Dean's Newsletter
September 28, 2009

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Genotyping and Education

Over the last several months a number of our faculty, students and staff have been engaged in discussion and debate about whether to offer personal genotyping to incoming medical students, selected groups of graduate students and incoming residents in internal medicine. Such an offering relates to the emerging field of "personalized medicine" and raises both opportunities and questions of enormous importance, relevance and controversy. It is very much the kind of discussion that should take place at Stanford. But, ironically, the debate, which raged during the summer and was sometimes heated as well as enlightening, began almost by happenstance.

It started on June 5th at the end of a departmental update to the School's Executive Committee when Mark Krasnow, Professor and Chair of the Department of Biochemistry, mentioned, almost in passing, a plan to offer personal genotyping to incoming medical students. At one level, the rationale seems meritorious and obvious. If students elected to be genotyped they would likely become more engaged and personally motivated to understand the underpinnings of molecular genetics and its relevance to the future of medicine. Independently, plans had been made to incorporate personal genotyping into the Advanced Genetics 203 course, and the Department of Medicine had concluded that personal genotyping would enrich the learning experience for incoming residents in Internal Medicine. In fact, these efforts were to have begun this fall.

Numerous faculty leaders, after becoming aware of these plans, began expressing concern – not about the educational value of participatory learning, but about a wide range of ethical conundrums. Some of these are relevant to anyone who elects to undergo personal genotyping. At the same time, the particular vulnerability of students – including the unintended coercion that might result from peer pressure or perceived student perceptions of faculty/teacher expectations – raised additional questions and concerns, which I also shared. Accordingly, within a couple of days after the revelation of the

aforementioned plans, I put a temporary moratorium on any plans or proposals to offer genotyping to students and trainees until we had more discussion and debate about the pros and cons, including potential consequences. On June 11th I appointed a Genotyping Task Force to review these broad and important questions.

The Task Force includes Charles Prober (chair), Russ Altman, Clarence Braddock, Pat Brown, Mildred Cho, Gil Chu, Hank Greely, Harry Greenberg, Ralph Horwitz, Louanne Hudgins, Ann James, Stuart Kim, Mark Krasnow, Phil Lavori, David Magnus, Kelly Ormond, John Pringle, Alan Schatzberg and Mike Snyder. This group clearly has broad expertise in genetics (including genetic counseling), basic and clinical science, law, ethics and education. The Task Force first met on June 12th and had a productive and "animated" discussion that addressed the potential benefits and liabilities of offering personal genotyping to students and trainees. One proposal was that this might be done through an "opt-in" approach, but concerns were raised about the need and role of IRB engagement and whether any informed consent could be free of potential coercion, even though unintended.

Issues about how anonymity and confidentiality could be ensured were also raised and, with these, the potential inadvertent impact of the results of student testing on family members. The need for genetic counseling (along with the resources to cover them) was also discussed in relation to news that might affect students who are already under considerable stress by the very nature of their work and study demands. Concerns were also expressed about potential or perceived conflict of interest, since some of our faculty have relationships with the two most notable companies involved with genotyping (e.g., 23&Me [https://www.23andme.com/] and Navigenics [http://www.navigenics.com/]).

Despite these concerns, the Task Force recognized that it is essential for our students and trainees (and I daresay our faculty as well) to be well informed about this rapidly emerging area of medicine and science. Individuals are already volunteering (and paying for) being tested and a number of faculty have also done so – some being very willing to share their own results publicly, including in education settings! Because of the importance of preparing students for the future of "personalized medicine" the Task Force considered whether alternatives might be considered at this juncture – such as the use of genomes already available in the public domain or the genotyping of the cadavers used by the students for anatomy. Although there was a diversity of opinion (and still is), most coalesced around a proposal that was presented by Dr. Gil Chu, Professor of Medicine and of Biochemistry.

Dr. Chu's proposal was discussed with our Executive Committee on Friday, September 18th. Because this is such an important topic, I am interested in engaging our broader community in the dialogue and discussion. In fact, this is an issue that will impact each of us as healthcare providers or healthcare recipients. While the details of Dr. Chu's proposal are specific, it is also their granularity that helps bring the topic into greater relief.

2009-2010 Proposal for Introducing Students to Genotyping

1. **A three-armed educational approach about the technology and clinical utility and ethical/social implications of genome wide association study data, and whole genome sequencing technologies.**
    a. ***The Molecular Foundations course (for MD students) will include*:**
        i. Introductory lectures will discuss principles important for understanding genotyping data. Topics include DNA hybridization, nucleic acid amplification, DNA sequencing, and microarrays
        ii. The course will include an interactive "case presentation" of a sequenced genome, derived from James Watson, Craig Venter, and/or Steven Pinker. The presentation will relate genotyping data to the known phenotype(s), introducing students to the utility, technical feasibility, and ethical implications of the genotyping data.
    b. ***The Human Genetics course (GENE 202*)** will provide approximately 4.5 hours of class-time on the clinical utility of genetic association studies and potential clinical utility of genome sequencing as follows:
        i. Introductory lectures
        ii. Lectures about the use of GWAS (Genome Wide Association Studies)
        iii. Facilitated discussion about the ethics and social implications of such data
        iv. There will also be a discussion-based lecture about the overall personal, family and social implications of genetic information, particularly predictive information. While not directly targeted to the genotyping education approach, it will also include relevant issues in a case-based format.
    c. Practice of Medicine (POM) course
        i. Information about genotyping will be included in the POM course.

2. **Assessment of the process, and of student attitudes towards the potential of genotyping**
    a. An appropriate assessment measure will be developed and will be approved by the IRB addressing pre- and post-assessments of knowledge and attitudes of students and trainees about genome wide association data, about the educational process employed this year, about student interest in genotyping, and about the potential implications of use in class (including risks/perception of possible coercion).

3. **The data from the various assessments will be presented to the Genotyping Task Force for review and discussion.**

We had a thoughtful and wide-ranging discussion at the Executive Committee, with many points of view and experience offered by clinical and basic science chairs. I encouraged the Executive Committee to reach out to our broader community of faculty and students to also engage them in this discussion, with the understanding that we will be revisiting it in coming months. I am also pleased that our students are wrestling with the issues – and some are writing about it as well. A notable example is the paper of MD/PhD student Keyan Salari (SMS 6) entitled "The Dawning Era of Personalized Medicine Exposes a Gap in Medical Education" in the Student Forum of the August issue of Public Library of Science (see: http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.1000138)

Please feel free to convey your thoughts and comments to Dr. Prober (so they can be shared with the Task Force) or directly to me.

Sowing the Seeds of Innovation and Discovery at Stanford

An important question in science is how to promote and support the most innovative and paradigm-changing research. By this I mean research that opens new insights and even shatters past beliefs, creating new ways of looking at the world. This is the kind of research every scientist dreams of doing but relatively few are able to attain. Of course, the reasons are complicated and include everything from true genius to serendipity. It is a matter not simply of research support but also of the very culture of science and the local environment that supports (or occasionally suppresses) individual and even collective creativity and innovation. The dynamics of the process of knowledge creation also play a critical role. New knowledge builds on past discoveries and assumed truths and may progress linearly for long periods, only to erupt from time to time in new bursts of creativity, insight and innovation. This is the history of science described in Thomas Kuhn's ***"The Structure of Scientific Revolutions"*** and more recently poignantly described by Steven Johnson in ***"The Invention of Air: A Story of Science, Faith, Revolution and the Birth of America."***

Without question biomedical research in the US is, at least to date, the most advanced and successful in the world. This largely reflects the long-standing and significant investments by the National Institutes of Health in funding basic research as well as the culture of discovery and innovation that has been fostered at our nation's research universities, medical schools and teaching hospitals. However, while peer-reviewed competitive funding has been a successful model, it does not always foster the most innovative or high-risk research. In fact, when research funding becomes more constrained, as has been the case during the past six years (except for the current burst of support associated with ARRA funding) investigators often become more cautious and less willing to propose research that is not likely to be successful. Concomitantly, funding agencies and reviewers become more risk adverse in funding proposals that seem to stray too far from pre-existing data.

Several years ago the NIH, to its credit, sought to change this pattern by funding generously a small number of highly competitively selected investigators who posed big and novel, but risky, questions that might be "paradigm shifting" but that not have gotten approved by the traditional peer-reviewed study section system. This led first to the NIH Pioneer Award followed by the New Innovator Award and more recently the Transformative R01 Award. In a sense these research awards represent a small scale but very important (and also prestigious) advance for American science and investigation. When the latest awards were announced by the NIH on September 24th, Stanford faculty once again fared remarkably well: four new Pioneer Awards, five New Innovator Awards and four Transformative RO1 Awards. This is of course wonderful news, and it poses additional interesting questions.

While Stanford is relatively small compared to its peer institutions, it has fared remarkably well in these highly competitive NIH awards for innovation. In fact, Stanford faculty received approximately 10% of this latest round of awards. Even more remarkably, of the 81 NIH Pioneer Awards that have been given since the program began in 2004, Stanford faculty has won 15 (18.5%). How is this continuous pattern of success explained?

I have been reflecting on this question and, while I recognize that my comments are speculative, I want to share them here – since our shared goal is to foster even more creative science – and scientists. Of course, a key factor of success is our remarkable talented individual faculty. But I also think that the environment and culture at Stanford have contributed to their individual and collective success. The seeds of new, creative scientific ideas need fertile soil if they are to flourish. Elements of our "soil" include Stanford's strengths as well as the culture of Silicon Valley that surrounds and interacts with it. A setting that brings together in close proximity faculty from the engineering, physical, computational and biosciences and that encourages interaction and collaboration is a unique attribute of Stanford. So too is the premium placed on recruiting and then supporting the very best faculty who can be identified and then encouraging them to push their personal limits of inquiry.

An important feature (that I must admit was initially foreign to me when I moved to Stanford from the East Coast) is the view that failure is not an end but a potential beginning. I don't want to suggest that working at Stanford (like any other premier institution) is not also associated with tremendous pressures and expectations, especially for junior faculty. And this is not to imply that the success of individuals or indeed our institution is a right. That said, I do think that Stanford's success in garnering a disproportionate share of awards for innovation is a testament to individual ingenuity, strong support and mentoring, the fostering of an entrepreneurial spirit and, of course, a hefty dose of luck. I also think that it reflects the commitment and support of our institutional leaders, especially the President and Provost, the very positive interactions among Stanford's seven schools and numerous centers and institutes and the support that we receive from our Board of Trustees and community. While it is important to give praise to the individual recipients of these recent awards, they are also tributes to the countless faculty, students and staff who work with the recipients to create an

environment that fosters creativity. We are fortunate that seeds of new ideas and fertile soil in which they can grow are both present in abundance at Stanford.

I end by offering congratulations to each of these new award winners. The details of their awards can be reviewed at http://med.stanford.edu/ism/2009/september/nih-awards.html. They include:

NIH Pioneer Awards

- ***Ajay Chawla, MD,PhD***, Assistant Professor of Medicine (Endocrinology)
- ***Chang-Zheng Chen, PhD,*** Assistant Professor of Microbiology and Immunology and member of the Baxter Laboratory in Genetic Pharmacology
- ***Markus Covert, PhD***, Assistant Professor of Bioengineering
- ***Krishna Shenoy, PhD***, Associate Professor of Electrical Engineering

New Investigator Awards

- ***Euan Ashley, MD, PhD***, Assistant Professor of Medicine (Cardiovascular Medicine)
- ***Sarah Heilshorn, PhD***, Assistant Professor of Materials Science and Engineering
- ***K.C. Huang, PhD***, Assistant Professor of Bioengineering
- ***Anna Penn, MD, PhD***, Assistant Professor of Pediatrics (Neonatal and Developmental Medicine)
- ***Justin Sonnenburg, PhD***, Assistant Professor of Microbiology and Immunology

Transformative RO1 Awards

- ***Andrew Hoffman, MD,*** Professor of Medicine (Endocrinology) and Chief of Endocrinology at the VA Palo Alto Health Care System
- ***Calvin Kuo, MD, PhD***, Associate Professor of Medicine (Hematology)
- ***Julie Parsonnet, MD***, George DeForest Barnett Professor of Medicine (Infectious Disease) and of Health Research and Policy
- ***Joseph Wu, MD, PhD***, Assistant Professor of Medicine (Cardiology) and of Radiology

Congratulations to each of the award winners – and also congratulations to Stanford for its partnership with each of them and their colleagues.

Anticipating the Future to Preserve Excellence

How the changing economic environment will affect the core missions of education, research and patient care that define and underpin academic medical centers was the focus of three groups with whom I met in the past two weeks: the Council of Deans of the AAMC (Association of American Medical Colleges), the Board of Directors

of the AAHC (Association of Academic Health Centers) and the Group of Principal Business Officers of Medical Schools (part of the AAMC).

Central to the discussions was the fact that education (which serves as the core mission of medical schools) is expensive for both students and institutions. The rising debt (now over $175,000) along with the long duration of education (when medical school is combined with residency and fellowship training) is impacting career choice, which in turn is directly affecting our healthcare system. A topic of particular concern was graduate medical education, which, over the next several years, could face some serious challenges in competition for available residency positions as a number of allopathic medical schools have increased class size and new schools have been launched. Not only has there been a failure to fund new ACGME approved residency slots, there is also considerable concern about whether the funding model for GME is sustainable. Currently it is embedded in Medicare, and there is increasing pressure on the Indirect Medical Education (IME) portion of GME funding – which will impact teaching hospitals most severely. At the same time, a number of residency program directors are recognizing that hospital based GME education needs revision so that it has a much greater focus on hospital ambulatory and community based education. Clearly these issues have significant ramifications for programs as we know them. But they are important and deserve consideration.

Coupled with these GME concerns is the reality that the cost of undergraduate medical education needs to be addressed. While I agree that this is important, I feel that this is not simply a cost problem but rather one that needs to focus on a reassessment of the models and formats used for medical education – many of which are carryovers from the 20th century. Thankfully, with the opening of the Li Ka Shing Center for Learning and Knowledge in 2010 we will have the opportunity to critically review the entire scope of our Stanford education programs.

With respect to research, every discussion, needless to say, begins with a focus on funding and the recognition that the last decade has seen more boom and bust economics than any time since the NIH was created. While virtually every school, including Stanford, is benefiting from the 2009 American Recovery & Reinvestment Act (ARRA), appropriate concerns are focusing on the funding for biomedical research in 2011 when ARRA disappears.

The impact of research funding has been experienced quite differently among various medical schools. Many built new facilities and recruited faculty only to find that it was difficult to support a research mission on an on-going basis. This should not really be a surprise since the model for research funding in the biosciences is highly leveraged on sponsored research support along with considerable institutional support. Unfortunately many schools have chased the goal of becoming a top funded school in NIH awards, which has often meant recruiting more faculty than they can support. Thankfully we have not made this mistake at Stanford since our recruitments have been more closely matched to faculty quality (rather than quantity) and our space constraints

(while painful) have compelled us to use research space more wisely and to plan new space by more realistic projections of future needs.

At the same time, we do need to critically examine our models for supporting research and to focus on how to better support an excellent but comparatively smaller research faculty than our peers. Importantly, we also need to examine more critically shared costs, especially for cores and functions that support broader communities of investigators and that are critically evaluated for function, effectiveness and cost. At the same time, we need to do all we can to advocate for sustained and predictable funding for biomedical research – an activity that I and many of our faculty leaders are actively pursuing.

The past couple of years have witnessed larger than expected margins in clinical income for physician practices and hospitals. These margins are covering the costs of education and research – as well as physician income and hospital programs (including facilities) at nearly all institutions across the country. While it is hard to predict the pace of change, this issue gives me significant concern. The assumption that payments for physician and hospital services will continue as they have in the past seems highly tenuous. Although it is hard to know the depth and pace of change at this moment, it seems inevitable that downward pressures on reimbursement for physician and hospital services, including GME, are inevitable. I have spoken to some of these issues in a second podcast led by Paul Costello, Executive Director of Communications, and my remarks can be heard at: http://med.stanford.edu/121/2009/pizzo_healthcare.html.

I won't repeat my comments or reflections here – and am first to give them a note of caution under any circumstance – but I do strongly believe that we cannot operate with the assumption that past models of success will carry us into the future. The notion that growth and greater volumes will yield better prices (while still true today) is not likely to be true in the future. Success will be measured more by evidence of quality, effectiveness, efficiency and cost containment along with evidence of innovation and discovery. While we have a long way to go to achieve the metrics of success that will be required in these likely new arenas, I am pleased that the alignments we have developed with our hospital partners at SHC and LPCH are focusing on these very issues. The immediate goal is to stay focused and aligned and recognize that while change is coming we can still play an important role in shaping that change. Without question the issues we will need to address over the next several years will engender internal as well as external debates, will pit one mission and constituency against another, and will compel us to stay focused on our core identity and mission. Stanford will not be spared the challenges that impact every academic center in the nation over the next decade and more, but it can be a leader if we don't lose sight of our mission: *To be a premier research-intensive medical school that improves health through leadership and collaborative discoveries and innovation in patient care, education and research.*

Stanford's "Mini-Med School" Begins with a Bang

On Tuesday evening, September 22nd we launched the first quarter of our first *"Mini Med School: The Dynamics of Human Health."* The Fall Quarter of this three quarter course begins with broad overview of science and medicine, from the role of the physician in society to the fundamental underpinnings of life and development to the interactions of humans with the microbes within and the environments outside them – including pandemics– changing healthcare reform and global health. In the Winter and Spring quarters we will continue with *"Medicine, Human Health and the Frontiers of Science,"* which will focus on human biological systems in health and disease.

The first edition of this course has proven amazingly popular. Even though we capped the class size at 250 participants for the first quarter, we are told that the registration for our Mini-Med School is higher than any Continuing Studies course in its 20-year history. This speaks to the interest of our community in topics related to science and medicine and the importance of engaging them in dialogue and education.

I am grateful to the outstanding faculty who have agreed to participate in this course. Our first speaker, Dr. Abraham Verghese, Professor of Medicine and Senior Associate Chair for the Theory and Practice of Medicine in the Department of Medicine, set the bar for excellence high. Dr. Verghese spoke about the role of the physician in past and modern society and also had an engaging dialogue with the participants.

I also want to thank Dr. Kathy Gillam, Senior Advisor to the Dean, for the tremendous amount of time and effort that she has put into the organization of this course.

Clinical Chairs Give Updates to Hospital Directors

It has become a tradition at the September meeting of the Stanford Hospital & Clinics (SHC) Board of Directors meeting to host a dinner event with our clinical department chairs. An important part of this is a brief presentation by each chair about various initiatives and activities going on in their departments. The event held on Wednesday, September 25th was both lovely and informative. The clinical chairs did an excellent job of describing some of the exciting work being conducted in their respective departments and, in doing so, offered a perspective on how broad and deep our clinical programs have become at Stanford Medicine. I know that the Hospital Directors were impressed and I was extremely grateful for all the work that faculty and our chairs are conducting.

Stanford Health Policy Forum – Cancelled

Due to a last minute scheduling conflict, the September 30th Stanford Health Policy Forum has been cancelled. The Forum will be rescheduled for later this fall and a new date will be posted on the Health Policy Forum's website at http://healthpolicyforum.stanford.edu.

For any questions or concerns, or to receive an email directly about this reschedule, please contact Lucy Wicks at 650-725-3339 or Lucy.Wicks@stanford.edu.

Upcoming Events

The Ninth Annual Jonathan King Lecture: *"Fiction is the Great Lie That Tells the Truth"*
Dr. Abraham Verghese, Professor and Senior Associate Chair for the Theory and Practice of Medicine in the Department of Medicine
Tuesday, October 6th
5:00 pm
Clark Center Auditorium

Symposium: "Stem Cells of the Gut and Endoderm"
October 16 & 17
Clark Center Auditorium

This symposium is co-sponsored by the Stanford Digestive Disease Center (DDC – an NIH NIDDK funded interdisciplinary center) and the Stanford Institute for Stem Cell Biology & Regenerative Medicine (SISCBRM). The DDC, under Harry Greenberg as PI/Director, is organizing Part I of the Symposium on Friday, October 16th, while the Institute for Stem Cell Biology is organizing Part II on Oct. 17th. Of note, the second day of the symposia will provide all with a chance to recognize Dr. Irv Weissman, Director of the SISCBRM.

An impressive line-up of invited speakers include Hans Clevers (Hubrecht Institute, The Netherlands); Vassilis Pachnis (National Institute for Medical Research, London); Sean Morrison (University of Michigan); Ken Zaret (University of Pennsylvania); Marcus Grompe (Oregon Health and Science University); Maria Millan (Stem Cells Inc., Palo Alto) along with Stanford faculty including Irv Weissman, Michael Clarke, Calvin Kuo, Seung Kim and Marius Wernig. If you are interested in attending the symposium please RSVP to lpjacob@stanford.edu.

Honors and Awards

Stanford Hospital & Clinics presented two awards to faculty: one for clinical excellence and the second for compassion in medicine. I am pleased to announce the award recipients:

- ***Dr. Christine Wijman***, Associate Professor of Neurology and Neurosciences and Director, Stanford Neurocritical Care Program received the Denise O'Leary Award for Clinical Excellence

- ***Dr. Stephanie Harman***, Director, Palliative Care Inpatient Consult Service and Instructor in Medicine received the Isaac Stein Award for Compassion in Medicine.

Please join me in congratulating Drs. Wijman and Harman