responsibility, Individual Integrity: Scientists Addressing Conflict of Interest in Biomedical Research.” The goal was to bring leaders from academia, industry and the NIH together to consider the impact of conflict of interest from the perspectives of scientists and academic institutions. The conference was prompted by the LA Times report (12/08/04) regarding violations of conflict of interest policies by NIH leaders and scientists and the unfortunate events that followed. My task at this conference was to focus on how we address these issues at Stanford.

Based on the perspectives offered by Dr. Elias Zerhouni, Director of the NIH, Dr. Bill Brody, President of Johns Hopkins University and Dr. Gail Cassel, VP for Infectious Disease at Eli Lilly, who spoke before me, I underscored my personal belief that we need to do everything we can as individuals and as institutions to address conflicts of interest in a responsive and transparent manner. It seems clear that this matter is now in the public eye. Further, I believe it would be irresponsible to assume that it will simply disappear as a source of concern or that it will not be pursued by the press or by legislative or regulatory bodies. Accordingly, it is imperative that we have clear institutional guidelines and expectations and that members of our community of scientists and physicians each take personal responsibility for acting in a manner that is beyond reproach. Given the events that occurred at the NIH last year and that have unfolded in the pharmaceutical industry within the past several months, it seems obvious that public trust has been seriously eroded – and that this is something that must be regained.

The reasons for concern – at least grounds for worry - are also compelling. For example, of 210 life science organizations surveyed in 1994, 90% reported some relationship with academia. More notably, 88% retained faculty as consultants and at one academic institution (which is likely representative) a third of the faculty had consulting, speaking or advisory board relations with industry. At top research universities, half or more of faculty had some consulting arrangement. With the passage of Bayh-Dole in

1980, these relationships are not surprising, but they do offer some grounds for concern, or at least reflective monitoring. For example, nearly 50% of academic investigators reported receiving “research-related gifts” from industry, including equipment, biomaterials, discretionary funds, student support, travel funds, etc. Moreover, nearly two-thirds of those academic scientists who received gifts reported that they were important to the progress of their research.

In addition to gifts, equity relationships have increased during the last two decades. While the actual number varies among institutions, one reported that 14% of its faculty were involved in such relationships (Boyd E and Bero L *JAMA* 2000;284:2209-2214). Obvious concerns are that such arrangements can affect academic openness, objectivity and bias among faculty and that they could jeopardize the training of graduate students and other trainees. Just this year two books addressing these concerns have been published: Jennifer Washburn, *University.Inc., The Corporate Corruption of American Higher Education*, Basic Books, February 2005, and Jerome Kassirer, *On the Take, How Medicine's Complicity with Big Business can Endanger Your Health*, Oxford University Press, September 2004. Both are receiving attention from regulators and lawmakers, among others. These publications underscore the increasing level of concern about the academic and medical community's evolving relationships with industry and about conflicts of interest.

While it is clear that the greatest risk and concern apply to conflicts of interest involving clinical trials and patient studies, it is also important to note that the dangers transcend these obvious areas. For example, the commentary by Brian Martinson et al entitled “*Scientists Behaving Badly*” published in the June 9th issue of *Nature* (435:737-738) raises many concerns. The authors describe an anonymous survey of 3,247 early and mid-career scientists. Of the respondents (there was a 52% response rate), 15.3% reported that they had changed the design, methodology or results of a study in response to pressure from a funding source. While overt fabrication and falsification was rare, over 10% admitted to overlooking others' use of flawed data or others' questionable interpretations of data, or dropping observations or data points from analyses based on a “gut feeling” that they were inaccurate. Amazingly, 27.5% reported “inadequate record keeping related to research projects.” Although some circumspection is appropriate in interpreting such a survey, it does seem that a worrisome pattern is evident. Particularly concerning is the inference that can be drawn from the data that scientists and physicians may be biased because of ties to funding sources, most notably to industry. These findings make it imperative that individual and shared responsibility be at the forefront of concern and institutional oversight.

We recognize the important benefits that accrue from productive relations with industry. Nevertheless, it is essential to remember that the primary responsibility of each faculty member is to Stanford University and to her/his participation in its primary missions of research, education and patient care. There is no question that sharing knowledge and scientific discoveries through lecturing, writing, etc. is an essential component of the academic process and that faculty are assessed on their national and international reputations, which can be enhanced by appropriate relations with industry.

These benefits have been well demonstrated with the important connections that accrued, for example, in genetic engineering – which arose in institutions like Stanford – and which spawned much of modern biotechnology. Similarly, there is every reason to believe that genome profiling and stem cell biology will have similar impacts in the future. Indeed, academic medical centers such as ours have an obligation to translate discoveries, which requires effective partnerships with industry. At the same time, academic medical centers have an equal obligation to conduct clinical research – and I would argue all research – without bias and in a manner that protects the integrity of the data as well as the public safety and trust.

It is for these reasons that all Stanford faculty are required to disclose any personal financial interests they may have regardless of the dollar amount, including honoraria and equity (stock, stock options, royalty for the faculty member, spouse/partner, or dependent children). These must be disclosed in the informed consent forms for faculty engaged in clinical research and in any public presentations and publications. While disclosure is mandated and while failure to disclose results in loss of investigator status, it is not unreasonable to query whether this policy is sufficient.

As I have commented in recent Dean’s Newsletters, the School of Medicine has established clear guidelines regarding conflict of interest and has published both guidelines and tips to faculty on how to manage potential conflicts (see <http://med.stanford.edu/conflict/>). One of the important aspects – and assets – of our policy is that our Office on Conflict of Interest and the appointed Committee on Conflict of Interest begin with the assumption that our faculty will do the “right thing” if appropriately informed and educated. Hence, I encourage you to seek guidance if you have questions or concerns. Our goal is not to impede your research or opportunities but to assure that they are consonant with our values and your role as a member of the University community.

As a general rule, if a personal financial incentive becomes a significant motivation, one is likely moving into dangerous waters where objective advice and guidance are needed. Similarly, it is always wise to ask whether basic academic values are being maintained, including an open academic environment. It is also essential to assure that there no restrictions on publication or dissemination of results, that fair licensing practices are upheld, that the research is appropriate to the mission of the university and that resources and facilities are appropriately used. It is critical as well to assure that students and trainees are not being exploited by any academic/industry relationship. While there are certainly many nuances, it should not be missed that conflict of interest is something that the public easily understands – as do journalists – so thinking about how one’s personal situation would look on the evening news or on the front page of a local or national newspaper is a good “smell test.”

I also think it is important to recognize that standards that have been accepted in the past will be more stringent in the future. Regardless of whether or not this change is manifested in new regulations or legislation, it seems implausible that this issue will disappear from public attention. It would be naïve to assume that conflict of interest will

be entirely avoidable, but there is every reason to expect that such conflicts can and must be managed, especially if the faculty member seeks guidance and follows institutional recommendations. This is both an individual and a shared obligation.

Whether we need to move to broader oversight over our institutions, as discussed at FASEB, is less clear to me. I think the ultimate key is making sure that we each take our personal and university responsibilities seriously. Should you have any questions about how our conflict of interest policies apply to your research activities, I strongly recommend that you engage our institutional resources to provide help and advice. Feel free to contact Ms. Barbara Flynn, Manager, Conflict of Interest Review Program (barbara.flynn@stanford.edu) or Dr. Harry Greenberg, Senior Associate Dean, Research, Department of Medicine (harry.greenberg@stanford.edu) with your questions or concerns.

Comparing Notes on Translating Discoveries

On Thursday June 16th, I participated in a Workshop on Translational Research and Medicine sponsored by the National Cancer Institute. My role was to reflect on how we are approaching this challenge at Stanford. In doing so I shared our still evolving efforts to integrate our overarching mission in *Translating Discoveries* across the spectrum of our programs, from education to research and patient care. While we have much work to do to fully realize our goals, I think we have made progress in many areas since our Strategic Plan *Translating Discoveries* was formulated in early 2002. These include:

- ***Medical Student Education*** – Our New Stanford Curriculum, which commenced in the Fall of 2003, has served to refocus our medical student education objectives toward developing a strong foundation in science along with its connection to patient care. The scholarly concentrations, which enable students to engage in specific areas of inquiry and research, are perhaps the most distinctive facet of our new curriculum (<http://med.stanford.edu/md/curriculum/>). In addition to the range of possible choices for scholarly concentration, I highlighted the one focused on clinical research since it relates directly (albeit not exclusively) to translational research. Indeed, I further emphasized that all students receive some training in clinical research, but that the scholarly concentration provides a deeper experience along with the opportunity to do research. That said, several of our other scholarly concentrations also afford opportunities to engage in clinical or translational research.
- ***Graduate Student Education*** – Our programs for graduate students begin with a focus on basic science. However we have recently introduced a number of courses that permit graduate students to learn more about the challenges in clinical medicine and the opportunities to engage in translational research. In addition, initiatives like the BioX innovation awards and the Biodesign program offer opportunities to engage graduate students in research or innovation that has a translational focus, as will the new Department of Bioengineering, which is

jointly held in the Schools of Medicine and Engineering. In addition, work is proceeding to develop a “Masters in Science” program for graduate students, and we are also participating in the Commission on Graduate Education, which is seeking to develop new opportunities for interdisciplinary education across the entire University.

- ***Postdoctoral Fellow Training*** – Although postdoctoral training has traditionally been more departmental or even investigator based, we are developing ways to integrate training across the continuum. One of the opportunities we are exploring is extending the scholarly concentrations developed for medical students into the clinical training years. Another is to develop the Advanced Residency Training at Stanford (ARTS), which is being modeled after the UCLA “STARS” program. ARTS will provide PhD training for residents and clinical fellows; we hope this program will be initiated by 2007.
- ***Faculty Development and Research*** – and its relation to patient care – are being orchestrated through the development of the Stanford Institutes of Medicine and the Strategic Centers. These are designed to promote interdisciplinary education and research and to foster translational research and medicine. These also complement the Centers of Excellence at both Stanford Hospital & Clinics and the Lucile Packard Children’s Hospital, as well as the broader BioX programs at Stanford.
- ***Support for translational research*** – To help facilitate our efforts in clinical and translational research, a number of programs are being put into place, most notably the STRIDE program, which will handle clinical data base development. Another important effort underway is the development of the Stanford/Packard Translational Research Medicine program. This initiative will facilitate protocol development and clinical/translational research through the provision of support for biostatistics, data management (including budgeting, contracting, automatic billing, accounting and audit), compliance, study source document archiving, research coordinator support, etc. These serve as a prelude to developing a Center for Translational Research at Stanford.

While each of these programs can be considered discrete, our attempt to integrate them and to draw associations and relationships between our missions in education, research and patient care and translational medicine and innovation will make us unique and will further shape the future of Stanford Medicine.

Getting Ready for a Review by the Association for the Accreditation of Human Research Protection Programs (AAHRPP)

The following commentary was prepared by Kathy McClelland, Director, Research Compliance Office, and Ann Arvin MD, Associate Dean of Research: Arthur Bienenstock, Vice Provost and Dean of Research and Graduate Policy, joins us in

announcing to our research community that Stanford University is seeking accreditation of its program of protection of human subjects in research through the Association for the Accreditation of Human Research Protection Programs (AAHRPP) (www.aahrpp.org). Voluntary accreditation of human subjects research programs is a new initiative that is being undertaken by academic research institutions throughout the U.S. Stanford's program includes human subjects research conducted at the University, Stanford Hospital and Clinics (SHC), Packard Children's Hospital (LPCH), the Veterans Affairs Palo Alto Health Care System (VAPAHCS), and Palo Alto Institute for Research and Education (PAIRE).

This process will involve all of us because AAHRPP accreditation is based on the principle that human research protection must be part of the fundamental culture of institutions like Stanford. In December 2005, AAHRPP will conduct an on-site review of all aspects of our human subjects research programs. This visit will involve examining documents and interviews with Stanford faculty and staff. The site visitors could choose to interview you, if you are an investigator or study coordinator conducting human research protocols. You will be notified in advance if you are selected to talk to AAHRPP site visitors. Their questions will focus on the mechanisms in place at our organizations and in your own research program to protect study participants.

An Advisory Board, led by Dean Bienenstock and Associate Dean Arvin, is helping to prepare for AAHRPP review and on-site evaluation. Members of the board are:

- Steven Alexander, MD, Director of ACCESS
- Penny Eckert, PhD, Chair, Non-medical IRB
- Harry Greenberg, MD, Senior Associate Dean of Research
- Rodney Johnson, JD, Senior Medical Center Counsel
- Steve Jung, Director, Internal Audit and Institutional Compliance
- Rick Kraemer, MD, Associate Chief of Staff, VAPAHCS
- Nancy Lee, RN, Vice President, Clinical Services, Stanford Hospital and Clinics
- Steve Leibel, MD, Medical Director, Stanford Cancer Center
- Vicki Link, RN, MBA, Director, LPCH Quality Management
- David Magnus, PhD, Director, Stanford Center for Biomedical Ethics
- Kathy McClelland, Director, Research Compliance Office
- David D. Oakes, MD, Chair, Medical IRB Panel #1
- Paul Yock, MD, Professor of Medicine-Cardiovascular Medicine, Bioengineering

Watch for updates and more information about AAHRPP in upcoming newsletters and announcements. Any immediate questions can be directed to: kathy.mcclelland@stanford.edu, 723-4697.

Differentiating the Cancer/Stem Cell Institute and Comprehensive Cancer Center

In December 2002 I announced the establishment of the Stanford Institute for Cancer/Stem Cell Biology and Medicine – the first of our four Stanford Institutes of Medicine. At that time the association of cancer and stem cell biology in a single institute made sense and seemed opportune. Cancer cells and stem cells share the common characteristic of self-renewal, and there seemed to be significant potential for convergence of the fields of cancer biology and stem cell biology in shedding light on each other and in the prospect of therapeutic insights and opportunities. Since then several important events have transpired. One, of course, was the passage of Proposition 71 in November 2004 and the formation of the California Institute for Regenerative Medicine (CIRM). The second has been our evolving efforts in planning to apply to the National Cancer Institute to become a designated Comprehensive Cancer Center. As reported in the June 13th Dean's Newsletter, our current plans are to submit our application to the NCI in February 2006.

While there remains considerable and appropriate overlap in the scientific underpinnings of cancer biology and stem cell biology – and it is likely that Stanford will be especially recognized for elucidating these interconnections – it is also clear that this titular connection engenders confusion.. Accordingly, to provide clarity we have decided to create a nominal separation between the two. Effective immediately, Stanford Institute for Cancer/Stem Cell Biology, which heretofore has included our planned Comprehensive Cancer Center, has been renamed as follows:

- ***The Stanford Institute for Stem Cell Biology and Regenerative Medicine*** will encompass our broad programs in stem cell research as well as the Program in Regenerative Medicine. The Director of the Institute will be Dr. Irv Weissman, the Ludwig Professor; the Associate Director will be Dr. Mike Clarke, who will be officially joining the School in September 2005 from the University of Michigan. The Program in Regenerative Medicine includes initiatives in Education (led by Dr. Minx Fuller), Research (led by Dr. Roel Nusse), Stem Cell Policy (led by Drs. Linda Giudice and Julie Baker), Bioethics (led by Dr. David Magnus) and Facility Planning (led by Dr. Michael Longaker). Dr. Michael Longaker serves as the Program Director. Of note, the Institute and Program have a close affinity to the current and future efforts of the CIRM.
- ***The Stanford Comprehensive Cancer Center***, which we hope will soon achieve an NCI designation, will include the programs and cores being developed for our planned application to the NCI in February 2006. Dr. Irv Weissman will be the Principal Investigator and Dr. Bev Mitchell, recently recruited from the University of North Carolina, will serve as the Deputy Director and Co-Principal Investigator. Dr. Karl Blume, who has been so incredibly instrumental in bringing forth our collective efforts for the NCI application, will serve as a Senior Program Advisor for the Comprehensive Cancer Center. They will be joined by several Associate Directors including Dr. Steve Leibel (Clinical Research), Dr. Mike Cleary (Basic Research), Dr. Ronald Levy (Translational Science), Dr. Dee West (Population Research), Yanru Chen Tsai, PhD (Shared Resources) and Ms Joanne Murphy (Administration).

I hope that this change will provide clarity to those who were confused about the connections between cancer and stem cell biology, and in particular about our institutional commitment to each of these areas. There is little doubt that there are – and should be – scientific, educational and patient care overlaps between these disciplines, as there will be with stem cell biology and our other three Stanford Institutes of Medicine. However, it is also true that making these efforts discrete will help us to communicate more effectively with those communities who are less familiar with our initiatives and unique research agendas.

California Health Care Institute Advocacy in Sacramento

In conjunction with other selected members of the Board of Directors of the California Health Care Institute I visited Sacramento on Monday June 13th to meet with the Governor's Executive Cabinet regarding issues of interest to the academic and biotechnology communities. One of the most important issues is our commitment to innovation. My task was to address the importance of the National Institutes of Health (NIH) in supporting academic research and our concern that the current downturn in the NIH budget will have deleterious effects on the California biomedical research enterprise. While we all celebrate the doubling of the NIH budget that was achieved in 2003, we have now witnessed two years of funding that has barely kept pace with inflation. Of concern is that the President's FY06 budget for the NIH provides less than a 1% increase, which is well below inflation and which decreases the amount of actual research dollars available. Despite the fact that Stanford can boast the highest amount of NIH research support per faculty member of any school in the nation, our real concern must be the support available to young faculty who are seeking their first competitive RO1. At a time when the biomedical research engine has perhaps the greatest promise ever, we face a period when the ability to support and develop new faculty is challenged. The consequences have enormous implications for academia as well as for innovation and thus are of interest to the Governor and the state.

Last year the Governor wrote to the President on behalf of NIH funding and it is our hope that he will do so again. Obviously advocacy for improving NIH funding is something that should be pursued through our individual and collective efforts, including through our various professional societies. Of concern is the fact that, whereas the NIH has long had strong bipartisan support, its recent tarnishing, especially in the area of conflict of interest, has the potential to impact adversely on the support it so needs to be successful. This is yet another reason to pay careful attention to the impact of public perception on science and medicine.

Honors and Awards

- *Stephen Baccus, J.D., Ph.D*, Assistant Professor of Neurobiology, was recently chosen as a 2005 Pew Scholar in the Biomedical Sciences. This award has been coveted for its intended flexibility, as it is designed precisely to enable scientists

to take calculated risks, expand their research and follow unanticipated leads.
Congratulations to Dr. Baccus!

- **Roger D. Kornberg**, the Mrs. George A. Winzer Professor in Medicine, received the Alfred P. Sloan Prize for his discoveries involving the inner workings of RNA and the role of genes as a cause of cancer. The Sloan Prize is given by the General Motors Research Foundation for contributions in basic science related to cancer research. Congratulations to Dr. Kornberg!
- **Dr. Eric Knudsen**, Professor and Chair of the Department of Neurobiology will share the Peter Gruber Foundation 2005 Neuroscience Prize with Dr. Masakazu Konishi of the California Institute of Technology, for the work on sound localization and neural plasticity. Each will receive a gold medal and \$200,000 in unrestricted cash at the Society of Neuroscience's Annual Meeting on November 13th in Washington, DC. Congratulations to Dr. Knudsen!
- **Dr. Michael Longaker**, Professor of Plastic and Reconstructive Surgery, has been named the recipient of the prestigious 2005 Joan and Julius Jacobson Award from the American College of Surgeons (ACS) in recognition of "an outstanding surgeon engaged in research advancing the art and science of surgery." The award will be presented at the fall meeting of the ACS. Congratulations to Dr. Longaker!

Appointments and Promotions

- **James Brooks** has been promoted to Associate Professor of Urology, effective 7/01/05.
- **Randy Buckner** has been appointed to Professor of Psychology, effective 9/01/05.
- **Sheau-yi Hsu** has been reappointed to Assistant Professor of Obstetrics and Gynecology, effective 9/01/05.
- **Lei Xing** has been appointed to Professor of Radiation Oncology, effective 7/01/05.