

HGM2008 plenary abstracts: genome functions and systems biology

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009: Systems Medicine, Transformational Technologies and the Emergence of Predictive, Personalized, Preventive and Participatory (P4) Medicine

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The challenge for biology in the twenty first century is the need to deal with its incredible complexity. One powerful way to think of biology is to view it as an informational science. This view leads to the conclusion that biological information is captured, mined, integrated and finally executed by biological networks. Hence the challenge in understanding biological complexity is that of deciphering the operation of dynamic biological networks across the three time scales of life-evolution, development and physiological responses. Systems approaches to biology are focused on delineating and deciphering dynamic biological networks and their interactions with simple and complex molecular machines. I will focus on our efforts at a systems approach to disease-looking at prion disease and cancer. I will also discuss the emerging technologies (measurement and visualization) that will transform medicine over the next 10 years. It appears that systems medicine, together with pioneering changes in DNA sequencing and blood protein measurements (nanotechnology) and as well as the development of powerful new computational and mathematical tools will transform medicine over the next 5–20 years from its currently reactive state to a mode that is predictive, personalized, preventive and participatory (P4). This will in turn lead to the digitalization of medicine-with ultimately a profound decrease in the cost of healthcare. It will also transform the business strategies for virtually every sector of the health care industry. These considerations have led ISB to begin formulating a series of national and international strategic partnerships that are focused on making P4 medicine a reality. I will discuss some of these strategic partnerships and discuss the implications arising from the globalization of science.

010: A robustness-based approach to systems-oriented drug design

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Many potential drugs that specifically target a particular protein considered to underlie a given disease have been found to be less effective than hoped, or to cause significant side effects. The intrinsic robustness of living systems against various perturbations is a key factor that prevents such compounds from being successful. By studying complex network systems and reformulating control and communication theories that are well established in engineering, a theoretical foundation for a systems-oriented approach to more effectively control the robustness of living systems, particularly at the cellular level, could be developed. Here, I use examples that are based on existing drugs to illustrate the concept of robustness, and then discuss how a greater consideration of the importance of robustness could influence the design of new drugs that will be intended to control complex systems.

011: Information processing by the intracellular signaling network

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The coordinated response of a cell to environmental cues such as growth factors and hormones is mediated through the activation of various signal transduction pathways. Our current perception of signaling pathways is that they constitute a highly complex network that, like most other complex networks, exhibits a scale-free topology. Consequently, the functional outcome of signal transduction would likely represent the integrated result of the intricate and varied interactions between the numerous individual constituents of the network. While overall topology of the signaling network has been revealed, mechanisms that regulate the pathways embedded within this network continue to remain enigmatic. For instance, the question of how the amplitude and rate of signal transfer are modulated is yet unclear. Stimulation of a given cell surface receptor with different agonists is known to evoke diverse cellular responses, although they all activate the same intracellular pathways. This is especially true in the case of lymphocytes, where variations in the nature of antigen receptor triggering can lead to the opposing and extreme outcomes of cell death on the one hand, to proliferation and differentiation on the other. While such observations point to the inherent plasticity of signaling networks, how this is achieved remains to be clarified.

Studies from our laboratory suggest that, during the process of signal transduction, the individual components of the network exhibit chaotic behavior. As a result, transmission of signal through the modules of the network occurs in a non-synchronized manner. Importantly, it is this feature of asynchronous transmission that provides the operational framework for signal processing in a combinatorial manner and thus accounts for the plasticity of the signaling network.

012: The \$10 Million Dollar Archon X PRIZE in Genomics

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Incentive prizes for technological breakthroughs have a long history of successfully advancing science and engineering. The X PRIZE Foundation has lead the way in creating a series of incentive prizes that will result in innovations that makes a lasting impact. Although a technological breakthrough can meet this criterion, so do prizes which inspire teams to use existing technologies, knowledge or systems in

more effective ways? As scientists gain knowledge from mapping the Human Genome, they will also find new ways to treat and even prevent disease. To build the library of information necessary to advance the field of genomic medicine, it is imperative that we develop DNA sequencing technology that is faster and affordable. To stimulate breakthrough innovation in the field of genomic sequencing and to help lay the groundwork for the era of personalized medicine, the X PRIZE Foundation has launched a global competition with a \$10 million (USD) prize for the winner of the Archon X PRIZE for Genomics. The \$10 million X PRIZE for Genomics prize purse will be awarded to the first non-governmental Team that can develop a system and use it

- to sequence 100 human genomes
- within 10 days or less
- with an accuracy of no more than one error in every 100,000 bases
- with sequences accurately covering at least 98% of the reference genome
- with complete Haplotype information
- at a recurring cost of no more than \$10,000 per genome.

The presentation will discuss the current teams in the competition, the rationale for the winning criteria, and the ways in which the X PRIZE Foundation is developing methods to deal with judging of the contest, validation of data and ensuring ethical standards for the individuals whose DNA is involved in the contest.