An Audacious Proposal

for Transforming and Democratizing Healthcare

Dr. Lee Hood, President and Co-Founder of ISB

At ISB, we remain committed to **inventing the future of human health**, with the ultimate objective of democratizing healthcare in developed and developing countries worldwide. In last year's annual report, we proposed a digital-age, Framingham-like longitudinal study over 25 years for 100,000 well individuals. Phase 1 of the **100K Wellness Project** launched in March 2014 with a group of "100 Pioneers" whose early results have been spectacular. Phases 2–4 will scale the study to 1,000 participants in 2015, 10,000 in 2016 and eventually 100,000.

This year, we want to make another **audacious proposal** that will leverage the striking response to the 100K study that we've received from many leaders at research institutions, medical centers and innovative health systems in the U.S. and abroad who have already initiated strategic partnership discussions with us. Internationally, we envision a franchise-like model with rigorous scientific and security standards and an agreement to aggregate and share data. This will enable seamless coordination across the countries that become early adopters.

The 100K study harnesses **ISB's systems approach to disease** and expertise in the integrated analyses of biological data. We first gather the genome sequences of participants and then collect blood, saliva, stool and urine samples every three months in order to measure microbiome diversity in the gut; clinical chemistries that are focused on nutrition; 1,600 blood metabolites; epigenetic (methylation) status of white blood cell DNA; blood organ-specific fingerprints from the brain, heart and liver; selected hormones; ongoing clinical histories, psychological tests, and data from "quantified-self" devices including heart rate, activity, sleep quality, blood pressure, weight, etc. These measurements form a **dynamical personalized data cloud** for each participant that enables us to study the molecular basis of health and disease. As the study grows, it will help distinguish between those who remain well or improve in health and those who transition into disease. This insight will allow us to construct multiparameter **metrics for wellness**—a term now defined by fuzzy psychological criteria—and study the initiation and progression of disease.

When integrated with health coaching and medical oversight, these metrics create **"actionable outcomes"** that allow participants to increase their wellness or to facilitate early transition from disease back to a wellness trajectory. So far, after having analyzed just a few types of data, we've found that 100 percent of the 100 Pioneers have multiple actionable possibilities—thus confirming our hypothesis that virtually all individuals will have the potential to improve their wellness and/or avoid disease.

Why ISB

The 100K Wellness Project emerged over the past decade from ISB's application of systems approaches to the study of disease. What we now term **"systems medicine"** has reached a tipping point and is changing the practice of medicine through ISB's many pioneering technologies and systems strategies: identifying disease genes through family genome sequencing, delineating panels of blood proteins that can distinguish benign from cancerous lung nodules, stratifying disease into its distinct subtypes, developing computational approaches to identify new drug target candidates, etc. Also, our faculty have expertise and interest in: genomic, proteomic, metabolomic and physiological assays; single-cell assays that serve as windows into human biology and disease; the microbiome's influence on health; and big-data analytics and predictive modeling.

The convergence of systems medicine, big data and patient-activated social networks has led to a medicine that is **predictive, preventive, personalized and participatory—P4 medicine.** P4 is proactive, focused on the individual and wellness, creates virtual dynamical clouds of billions of data points for each patient that can be used to optimize wellness and minimize disease, contends that clinical trials should be done in the context of individuals rather than large populations, and employs patient-activated social networks for crowd sourcing, learning and advocacy. Contemporary medicine is focused almost completely on disease. **The 100K study embodies P4** principles and serves as a pilot project for bringing P4 medicine to the U.S. healthcare system and, perhaps, to those of other nations.

The benefits of the 100K initiative are truly staggering. The collected data will reveal actionable possibilities for optimizing wellness and minimizing disease. Creating multiparameter metrics for wellness will quantitatively define such fundamental human aspects such as stress, resilience, energy and physiological versus chronological age. Identifying and treating diseases at the earliest transitions will **save billions of healthcare dollars**. This project will push essential advancements in technology from mobile applications that can measure, for example, a droplet of blood to the development of a global IT for healthcare.

With the introduction of P4 medicine into the healthcare system, industry will have to rewrite business and clinical plans to remain competitive. A lucrative industry will emerge as bold innovators become the Googles and Microsofts of wellness. And as P4 spreads through developed and underdeveloped nations, the cost savings will enable the P4 practices worldwide that will **democratize healthcare**.

The Potential for U.S. Leadership

The U.S. can be at the forefront of this transformation by positioning itself as a global innovator through the advancement of science, technology, IT for healthcare (big data) and medicine. This would fundamentally transform the nature of healthcare through the introduction of **the concept of wellness as the foundation for medicine of the 21st century**, thus fostering innovation and spurring investment in the U.S. economy.

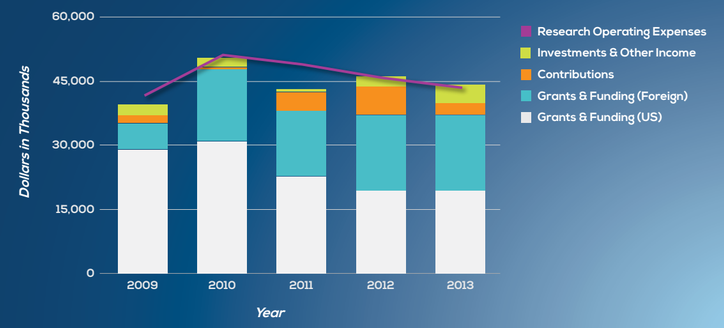
We are building a **coalition of like-minded colleagues** to successfully engage Congress and the Administration to create a nationally supported 100K Wellness Project. A bipartisan federal initiative would ensure that the U.S. maintain global leadership in P4 medicine. Success will require broad scientific collaborations and partnerships with visionary policy makers who **value as a national priority the improved health of our citizens**, the concomitant healthcare savings, and the explosion of private industry opportunities.

Financial Statement

Year Ending December 31, 2013

5-Year Overview

Research Operating Expenses vs. Total Revenue



Balance Sheet

Dollars in Thousands

Assets	$
Cash & Investments	23,714
Other Assets	10,978
Property & Equipment (Net)	12,961
Total Assets	**47,653**

Liabilities	$
Accounts Payable & Accrued Expenses	18,810
Deferred Revenues	2,981
Notes Payable	7,823
Total Liabilities	**29,614**

Net Assets	$
Unrestricted Net Assets	375
Temporarily Restricted Net Assets	8,992
Permanently Restricted Net Assets	8,672
Total Net Assets	**18,039**

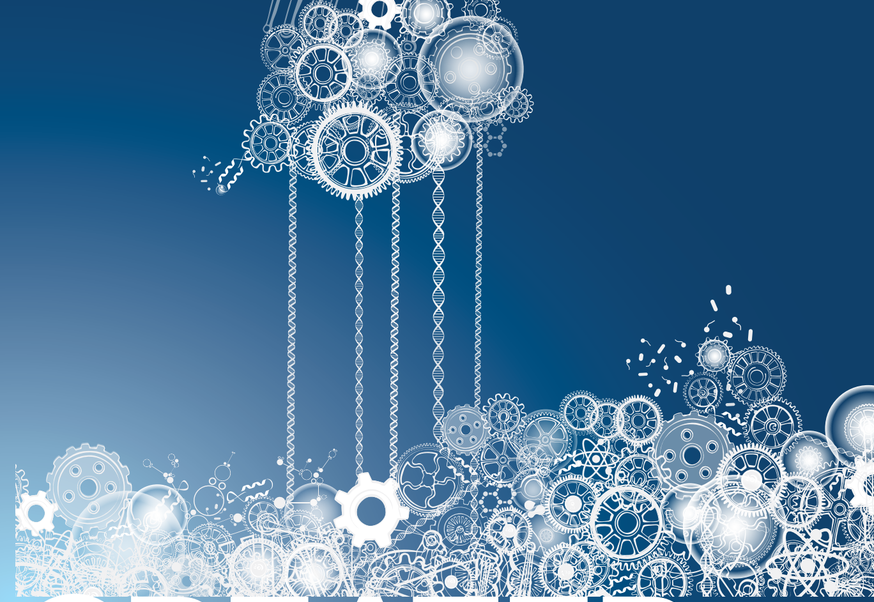
Statement of Activities

Dollars in Thousands

Revenues	$	%
Grants & Contract Revenue	37,449	85.0
Contributions	2,276	5.2
Investments & Other Income	4,330	9.8
Total Revenues	**44,055**	**100.0**

Expenditures	$
Research & Other Direct Costs	32,737
Management & General	10,441
Fundraising & Other	193
Total Expenditures	**43,371**
Increase in Net Assets	**684**

Scan this QR code for the full 2013 annual report



GREATER THAN THE SUM

annualreport.systemsbiology.net

2013 ISB Annual Report

Institute for Systems Biology

Revolutionizing Science. Enhancing Life.

At Institute for Systems Biology, it's *how* we do it that matters most. The systems approach that we pioneered and exemplify continues to distinguish our ability to tackle the most complex biological and environmental challenges today. Because of how we apply our hallmark collaborative, cross-disciplinary and integrative approach, our collective success is GREATER THAN THE SUM OF ITS PARTS.

For ISB's full 2013 annual report, please visit:
annualreport.systemsbiology.net

NEXT GEN SCI STANDARDS

At ISB, supporting science education is not just a box that we check.

ISB's education team was instrumental in the two-year process to help Washington State adopt the Next Generation Science Standards (NGSS), which became official in October 2013. The process involved review sessions at the state level, followed by sessions for educators and administrators. ISB also hosted workshops on implementation strategies. It's unusual for a nonprofit scientific research organization to play such an integral role in the development and implementation of educational standards.

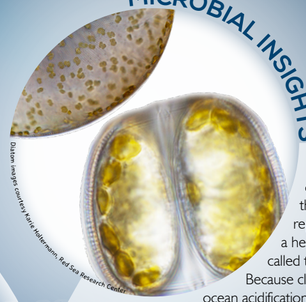
BENCH TO BEDSIDE

This blood biomarker panel has the potential to save the healthcare system billions of dollars by reducing the number of unneccesary invasive surgeries.

When it comes to determining whether lung nodules are benign, a patient typically faces an invasive biopsy. In 80 percent of cases, it turns out the surgery is unnecessary. A study, co-authored by researchers at ISB and Indi (Integrated Diagnostics, an ISB spinout company) and published in October 2013 in *Science Translational Medicine*, suggested that a blood test could save countless patients the trauma and expense of surgery. Indi has since started commercializing the blood test, called Xpresys™ Lung, which is based on technology that uses mass spectrometry to detect specific proteins in the blood and eventually can be applied to other diseases such as cancers and neurodegeneration.

KNOWLEDGE TRANSFER

MICROBIAL INSIGHTS



Diatom images courtesy Kara Shallenberger, Red Sea Research Center

Nearly 25 gigatons of carbon is cycled annually through the oceans, replenishing resources for a healthy planet in a process called the microbial loop. Because climate warming and ocean acidification affect the water column and supply of nutrients, understanding how algae respond to changes in environmental conditions can help scientists develop realistic and predictive models for how to counteract those shifts. ISB researchers published two papers in 2013 related to ocean acidification and also received a $1.8 million grant from the National Science Foundation toward ongoing studies.

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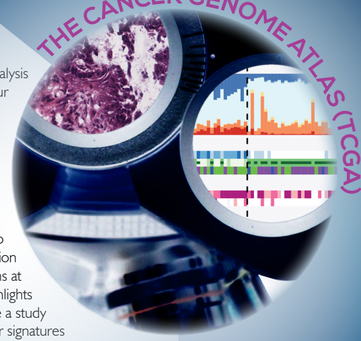
Publications in journals such as *Cell, Nature Nature Methods, PLOS One, PNAS* and *Science Translational Medicine.*

WHY CANCER THERAPIES FAIL

The main reason for the failure of cancer therapies is the unfathomably rapid development of drug resistance. It is commonly believed that therapy resistance is similar to how bacteria evolve and develop resistance to antibiotics: a process of Darwinian evolution, driven by random mutations and survival-of-the-fittest cancer cell. But ISB researchers discovered that cancer therapy resistance does not follow the Darwinian mechanism of evolution but, instead, cancer cells actively adapt to the external threat.

This new principle sheds light on the evasiveness of cancer cells.

THE CANCER GENOME ATLAS (TCGA)



ISB continues its participation as one of seven data analysis centers for TCGA. Our unique contribution to TCGA is our profound ability to develop methods and software tools to analyze, integrate and visualize massive swaths of existing data in order to unearth new information and draw connections at multiple scales. Highlights from 2013 include a study on the molecular signatures of endometrial cancer subtypes that was published in *Nature* and a paper on the largest catalog of glioblastoma tumors that appeared in *Cell*.

PUSHING FRONTIERS

We now know that infectious viral proteins exploit nuclear pore complexes to gain control of cells.

One of the next frontiers in basic science research is organizing and achieving a four-dimensional understanding of the data that the Human Genome Project generated. The National Institutes of Health is spearheading new projects such as the "4D Nucleome" to study nuclear architecture as related to gene expression and cellular function. Since ISB's inception in 2000, our scientists have been contributing to the collective understanding through our research on nuclear pore complexes, which play a key role in determining nuclear architecture and controlling gene expression. Recent work, done in collaboration with Seattle BioMed, was published in the journal *Cell*.

BIOLOGICAL DISCOVERIES

THE POWER OF PROTEOMICS

ISB is home to one of the largest mass spectrometry labs on the West Coast and our researchers have had a long history as leaders in developing proteomics technology and open-access databases. Examples of the impact of our research on the study of proteins—which are involved in virtually all cellular processes—include a complete mass spectrometric map for analyzing the yeast proteome (published in *Nature*) and also an update of the latest advances related to ISB's PeptideAtlas, a project that has cataloged the proteins observed in thousands of proteomics experiments as an open-access resource for researchers everywhere.

OPEN-ACCESS TOOLS

We have a responsiblity to share what we learn.

A hallmark of ISB's systems approach is the cross-disciplinary and collaborative culture necessary to make sense of the complexity. Our researchers engineer tools that make it easier and faster to integrate and analyze disparate forms of data and, because of our open-access philosophy, enable the global community of scientists to explore data resources more efficiently. Two examples of published research from 2013 include a decision-tree software that can help predict cellular actions and a computational strategy that helps researchers capitalize on existing large data sets.

BIG DATA SCIENCE