Dean's Newsletter
July 24, 2012

Table of Contents

- Welcome to Provost Lloyd Minor as the Next Dean of the School of Medicine
- Precision Medicine and the Health of Individuals and Communities: Managing Expectations
- Personalized Medicine Witnessed Through an Individual Lens
- The Convergence of Individuals and Institutions: Celebrating 50 Years Clinical Trials Research on Hodgkin's Disease and 51 Years of Contributions by Dr. Saul Rosenberg
- Upcoming Event: Medicine X Conference, September 28-30
- Awards and Honors
- Appointments and Promotions

Welcome to Provost Lloyd Minor as the Next Dean of the Stanford University School of Medicine

I am extremely pleased to extend my personal welcome to Dr. Lloyd Minor, who will succeed me as Dean of the School of Medicine on December 1st. Dr. Minor's contributions in science and medicine and currently as Provost of The Johns Hopkins University School of Medicine were well delineated in the announcement of his appointment on Wednesday July 18th (see: http://med.stanford.edu/ism/2012/july/minor.html). Over the weeks that I have interacted with Dr. Minor since the Search Committee and Provost completed their deliberations, I have been very impressed by the thoughtful and thorough way he has sought to learn about Stanford as a medical school and university. Dr. Minor's commitment to excellence is evident from his many past accomplishments and important leadership positions, and I am sure that he will work in a visionary and insightful manner with faculty, students, staff and leaders across the Medical Center and University to guide the future of Stanford Medicine to even greater heights and accomplishments.

While I will do so again in my last Dean's Newsletter this November, I also want to thank our entire community for their dedicated commitment to making Stanford Medicine a truly outstanding institution and community of excellence across all its missions. Despite the many challenges facing academic medical centers, the future for Stanford Medicine is exceptionally bright and is made even more so by the appointment of Dr. Minor as the next dean.

Precision Medicine and the Health of Individuals and Communities: Managing Expectations

Hardly a day goes by when there isn't a report about a promising new discovery, insight, technologic breakthrough, new test or potential treatment from the rapidly advancing world of human genomics - and the modifying impact of epigenomics,

proteomics, microbiomics, and metabolomics, now gathered under the banner of "omics." Indeed, it is a very exciting time in science and medicine, but it is also a time when enthusiasm and passion can give way to expectations that exceed current knowledge. This is a story we have witnessed many times, when enthusiasm and oversimplification can be taken for fact and when promissory messages advance beyond current realities.

At Stanford, exciting new technologies and opportunities have unfolded from the work of a number of scientists. One of the most notable is the recently reported "integrative personal genomics profile" described by Dr. Mike Snyder and his colleagues. They collected billons of bits of data serially, thus permitting a unique (and highly individualized) glimpse into how his genes and proteins responded to changing conditions of health and disease. In a seminal paper published in the March 16, 2012 issue of the journal ***Cell*** (http://www.sciencedirect.com/science/article/pii/S0092867412001663), Snyder and his colleagues reported on the monitoring of some 20,000 distinct transcripts that coded for some 12,000 genes and measured the levels of over 6,000 proteins and over a thousand metabolites. The amount of data generated from this study of a single individual is staggering and illustrates that the rate-limiting step in the future will be how to gather, store, analyze and utilize massive amounts of data. While the technology permits rapid sequencing and unique measurements to be done in humans, it will be the wisdom and subsequent algorithms developed by biostatisticians and informaticians that will permit such data to be useful in day-to-day clinical settings. Clearly these opportunities are exciting, but they are also fraught with hazard – not just because of what is now known, but also more importantly because of what remains to be learned and analyzed. Generalizing from unique individual experiences minimizes the incredible technologic, analytic and evidence based medical and even ethical issues that must be understood.

The excitement and potential of the opportunity has gone hand in hand with recent promises being made by medical centers around the nation – nearly all of which are forecasting personalized medicine as imminent and transformative. While it is easy to share in the excitement, we also have a responsibility to be cognizant of what we do know and can do now, versus what we think we can do but really don't know if we can accomplish. As in the past there is a competitive rush among academic medical centers and biomedical research institutes to be the "leader" in this endeavor. At Stanford we are fortunate to have among the most talented scientists in the world in this rapidly emerging discipline – from the molecular to the population levels. We also have the advantage of incredible depth in computer science, engineering, informatics and statistics. There is every reason to aspire to lead this field – as long as we do so with evidence and responsibility. Some of the challenges dealing with the massive deluge of data are the topic of the newly published Summer 2012 issue of Stanford Medicine (see: http://stanmed.stanford.edu/2012summer/). I encourage you to read these excellent and timely articles.

Some very difficult lessons have been learned from centers where perceived potential became a marketing tool for cancer treatment – as was evidenced by the serious problems that impacted the Duke Cancer Center in recent years (duke

http://www.nytimes.com/2011/07/08/health/research/08genes.html?_r=1). A recent series of articles in the *New York Times* also illustrates some of the extraordinary areas of promise as well as disappointment in cancer genomics (see: http://www.nytimes.com/2012/07/08/health/in-gene-sequencing-treatment-for-leukemia-glimpses-of-the-future.html?ref=ginakolata and http://www.nytimes.com/2012/07/09/health/new-frontiers-of-cancer-treatment-bring-breathtaking-swings.html?ref=ginakolata and http://www.nytimes.com/2012/07/10/health/genetic-test-changes-game-in-cancer-prognosis.html?ref=ginakolata). Of course the cycle of promise and disappointment is hardly new to scientists, physicians – or the patients and public we serve. But they are reminders to approach new knowledge with respect, thoughtfulness and evidence – as well as with enthusiasm.

The need for such balance prompted the Institute of Medicine of the National Academy of Sciences to issue a March 23, 2012 report entitled the "Evolution of Translational Omics: Lessons Learned and the Path Forward" (see: http://www.iom.edu/Reports/2012/Evolution-of-Translational-Omics.aspx). In the précis to this report, IOM notes that *"Genomics, proteomics, and other branches of molecular bioscience offer the prospect of greater precision in medical care, but some clinical tests based on "omics" research have proved invalid and highlighted the challenges of dealing with complex data. To enhance the translation of omics-based discoveries to clinical use, a new report by the Institute of Medicine recommends a detailed process to evaluate whether the data and computational steps underlying such tests are sound and the tests are ready to be used in clinical trials. The proposed process defines responsibilities and best practices for the investigators, research institutions, funders, regulators, and journals involved in development and dissemination of clinical omics-based technologies."* While the cautions and caveats noted by the IOM are important, it is not really feasible for each institution to define best practice in isolation. Rather, this is something that should be part of a national standard setting – although individual institutions, including Stanford, can help pave the way to a national dialogue.

Recognizing that the national dialogue is really in its nascent stages, it seems important to provide some guidance for how we should proceed with the "omics revolution" within the Stanford University Medical Center. Accordingly, the CEOs of Stanford Hospital and Clinics along with the Dean of the School of Medicine and the Vice Provost for Research have recently assembled two committees – one to address "omics" in clinical care at SUMC, and the second to provide guidance and recommendations on the infrastructure needed to support "omics" at SUMC. Each of the Committees includes representatives from SUMC and the University. They will be led by Dr. Steve Galli, The Mary Hewitt Loveless Professor and Chair of Pathology, and will provide a white paper report to the SUMC and University leadership by December 2012. These two Committees have just begun their work in the past week. Because this is such an important issue for our entire community I am taking the liberty of sharing the charge to each of these committees, recognizing that the scope and depth of their work and deliberations will almost certainly evolve as they get underway this month. Here are the charges:

1. ***To the Guidelines and Policy Committee: make recommendations and develop guidelines regarding the use of genomic and other "omics"-based data (such as those derived from assessments of patients' transcriptomes, proteomes, metabolomes, microbiomes, etc.) for the clinical care of patients at SHC and LPCH. Specific charges include***:

   - Make detailed recommendations regarding how to provide such "omics-guided" clinical care in a manner that advances the goals of providing leading edge and coordinated patient care and ensuring that Stanford take a leadership role in such efforts, while also maintaining full compliance with all applicable certification requirements, regulations, and policies that apply to such testing, including HIPAA, CLIA, and Joint Commission/CAP/ASHI.

   - Ensure that the recommendations set guidelines for the appropriate use of "omics testing" that: (1) clearly differentiate between the requirements to define the analytical and clinical validity of such testing, and those required to document clinical utility; (2) differentiate between the use of such testing for research vs. clinical care; (3) ensure that SUMC physicians and their patients who agree to have omics testing performed (whether on themselves or on dependents such as minor children) understand when the testing is being done solely or partly for research as opposed to when and how such testing can be used solely or partly for clinical care, including the limitations of testing that does not have documented clinical utility; and (4) develop guidelines for when the availability or use of such testing can be reported in any news releases, advertising, or fund-raising activities of the SOM, SHC or LPCH and how the clear distinction between the research and clinical uses of such testing should be maintained.

   - Provide estimates of the costs of various approaches to implementing its recommendations.

   - Propose a mechanism to provide scientific and clinical oversight of this ongoing effort.

   - Recommend an oversight mechanism that ensures that such testing is developed and performed in full compliance with Stanford's policies regarding individual and institutional conflicts of interest.

   - Produce a white paper document to convey these recommendations to the SUMC and University leadership.

2. ***To the Infrastructure Committee: make recommendations regarding the requirements for data storage, security, and use for employing human genomes and other large data sets (such as those derived from other "omics" analyses, or***

from digital anatomic pathology or radiology) for the care of patients at SHC and LPCH

- Make recommendations regarding the requirements for: (1) acquiring and managing the amount of data storage capacity (whether within SUMC or elsewhere), (2) security provisions, and (3) IT functionality needed in order to use large data sets such as those derived from genomic and other "omics" studies to care for patients at SHC and LPCH in a manner that is fully compliant with all applicable certification requirements, regulations, and policies that apply to such testing, including HIPAA, CLIA, and Joint Commission/CAP/ASHI. The recommendations should specifically address the issue of whether patients' individual genomes or other large data sets should be embedded in the patients' SHC or LPCH EMRs, or instead should be accessible when needed for clinical care but stored outside of the standard EMR.

- Define the: (1) facilities, (2) personnel (professional and support), and (3) institutional capabilities required for the bioinformatic analysis of the results of such testing, and for linking such data, and such data analysis tools to the electronic medical records of SHC and LPCH.

- Provide estimates of the costs of various approaches to implementing its recommendations.

- Propose a mechanism to provide scientific, IT and clinical oversight of this ongoing effort.

- Recommend an oversight mechanism that ensures that such bioinformatics analysis and other IT functionality is developed and performed in full compliance with Stanford's policies regarding individual and institutional conflicts of interest.

- Contribute to a white paper document to convey these recommendations for the SUMC and University leadership.

There is little question that these deliberations will be a work in progress that will be informed by new insights along with data emerging from Stanford as well as from institutions around the nation and world. Importantly, these Committees will also help inform other major initiatives underway to align precision medicine with population health sciences. The goal of this alignment is to create a bidirectional flow of knowledge on the inherent biological and environmental factors affecting health and disease for individuals as well as for communities. These are exciting opportunities that will change the way we think about human biology and establish new paradigms for how we care for communities.

Personalized Medicine Witnessed Through an Individual Lens

Appropriately, there is a much greater focus on preserving health and wellness now, as part of the evolving health care reform debates and discussions in the US, than in previous eras. Of course, an important component of preserving health is personal responsibility. We all recognize that there are features of health and disease that we can't control as individuals because of genetic or epigenetic risk factors (as discussed above) or because of just bad luck. Often when physicians or the public think of preserving health, diet and exercise quickly become prominent in the discussion. And for good reason! There is no question that obesity is becoming a major health liability in the US and that it is rapidly emerging as a worldwide problem, with short and long-term consequences to individuals and societies. We also recognize how valuable exercise is to physical wellness – from cardiovascular health to helping prevent dementia – and we know as well that lack of exercise impacts obesity and that obesity negatively impacts exercise.

In a number of ways I have not been shy about sharing my personal views on personal health as well as broader topics about healthcare in the US. I have tried to "practice what I preach" about personal health and wellness, and I thought I was making good decisions about exercise and diet. But I missed a simple health maintenance practice that has had a number of negative personal consequences and that has compelled me to consider another facet of wellness through a different lens. Moreover, as I have become more attentive to this practice, I also see it is one overlooked by many of my colleagues as well, probably including a number of you. It came to my personal attention in an ironic way.

In late April of this year I was preparing to leave on the red eye to DC (a regular itinerary for me) that was to include a meeting the next day with the Office of the Secretary of the Department of Health and Human Services about a report that I had chaired for the Institute of Medicine. Having spent nearly eight intense months with a dedicated committee, our report, entitled ***"Relieving Pain in America"***, addressed the public health problems associated with chronic pain. More than 100 million American adults experience chronic pain from various causes at a cost of $560-635 billion dollars per year. That's more than we spend as a nation on cardiovascular disease, cancer and diabetes combined. Despite these expenditures and the incredible toll on individuals and the nation, we lack many of the tools to accurately diagnose, treat and prevent chronic pain. Our report proposed *"A Blueprint for Transforming Prevention, Care, Education, and Research"* (which published in November 2011 by the National Academies Press). What I didn't realize as I helped prepare the report on pain in America and got ready to return to Washington to help continue to foster its implementation was that I would soon be one of the 100 million. It began, as it often does, with a simple act that was soon accompanied by acute back pain that has been followed by a long chronic phase mandating a number of changes and accommodations. I was first surprised but, in retrospect, recognize that I had not taken the personal responsibility to avoid or prevent this injury.

Part of the problem was that until this personal health challenge arose, I thought of myself as in "great shape." For many (many) years I have run 50-70 miles per week,

without any real joint aches or pains, seeming to defy the conventional wisdom that one gets out of balance. Of course, what I hadn't done (despite many cautions to do so) was to also pay attention to building "core body strength" and preserving a healthy posture. In fact I had done terribly in both areas. Since April, I have now done what tens of millions of Americans have had to do, to greater or lesser extents. I have sought medical advice, had MR scanning, had physical therapy, utilized acupuncture, done lots of exercises and stretches - and engaged in posture training (which has been particularly challenging for a body with decades of sitting and standing in the wrong directions).

So, why I am sharing this personal saga with you? I now recognize that my problems, probably like tens of millions of others, is a result of not paying attention to well known features of personal wellness. Of course I realize that sharing my personal experience as advice is starting to sound paternalistic – although I remember well the admonitions of friends and colleagues about how poor my posture was. But that is not the reason for this commentary. Now that I am actually paying more attention to posture for my own health and wellness, I am also more attentive to how significant an occupational hazard it is in our community. Over the years I have heard from countless surgeons and anesthesiologists about their personal encounters with neck and back pains that not infrequently curtailed or limited their clinical practice and that were the result of their posture and position in the operating room,. It is not, however just in the operating room, since most of us are slumped over computers, just as I am now trying **not** to do as I type this Newsletter. Accordingly, I have used my personal experience to also address this topic with a number of our surgical leaders and colleagues, encouraging them to include posture and ergonomic management for new trainees to help them prevent adopting sitting and standing patterns that will ultimately have a consequence on personal well-being. Similar concerns really apply to all of us whether we are caring for patients, working at the bench or sitting in front of computers.

As I have noted above, the expense of treating pain in America is truly astounding. And ascertaining one's personal genomic sequence would influence almost none of the outcomes, including early diagnosis and management. But many billions of dollars that are spent on lost productivity in the workplace, as well as the cost for medical interventions, could be saved if we devoted more attention to posture, ergonomics and core strengthening, in addition to diet and exercise. I see this more clearly through my personal experience – and I also see lots of my colleagues who are in the queue for a similar experience to mine unless simple health and wellness procedures are exercised, literally and figuratively.

The Convergence of Individuals and Institutions: Celebrating 50 Years of Clinical Trials Research on Hodgkin's Disease and 51 Years of Contributions by Dr. Saul Rosenberg

Friday, July 13th featured a ***"Celebration of Success in the Treatment of Hodgkin's Disease"*** (see also http://med.stanford.edu/ism/2012/july/hodgkins-0716.html

). Fifty years ago the first clinical trial on Hodgkin's disease was done at Stanford led by the pioneering partnership of Drs. Henry Kaplan and Saul Rosenberg. Five decades later the world of cancer biology and Hodgkin's disease has changed dramatically and serves as a remarkable beacon for discovery and innovation in science and medicine. Work begun at Stanford in Hodgkin's disease in 1962 created collaborations and debates of global significance. Studies in Hodgkin's disease helped shape the field of radiation oncology (largely because of the invention by Kaplan and Ginzton of the linear accelerator). This work also helped define the use of cancer chemotherapy as well as the role of combination chemotherapy and multi-modal therapy. It shaped the way clinical trials were conducted at single institutions and as multi-institutional trials.

This work gave rise to the concept and use of multidisciplinary teams, tumor conferences and collaboration between specialists in medical and pediatric oncology, radiation oncology, surgical oncology, pathology, and supportive care. The follow-up of Hodgkin disease survivors gave evidence of long-term complications (including second malignancies and organ damage) that, in turn, shaped the direction of subsequent clinical studies. As one looks at the history of Hodgkin's disease one can witness the story of cancer diagnosis, treatment and prevention that shaped the latter part of the 20th century and that is being reconfigured with more specific diagnostic tools and treatments in the 21st century. (Parenthetically, a highly readable book that tells the story of Hodgkin's disease and other important malignancies in the Pulitzer Prize winning 2010 book entitled ***The Emperor of All Maladies: A Biography of Cancer,*** by Dr. Siddhartha Mukherjee).

The symposium on July 13th also brought together many of the seminal investigators from around the world who contributed to the successful treatment of Hodgkin's disease. Importantly, this event appropriately celebrated the 51 year career of Dr. Saul Rosenberg on the Stanford faculty and his transformative role in defining and finding successful treatments for Hodgkin's disease. It is a unique story of individuals and institutions with pioneering ideas and the dedication to bring them to fruition for the benefit of patients. The institutional star of Stanford and Dr. Saul Rosenberg's own star shine very brightly in this story.

Special thanks to the Stanford Lymphoma group and especially Drs. Richard Hoppe and Ranjana Advani for their incredible efforts in making the event possible – and for their own important roles in contributing to the successful treatment of Hodgkin's disease.

UPCOMING EVENTS

Medicine X Conference
September 28-30
Li Ka Shing Center for Learning and Knowledge
Discount available for Stanford community

Medicine X is an exciting new conference that explores how emerging technologies will reshape the practice of health and medicine. The conference takes place Sept. 28-30 at the Li Ka Shing Center for Learning and Knowledge. The conference will

feature two days of talks by leaders from around the world, a Self Tracking Symposium, and once-in-a-lifetime chance to participate in a design workshop at design firm IDEO. Discounted tickets (up to 56 percent off) are available for faculty, staff, students, and alumni until Monday, August 6th. STAP funds may be used for reimbursement of the registration fees with your supervisor's approval. For more information, visit: http://stan.md/medxstanford

Awards and Honors

- ***Dr. James Brooks*** was named the first incumbent of the Keith and Jan Hurlbut Professorship in Urology at a wonderful celebratory dinner on July 11th. Congratulations to Dr. Brooks.
- ***Dr. Tracy Rydel,*** Clinical Assistant Professor of Medicine, and ***Dr. Sermsak (Sam) Lolak,*** Clinical Assistant Professor of Psychiatry and Behavioral Sciences, have been selected as Rathmann Family Foundation Educators-4-CARE (E4C) Medical Education Fellows in Patient-Centered Care for 2012-2013. This program provides the part-time salary support for a Stanford faculty, fellow, or chief resident to pursue further study and activities focused on the promotion of patient-centered care in medical education. The Educators-4-CARE program, launched in 2008, formally recognizes the critical importance of mentors and clinical teachers by providing tangible support to a cadre of skilled and dedicated teachers of the practice of medicine
  Please join us in congratulating Drs. Rydel and Lolak for this important achievement.
- ***Dr. Joseph P. Garner***, Associate Professor of Comparative Medicine, has just been named the recipient of AALAS' 2012 Bhatt Young Investigator Award. This prestigious award is given to an outstanding young scientist who has made significant contributions to the fields of laboratory animal science or comparative medicine. Joe's research on animal behavior and animal models of human psychiatric disorders have truly advanced these fields.
- ***Dr. John Pringle,*** Professor of Genetics, has been selected to receive the Lifetime Achievement Award from the Genetics Society of America. This major recognition is given for lifetime contributions in the field of yeast genetics and outstanding community service. The award will be presented to Dr. Pringle at the Yeast Genetics and Molecular Biology Meeting on August 3rd at Princeton University.
- ***The Arnold Gold Foundations Award for Humanism and Professionalism in Medicine*** was awarded to 16 medical students based on recommendations of their peers and colleagues at a celebratory event on Friday July 20th. The honorees include:
  - Yi An, SMS 5
  - Joseph Carpenter, SMS 4
  - Andrew Chang, SMS 5
  - Stesha Doku, SMS 5
  - Harry Flaster, SMS 5
  - Deepa Galaiya, SMS 5

- Jeremy Harris, SMS 4
- Walter Igawa-Silva, SMS 6
- Ahlia Kattan, SMS 4
- Ashley Koegel, SMS 5
- Anna Krawisz, SMS 5
- Temitope Lanre-Amos, SMS 4
- Julia Pederson, SMS 4
- Stephanie Smith, SMS 4
- Amy Waterlain, SMS 4
- Joslyn Woodward, SMS 5

Please join me in congratulating this year's recipients of the Arnold Gold Foundation Award for Humanism and Professionalism in Medicine.

Appointments and Promotions

Daniel T. Chang has been promoted as Associate Professor of Radiation Oncology, effective 6/01/12.

Hayley Gans has been reappointed as Assistant Professor of Pediatrics, effective 8/01/13.

Robert Harrington has been appointed as Professor of Medicine, effective 7/01/12.

Stephen Luby has been appointed as Professor of Medicine, Senior Fellow at the Freeman Spogli Institute for International Studies and Senior Fellow at the Woods Institute for the Environment, effective 9/01/12.

Josef Parvizi has been promoted as Associate Professor of Neurology and Neurological Sciences, effective 6/01/12.

Lee Sanders has been appointed as Associate Professor of Pediatrics, effective 6/01/12.

Stephen L. Skirboll has been promoted as Associate Professor of Neurosurgery, effective 6/01/12.

Justin L. Sonnenburg has been reappointed as Assistant Professor of Microbiology and Immunology, effective 6/01/12.