Systems Biology: A Disruptive Technology

By Ken Rubenstein, PhD

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This report focuses on the current and future applications of Systems Biology in drug discovery, specifically in pinpointing optimal individual targets, and combinations of targets, to overcome metabolic pathway redundancies, leading to efficacious and safe products. Topics covered include:

• Application successes at AstraZeneca, Pfizer, and J&J
  • Landscape of the Systems Biology marketplace and its future
  • Implications of innovative predictive modeling and global transcription epigenetics analysis
  • Review of 18 Systems Biology company business models
  • How SB will enable pharmacological progress in biologically complex “money” diseases
  • Projections on the future for Systems Biology in leukemia, Alzheimer’s, and Huntington’s diseases.

Continued on next page
Systems biology (SB) is challenging the existing dominant drug discovery approaches and on track to becoming a classic disruptive technology. This report describes examples of SB successes in big pharma and current SB applications as well as the radically new concepts emerging from basic SB research.

The report provides a survey on the origins of SB and the varying definitions in common use and then moves to a review of the current bioanalytical- and bioinformatics-based technologies for making sense of omic’s data through enabling pathway and network analysis. Pathway analysis, cell modeling, and disease modeling technologies today dominate the bioinformatics branch of systems biology. Database-mediated pathway analysis studies, which are particularly popular today, help to discover meaning in global biological data for drug discovery and diagnostics. As examples, systems biology approaches played a key role in understanding AstraZeneca’s Iressa (gefitinib), liver abnormalities were identified by Pfizer, and Johnson & Johnson identified a kinase inhibitor mechanism. Next, the report provides an overview of the recent explosion of academic SB activity and implications for highly novel approaches to drug discovery and diagnostics not envisioned today. Examples include nanosystems studies to construct a predictive model for transcription control, ChIP-on-chip technology for global transcription factor identification, and methylation-specific polymerase chain reaction (PCR) for global DNA methylation detection as an entry point to epigenetics.

**Systems Biology: A Disruptive Technology** provides an analysis of the commercial activities of 18 small systems biology companies reviewed in the context of the nature and dynamics of the systems biology market: the business models, deals, scope, and prospects. As examples, commercial databases and software programs from companies such as Ingenuity Systems (Redwood City, CA), GeneGo (St. Joseph, MI), and Ariadne Genomics (Rockville, MD) provide enhanced usability and comprehensiveness. Genstruct’s Knowledge Assembly platform enables “knowledge-driven systems biology;” Gene Network Sciences’ (Cambridge, MA) REFS (Reverse Engineering and Forward Simulation) systems permit reverse engineering and hypothesis generation from omic data; and Entelos’ (Foster City, CA) PhysioLab biosimulation models, which incorporate both molecular and higher-order disease data, permit construction of “virtual patients.”

**Systems Biology: A Disruptive Technology** concludes with a discussion and speculation as to the future for SB, supported by interviews with scientists and managers deeply engaged in this space. This analysis explains how and why pharma and diagnostics industries will benefit from advances in SB by leading to highly novel approaches for application to drug discovery and diagnostics discovery and development.

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About the Author: Ken Rubenstein, PhD, a biochemist and molecular biologist, received his PhD at the University of Wisconsin and postdoctoral training at the University of Pennsylvania School of Medicine. He was a key innovator and research manager for Syva Company, the diagnostics branch of Syntex Corporation. During his 13 years with Syva, Dr. Rubenstein became vice president, scientific affairs, a function that included strategic planning. Since 1983, he has served as a technology and marketing consultant to biomedical companies and an industry analyst, with more than 40 published studies to his credit.
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Colin Hill, CEO, President, Chairman, and Co-Founder, Gene Network Sciences, Cambridge, MA
David Lester, PhD, President and Founder, ITHW, Inc., Morristown, NJ
Stephen Naylor, PhD, Chairman, CEO, and Co-Founder, Predictive Physiology and Medicine (PPM), Bloomington, IN

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