

P4 Medicine: Personalized, Predictive, Preventive, Participatory A Change of View that Changes Everything

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Medicine is now undergoing a major revolution that will transform the nature of healthcare from reactive to preventive. The changes will be catalyzed by a new systems approach to disease that will trigger the emergence of personalized medicine — a medicine that focuses on the integrated diagnosis, treatment and prevention of disease in individual patients.

This change is rooted in new science². The convergence of systems approaches to disease, new measurement and visualization technologies, and new computational and mathematical tools can be expected to allow our current, largely reactive mode of medicine, where we wait until the patient is sick before responding, to be replaced over the next 10 to 20 years by a personalized, predictive, preventive, and participatory (P4) medicine that will be cost effective and increasingly focused on wellness.

Key benefits of P4 medicine, to the patient and to the system, include new abilities to:

- Detect disease at an earlier stage, when it is easier and less expensive to treat effectively
- Stratify patients into groups that enable the selection of optimal therapy
- Reduce adverse drug reactions by more effective early assessment of individual drug responses
- Improve the selection of new biochemical targets for drug discovery
- Reduce the time, cost, and failure rate of clinical trials for new therapies
- Shift the emphasis in medicine from reaction to prevention and from disease to wellness

P4 medicine promises to sharply reverse the ever escalating costs of healthcare – introducing diagnosis to stratify patients and disease, less expensive approaches to drug discovery, preventive medicine and wellness, and exponentially cost-decreasing measurement technologies. P4 medicine also promises to improve patient outcomes, and to empower both the patient and the physician. Having much more, and more accurate, information to be used by the patient and the doctor to make decisions about prevention and treatment is at the heart of this future medicine.

We must accelerate this transformation by promoting the necessary scientific research and at the same time dealing with the societal challenges presented by P4 medicine. The healthcare industry, public policy sector, and consumer industries will of necessity be required to develop new and creative business models and products. There is a unique opportunity now to enable and accelerate change by eliminating the key technical and societal (ethical, societal, policy, legal, economic, etc.) barriers that will prevent the full realization of the revolution of P4 medicine.

¹ For the most current version of this essay, as well as related essays, visit <http://www.cra.org/ccc/initiatives>

² Hood, Leroy. A Personal View of Molecular Technology and How It Has Changed Biology. *J. Proteome Research*. 2002.
<http://lazowska.cs.washington.edu/initiatives/JPR.pdf>

On the scientific front, a broad interdisciplinary approach, employing scientists and engineers of all types, is essential to this change – systems biology, including computational methods, technology development and global measurement and analysis of biological systems is essential. Much of the conventional medical research and practice will have to be replaced with systems approaches to catalyze this transformation.

On the policy front, we must make sure that policies with respect to privacy, non-discrimination, and access to health insurance, all critical for any health care system, are aligned to maximize both the protections and the benefits to patients. The opportunity arises for unusual strategic partnerships between government, the academy and the commercial sectors. The societal, ethical and healthcare policy issues attendant to the anticipated changes will be profound. These changes must also be planned for so that the barriers to delivery of the benefits of the coming technical advances will not prevent their adoption.

Scientific/Technological Objectives

A coordinated and integrated program can be envisioned, based on the following key objectives, to accelerate solving the technical challenges of P4 medicine.

- Methods for determining individualized genomes – personalized genome sequencing – new methods and approaches are necessary, but to deploy its predictive power these data will have to be integrated with diagnostic measurement data.
- Methods for determining the levels of organ-specific proteins, microRNAs and other possible biomarkers, including cells, in the blood to assess the health or disease in all major human organ systems and thus monitor the earliest onset of disease with its implications for more effective treatment.
- Digitize medical records and create effective and secure databases for individual patient records (new, data intense records with gigabytes of data). When the diagnostic methods are available the medical interpretation of the patterns observed from blood data will become increasingly rich and informative as science and databases advance.
- Develop new mathematical and computational methods for extracting maximum information from molecular information on individuals (including their genomes), and from other clinical data and history. Develop new computational techniques for building dynamic and disease-predictive networks from massive amounts of integrated genomic, proteomic, metabolomic and higher level phenotypic data. This is the heart of the new medicine: new methods for interrogating and understanding the interaction between the environment and the genome of the individual.
- Drug perturbations of biological networks to be understood in a predictive sense. These problems are experimental and computational. Therapeutic perturbations of biological networks re-engineering of networks in higher organisms with drugs (diseased back to normal).
- Among the great opportunities here are new methods for creating pluripotent cells (stem cells) from normal, differentiated cells, and then differentiating them to specific body cell types. The practical methods are developing rapidly, but the understanding will be complex and very important. The ability to create stem cells with a given individual's genome will be remarkable, understanding it will be revolutionary.
- Imaging molecular disease indications. New *In vivo* molecular imaging methods and analysis methods to follow disease, drug response, drug effectiveness, drug dosage determinations etc. This

technology is developing rapidly. Integrating this kind of data with all the other measurement data to make predictions and diagnoses is an important challenge.

- Handling the enormous personalized data sets—policies, security, quality control (validation), mining, reporting, modeling, etc. Technically challenging, requiring significant investment and effort, but completely achievable. The challenges here are large, but they include the challenge of making transparent interfaces for researchers, basic and clinical, to mine, analyze and visualize this data. All these are essential for its effective use in future.
- Education of patients and physicians about P4 Medicine. For the full effect of the changes discussed here to be felt patients must be well informed about their personal choices in many different ways. At least as important is a profound change in the way that physicians understand the medical issues (therefore medical school education must be radically changed) and how they relate to their patients. The patient-physician relationship will undoubtedly change dramatically. These issues are key to how information can be presented effectively to physicians, practitioners and patients.

Policy Requirements

- Invest in public health and education: Put fitness curricula back into schools and promote access to healthy foods.
- Reorient care delivery: Implement a patient advocate role, reinvent primary care, change the medical curriculum and recognize patient choices.
- Empower and activate patients: Shift behavior from “system” to individual responsibility. Support personalized medicine.
- Establish leadership: Create a national imperative around wellness and health. Shift resources to quality of life versus end of life.
- Conduct research aggressively: Develop clinical and scientific consensus on what works, overcome technical barriers, and better define healthcare goals and desired outcomes. Develop and promote science and technology to find and deliver cures, and access the pools of capital waiting for solutions.
- Create metrics and goals: Set a benchmark for the U.S. to become the “healthiest nation,” like putting a man on the moon. Define wellness and health, by age cohort from birth to death. Measuring wellness is the “true north.”
- Foster the development of an Information Infrastructure: Leverage technology and automation that will drive patients to engage with their physicians. Patients need an algorithm of choices.
- Redesign incentives: Change the reimbursement system. Stop paying for volume and start paying for quality. Provide government incentives to create investments in wellness. Create incentives to achieve better collaboration and to keep people healthy.
- Address the lack of leadership and systematic coordination among key stakeholders in addressing key complex problems that is preventing the acceleration towards the adoption of personalized medicine. This means optimizing the interactions of a complex network of interacting healthcare constituents.
- Address uncertain regulatory requirements, insufficient insurance reimbursement for diagnostic tests linked to pre-emptive care, incomplete legal protections to prevent genetic discrimination, and lack of a comprehensive healthcare information technology system and standards, all of which erode the potential for the future.