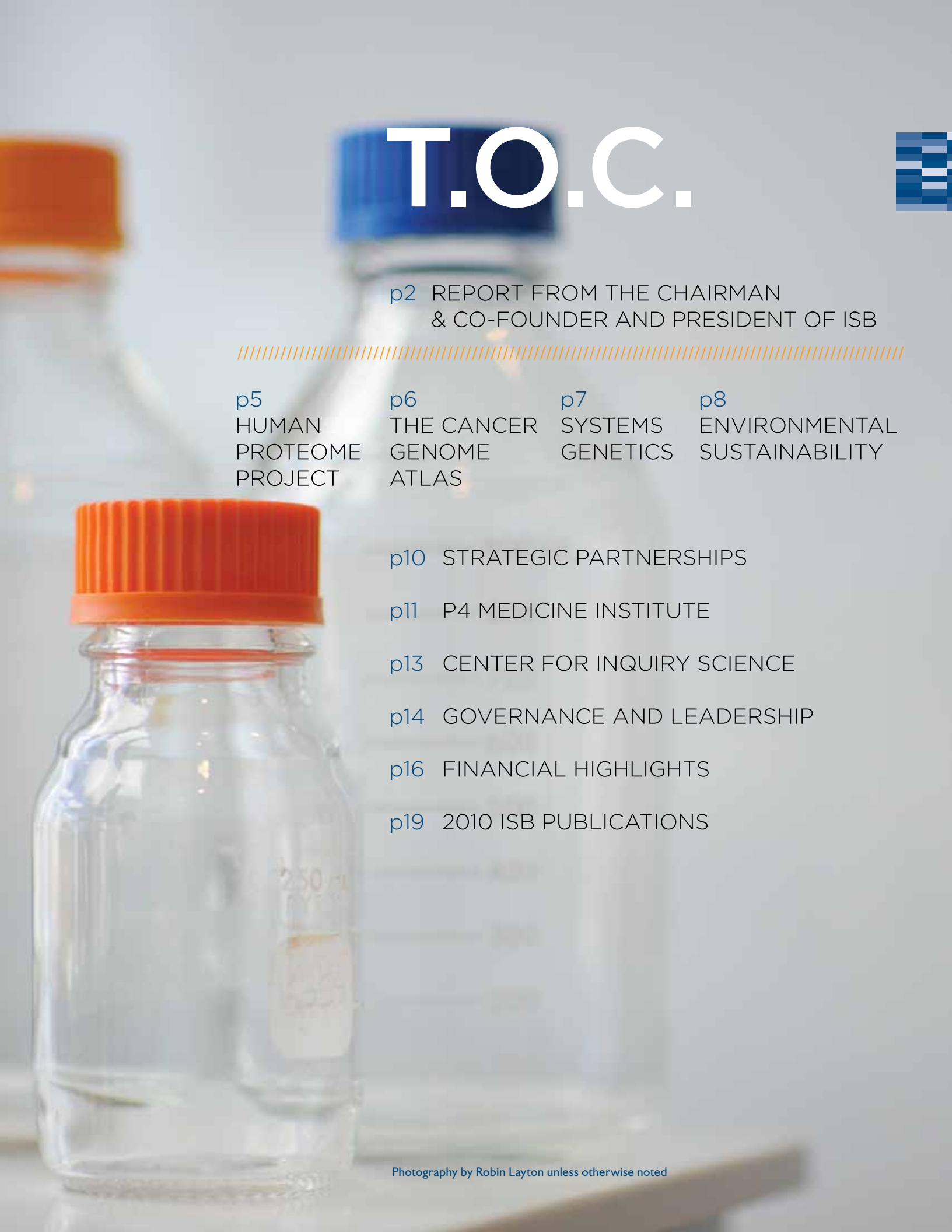
Institute for Systems Biology

Institute for Systems Biology
Annual Report 2010

Pushing Boundaries

Revolutionizing Science. Enhancing Life.

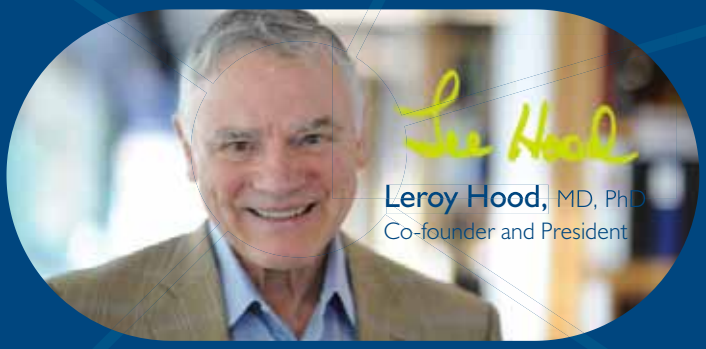
T.O.C.



Photography by Robin Layton unless otherwise noted

REPORT FROM THE CHAIRMAN & CO-FOUNDER AND PRESIDENT

As we formally celebrated the Institute for Systems Biology's (ISB's) 10th Anniversary, we had a wonderful year with outstanding science. As we reflect on our first decade at ISB – building a remarkable track record of achievement and creativity – and this year's accomplishments, we want to also provide you with a snapshot of our vision for the future.



Pushing Boundaries

Complexity is the grand challenge for all scientific and engineering disciplines in the 21st century. Systems approaches allow us to decipher this complexity. ISB is at the forefront of using this strategy to attack big and small problems in biology and medicine.

We are pioneering a systems-driven, big science approach, which is holistic rather than atomistic. We are working across disciplines and research specialties to confront societal problems in human health and environmental sustainability – in ways that will improve people's health around the world and improve the health of the planet.

As a small, non-profit research institute with 300 employees and collaborators, ISB remains agile and responsive to new opportunities. We have created a unique, cross-disciplinary environment at the Institute. Biologists, chemists, computer scientists, engineers, mathematicians and physicists are doing science in a new and different way that is fostering creativity and "out of the box" thinking. Working side-by-side and learning to speak the languages of other disciplines, they are collaborating in teams to solve big, fundamental problems in biology as well as more detailed small problems.

We are deploying integrated, systems-level strategies, which require the development of new technologies that allow new dimensions of data space to be explored both for biology and medicine. We are creating new analytical tools for acquiring, storing, validating, mining, integrating and modeling the exponentially increasing amounts of genomic, proteomic, cellular and phenotypic data. We are committed to an open source policy, making our data and software immediately available to all scientists.

Poised between academia and industry, we are passionate about transferring knowledge to society—pioneering a systems approach to K-12 science education, bringing P4 Medicine to patients and educating society and our colleagues about 21st century science. We have also focused on launching new companies through Accelerator and ISB spin-outs, and have raised more than $375 million in venture funding since 2003, for companies that employ more than 300 people.

ISB's Mission and Areas of Focus:

- **Systems Biology** – pioneering the strategies, tools and analytical algorithms of systems science for application to the life and environmental sciences
- **Human Health**
  - **P4 Medicine** (Predictive, Preventive, Personalized and Participatory) – catalyzing a revolution in healthcare focused around an informational view of medicine, which will utilize an individual's genomic, proteomic, and molecular diagnostic information to quantify wellness and demystify disease
  - **Global Health** – employing the systems approach to address the challenges related to infectious diseases and vaccine development, the emergence of chronic diseases, and maternal, newborn and child health
- **Environmental Sustainability** – using systems science to harness the power of microbes to attack real-world environmental problems such as climate change

With this summary of what ISB has become in just a decade and our vision for the future, let us consider what happened over the course of 2010.

Pioneering Discoveries

In 2010, the Institute launched a number of new biological and technological initiatives to address a series of big problems arising from earlier groundbreaking discoveries from ISB.

- First, we pioneered complete genome sequencing of the members of human families to attack a variety of simple and complex genetic diseases. Family genome sequencing integrates genetics and genomics and is a driver in a new discipline called systems genetics. This has allowed us to readily identify disease genes for simple diseases.
- Second, ISB, in collaboration with ISB co-founder Ruedi Aebersold, now at the ETH-Zurich, we pioneered four proteomics techniques that have allowed us to create highly sensitive targeted mass spectrometry measurements for each of the more than 20,000 human proteins. As a result, ISB is leading a global movement to undertake the "next big thing" in human biology since the completion of the Human Genome Project (a $3.8 billion dollar investment that drove almost $800 billion in economic impact, created more than 300,000 jobs and launched the genomic revolution). The Human Proteome Project will be made possible by these pioneering efforts at ISB.

INNOVATE, ACCELERATE, COLLABORATE

- Third, ISB is pioneering the development of a host of clinical assays employing genomic, proteomic, single-cell, and phenotypic measurements. These quantitative measurements will allow new dimensions of patient data space to be explored in the context of P4 Medicine, which will provide insights into deciphering the complexities of disease.
- Finally, ISB is exploring new techniques and strategies that will make blood a window for health and disease, which is a critical platform for P4 Medicine and in new advances in determining effective drugs for disease. These approaches focus on using organ-specific blood proteins and blood miRNAs (using mouse models of neurodegenerative and liver toxicity) to demonstrate that these blood biomarkers can achieve pre-symptomatic diagnosis, the stratification or specification of the different subtypes of a single disease (e.g. breast cancer) and the ability to follow the progression of disease.

Forging Partnerships

At ISB, we recognized early on that the key to attacking the big problems in biology and medicine is the creation of strategic partnerships. We understood that partnering with a broad cross-section of the world's best talent and expertise would foster innovation and achievement; accelerate discovery; and create new and unique funding opportunities for the Institute.

We have reached out to some of the world's best scientists and engineers to tap into expertise not available at ISB. Through the establishment of a wide range of relationships from academia, industry and government, we are developing and deploying the exciting new technologies and analytical tools required to address these big problems. Some of these partnerships include the Grand Duchy of Luxembourg, Ohio State University's Medical Center, Gladstone Institute, Caltech and Proctor & Gamble.

Transferring Knowledge to Society

One of the significant features of ISB is that it has created three unique institutions dedicated to transferring knowledge to society in a variety of different ways:

- First, the **Center for Inquiry Science,** embedded in ISB, has six full-time employees that are committed to a systems approach to K-12 science education to train the workforce of tomorrow; produce citizens that understand the relationship between science, technology, and society; and to encourage future scientists and engineers. We have demonstrated striking success in improving students' learning of science, notably student achievement in schools with the highest levels of poverty show the greatest gains.
- Second, in 2010 we launched the **P4 Medicine Institute** (P4MI), an independent, non-profit institute that is committed to bringing P4 Medicine to patients. It is focused on creating partnerships with a small network of clinical centers to employ relevant ISB clinical assays in the context of pilot projects that will demonstrate the power of P4 Medicine to the medical community.
- Finally, ISB participated in the creation of **Accelerator,** a for-profit company headquartered in Seattle. It provides resources to test emerging company ideas at a very early stage, and, if successful, facilitates funding to create a traditional start-up company. ISB provides scientific and technical expertise to these companies. Since 2003, Accelerator has supported the launch of 12 companies and has reviewed more than 750 business plans, to date. Eight companies are still in existence today, focusing on a wide range of promising discoveries such as improved biotherapeutics, vaccines, and biomarkers.

Looking Ahead

With a decade of accomplishments behind us and exciting opportunities ahead, there are several metrics worth noting because they are a testimony to the success of systems biology and ISB: 1) When ISB was launched 10 years ago, it was the only institution dedicated to systems science, and today, there are approximately 70 systems biology institutions worldwide; 2) a National Academies report on "A New Biology for the 21st Century" perfectly describes systems biology and predicts that it will be the key to biology and medicine in the future; and 3) the SCImago Research Group released a report evaluating research-centered organizations worldwide, which showed that over a four year-period ISB's research papers had the highest scientific impact in the United States and the third highest in the world.

As we move into the second decade of 21st century, it is an exciting time for ISB. Utilizing systems science, state-of-the-art technologies, and computational and mathematics tools -- we are leading the way in revolutionizing biology and medicine. We are well positioned to remain at the frontiers of science, pushing boundaries and continuing to transform the way science is done globally.

Accelerate

Researchers at ISB are generating results that can be applied to some of society's most perplexing problems in human health and environmental sustainability.

THE HUMAN PROTEOME PROJECT: EXPLORING THE NEXT FRONTIER

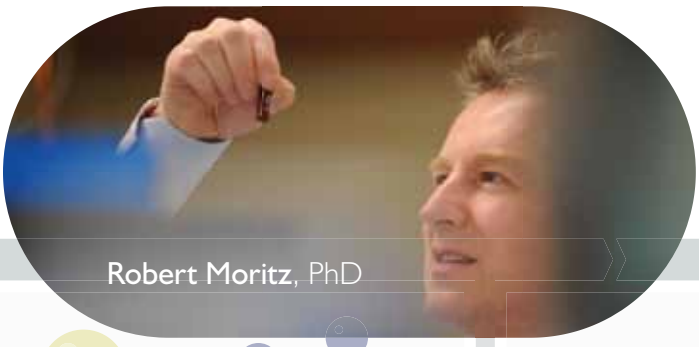
The **Human Genome Project** (HGP), often referred to as *the book of life* – demonstrated explicitly how the needs of biology can lead to transformational new technologies that, in turn, can revolutionize biology and catalyze new major scientific discoveries. Some of the major contributions of the HGP include:

- The first ever comprehensive "parts list" of all genes, which enabled the new discipline of systems biology
- Pioneering the applications of computer science and mathematics to biology
- The first biological project with an open source policy for all data, which enabled the global scientific community to analyze new information in real-time
- The transformation of medicine, allowing for early detection of disease and stratification of complex diseases into subtypes, making it possible for physicians to apply more appropriate drugs and other therapies

Tackling the "Next Big Thing" in Human Biology

Once again, scientists will have a transformative impact on biology through the **Human Proteome Project** (HPP), which over the next decade will generate the map of the proteins that will enable biologists to understand how these molecular machines of life function. Pushing the frontiers of science to a new level, this massive undertaking will have extraordinary benefits for society. Upon completion, the HPP is expected to:

- Make the study of all human, animal, plant and microbial proteins readily accessible, catalyzing fundamental changes in our understanding of every aspect of biology and medicine
- Transform how biologic research is conducted
- Provide deep insights into health and disease and lead to better prediction, prevention and treatment of disease
- Promote wellness of humans and the environment
- Create an enormous range of economic opportunities – from transforming drug target discovery and the creation of many exciting new companies – to the development of sustainable energy resources



Robert Moritz, PhD

"At ISB, we are leading the way in tackling the "next big thing" in human biology – the Human Proteome Project. Because proteins are the molecular machines of life and execute most of the important functions in human biology, this massive undertaking will transform how biologic research is done."

–Robert Moritz, PhD – ISB Faculty Member – Associate Professor

Still in its infancy, the Human Proteome Project is being made possible through groundbreaking efforts at ISB. A team of biological and computational scientists, led by Robert Moritz PhD, has developed the technical building blocks and unique software that have enabled the formal launch of the project. They include a database of all publically available protein mass spectrometry data; a pipeline for assessing the quality of mass spectrometry data; and techniques that allow for the quantification of hundreds of proteins in an hour. These efforts comprise of two of the three pillars of the HPP pioneered by Ruedi Aebersold, PhD, ISB co-founder and collaborator who is now at the Swiss Federal Institute of Technology (ETH-Zurich).

As a result of these other new technologies and tools developed at ISB, the Moritz group has generated "gold standard" reference mass spectrometry spectra (SRM) for each of the proteins encoded by the 20,300 genes in humans. ISB has now completed the human SRMAtlas in record time, which will provide digital open source access to these assays for researchers around the globe. It will enable researchers to detect and quantify human proteins in biological samples and analyze data generated by mass spectrometry techniques faster, cheaper and more reliably.

ISB and ETH jointly released the human SRMAtlas at the Human Proteome Organization Annual World Conference in September 2010 in Sydney, Australia. It was recognized globally by the scientific community as the first critical step forward in the Human Proteome Project.

As the Human Proteome Project expands, it will include researchers from around the globe. This colossal effort will include the development of new assays, technologies, and computational tools – and many of those will come from ISB.

THE CANCER GENOME ATLAS

Since ISB launched a decade ago, its researchers have been at the forefront in the field of computational biology – developing suites of software for analysis, integration and mathematical modeling of large data sets, which are critical in solving big, fundamental problems in biology and medicine.

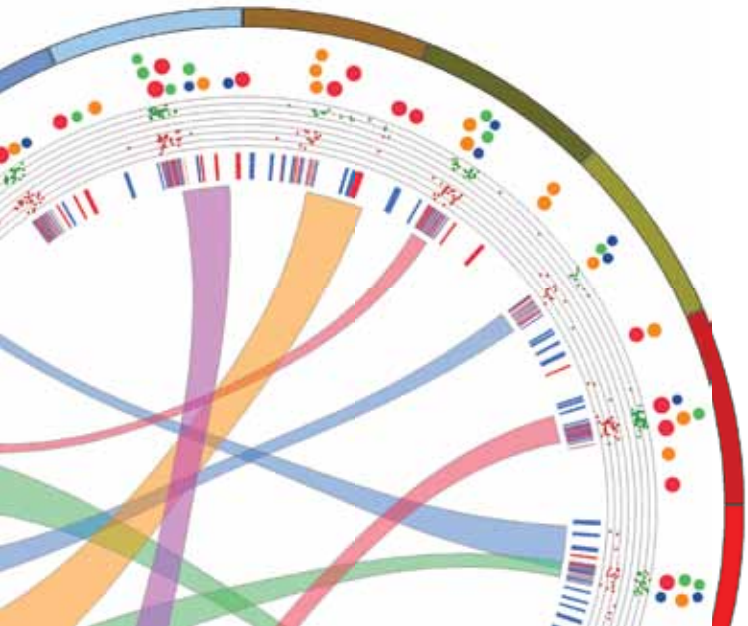
"An important part of our role at ISB is to create mathematical models that will help researchers understand and predict the progression of a tumor. We are building models of molecular networks and showing how they are disrupted in cancer. Ultimately, this will lead to the development of early detection tools and information that doctors and patients can use in making more informed treatment decisions." *Ilya Shmulevich, PhD – ISB Faculty Member – Professor*

Researchers are utilizing ISB's novel tools and technologies to unravel the complexities of common cancers.

The Cancer Genome Atlas (TCGA) is a joint project of the National Cancer Institute and National Human Genome Research Institute at the National Institutes of Health. Its goal is to provide the scientific community with comprehensive catalogs of the major genomic changes in more than 20 different types of human cancer to advance the development of more effective ways to diagnose, treat and prevent this dreaded disease.

ISB received an $8 million grant to participate as one of several national computational centers involved in The Cancer Genome Atlas project.

Led by ISB faculty member Ilya Shmulevich, PhD, the Institute's role is to develop state-of-the-art computational tools and software to enable comparison and integration of large cancer datasets and to develop predictive models of disease progression. ISB's new tools are allowing researchers to interactively explore, visualize, integrate and analyze cancer genomics and associated clinical data.



Ilya Shmulevich, PhD

Accelerating Discovery

As recently as a few years ago, finding changes in the genomes responsible for different cancers would have seemed impossible because it would have been too costly and too complicated scientifically. However, the cost of genome sequencing has dropped dramatically, and the software tools such as those being developed at ISB – critical for analyzing large data sets – are improving rapidly.

By studying tumors from 10,000 patients, researchers will be able to identify the genomic changes in breast, lung, ovarian, brain and many other cancers. Researchers are analyzing hundreds of samples for each type of cancer and comparing a patient's DNA in samples of both normal and cancer tissue, which allows them to identify changes specific to a particular cancer.

The Road to Personalized Medicine

Researchers are combining molecular information derived from the samples with clinical information about patients participating in the program to gain a better understanding of what makes one cancer different from another. By cataloging all the changes in large numbers of samples from many different cancer types, scientists can begin to identify patterns. Some of these changes may help researchers find new drug targets and develop more effective and personalized treatment strategies for cancer patients. Others will show a link between a specific change and its impact on disease progression or a recurrence of the cancer.

SYSTEMS GENETICS AT ISB: FROM MOLECULES TO LIFE

Powerful new approaches for understanding complex interactions between genetics and the environment

What are the principles that guide development, life and aging?

What maintains our health?

How do we prevent disease?

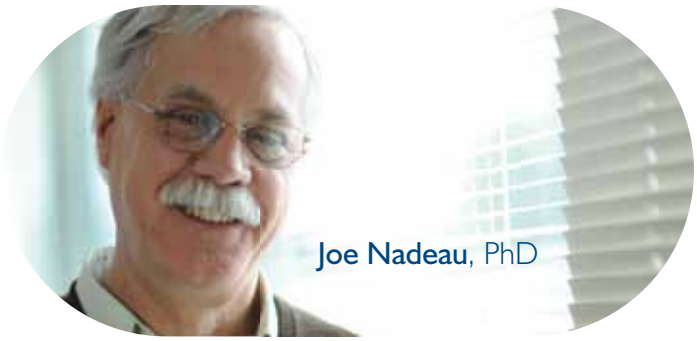
Researchers at ISB are pioneering a new discipline called systems genetics, which integrates genetics and systems biology. By introducing novel strategies, technologies and computational tools to model the interactions between an individual's genomes and his or her environment, scientists are now transforming how genetics can be used to broaden our understanding of health as well as evaluate and modify disease risk. The systems genetics perspective will result in tangible health benefits for society because it will enable scientists to see simultaneously the big biological picture, as well as the underlying molecular details.

Systems genetics uses modern genetic strategies together with bioinformatics and computational methods to incorporate genetic variation in models of complex traits and in studies of human disease and animal models, leading to a greater understanding of society's most common and pressing health risks. Combined with advances in genomic, proteomic and molecular diagnostic information, systems genetics will serve as a window into an individual's health and disease states, and provide the information necessary to more effectively tailor disease management.

Many of the novel methods and approaches that are enabling systems genetics research at ISB are made possible through partnerships and collaborations with other institutions.

"There is an urgent need to discover ways to treat and perhaps even prevent common human diseases. But it is extremely important that we approach this task in a way that not only enables great science, but that also leads to measureable improvements in people's lives."

–Joe Nadeau, PhD - Director of Research and Academic Affairs



Joe Nadeau, PhD

2010 Highlights

- The Family Genomics Group at ISB is developing state-of-the-art software that will re-invent the basic tools of genetics from the ground up. These new, more precise tools will enable researchers to extract biological meaning from whole-genome sequences in the context of human families. By identifying violations of the basic laws of genetics, noise in the data can be suppressed and a database of all known genetic variation can be created with high accuracy. This will enable scientists to identify novel and rare variants that may cause genetic disease and susceptibility to disease.
- Because many diseases such as heart disease, diabetes, and asthma result from combinations of changes in many genes that interact with each other and with the environment in complex ways, the Dudley lab at ISB is using a model organism (baker's yeast) to develop new experimental and computational methods for understanding these complex traits.
- ISB and the Gladstone Institute of Neurological Disease announced a collaboration that for the first time will leverage the power of ISB's whole-genome sequencing. It will focus on identifying genes and novel drug targets related to the onset and progression of Huntington's disease, as well as use induced pluripotent stem (iPS) cells from patients with the disease to screen for drugs that might delay, prevent or even reverse this devastating condition.
- ISB and Proctor & Gamble established a partnership to focus on how biological systems function in various skin conditions, including skin aging, inflammation and rhinovirus infection. Leveraging ISB's expertise in regulatory network inference and modeling, and P&G's in skin biology and dermatology, the effort will focus on characterizing and developing models of the global molecular changes that occur in skin under different conditions.

ENVIRONMENTAL SUSTAINABILITY

CREATING A SUSTAINABLE FUTURE THROUGH SYSTEMS SCIENCE
Focusing on environmental, economic and community health

Achieving environmental sustainability is one of civilization's historic challenges. For the past decade, ISB has been using systems science to improve the understanding of the interactions of microbes and ecosystems and create a new generation of sustainable tools and strategies that can be deployed to address this challenge.

This systems understanding is essential to explain and predict consequences of complex phenomena such as climate change, so that responsible and sustainable strategies for addressing these real-world issues can be developed.

How do microbes, or whole networks of microbes, react and adapt to environmental assaults?

How do microbes affect ecosystems? How can they be used to improve environmental sustainability?

A Transformational Opportunity

These systems approaches at ISB are allowing scientists to address biological complexity in novel and powerful ways. Under the scientific direction of Nitin Baliga, PhD, the Institute is at the forefront of understanding mechanisms of biological responses at the molecular level – not only within the networks of one microbe, but among the interactions between diverse microbes within ecological communities.

ISB is developing robust new technologies and computational modeling tools to demonstrate that it is possible to apply systems approaches to tackle this complexity and develop a predictive understanding of how biological systems work. This opens the door to more effective and responsible strategies for a variety of biotechnological applications such as bioremediation, bioenergy and climate stabilization.

Bioremediation, Bioenergy and Climate Stabilization

ISB's systems approach is enabling a better understanding of microbial ecosystems and how they can be be marshaled to detoxify hazardous materials, convert wastes to renewable energy and other valued products and reduce greenhouse gas emissions.

2010 Highlights

Cells: Adapting to Extreme Stress

The evolutionary success of an organism demonstrates its inherent capacity to keep pace with environmental conditions that change over time. The Baliga lab published a series of peer-reviewed scientific articles on how organisms respond to environmental stress at a molecular level, leveraging powerful new technologies and software tools developed at ISB – that can probe molecular phenomena at a systems scale. Several of these studies uncovered networks that confer extraordinary capabilities to those organisms, enabling them to withstand extreme levels of stress.

Increasing Science Literacy and Environmental Stewardship

In 2003, the Baliga lab launched a high school program in collaboration with school districts and other stakeholders in Seattle. Today, the collaborations have extended to other districts in Washington, as well as Kansas, Montana and Pennsylvania. Using real-world environmental challenges such as climate change, the team has developed a series of curriculum modules to engage students to apply systems thinking in the life and marine sciences. Working together in interdisciplinary groups, the students utilize systems biology techniques to solve complex problems. The lab has developed several curriculum modules, including one on the effects of increasing carbon dioxide on ocean systems.

All organisms, regardless of their complexity, live in, and rely upon diverse and interconnected communities.

"The systems approach has proven to be extraordinarily successful in achieving a molecular level understanding of complex biology. This is a critical step if we are ultimately going to engineer cells back to health or reengineer organisms to improve the health of the planet." *–Nitin Baliga, PhD - Director, Integrative Biology*

Pioneer

ISB's sustainability goal is to understand biological mechanisms and consequences of environmental change at the molecular level, so that it can reengineer these mechanisms to create new tools and sustainable strategies for bioremediation, bioenergy and climate stabilization.

STRATEGIC PARTNERSHIPS

THE POWER OF PARTNERSHIPS
Revolutionizing Medicine to a P4 Mode:
Predictive, Preventive, Personalized and Participatory

ISB has established a history of successful partnerships, which has broadened its reach through enhancing access to world-class talent, expertise, complementary fields of research and resources such as patient-based samples and data.

ISB and the State of Luxembourg

New tools and strategies for transforming medicine

Systems approaches to biology and medicine have already been transformational in laying the foundation for P4 Medicine and will have even more impact in the future in accelerating innovation in ways that will revolutionize healthcare.

P4 Medicine is emerging out of the new capabilities provided by a fundamental transformation of the science of biology. Within the last few years, biology has increasingly become an information-based discipline focused on a holistic understanding of complex biological systems.

Within the next ten years, patients will be surrounded by virtual clouds of billions of data points and researchers will utilize information technology to translate this information into accurate health predictions for each individual.

2010 marks the second year of the historic five-year partnership agreement between ISB and the Grand Duchy of Luxembourg, which is providing $100 million in funding for ISB to engage in innovative science initiatives related to P4 Medicine. This unprecedented model leverages funding from outside of the United States to support science and training at ISB.

Within Luxembourg, this multi-faceted effort involves most of the science and clinical institutions, a newly created biobank and the recently established Luxembourg Centre for Systems Biomedicine (LCSB). This nascent relationship between ISB and Luxembourg has already yielded significant discoveries with the publication of more than 30 scientific papers.

2010 Highlights

- In February, groundbreaking occurred for the Luxembourg Centre for Systems Biomedicine, which will serve as the nucleus for all cutting-edge biological science throughout the country. Internationally renowned geneticist Rudi Balling, PhD, is leading this exciting new initiative and by the end of 2010, he had recruited more than 30 researchers to the Centre.

- ISB has been a pioneer in advancing the field of genomics and in a paper published in *Science*, the Institute announced the sequencing and analysis of the complete genomes of a family of four. This study demonstrated the value of sequencing entire families, including lowering error rates, identifying rare genetic variants and identifying disease-linked genes. This paper was named the fifth most important science story of 2010 by *Discover* magazine.

  - In addition, ISB fully sequenced more than 100 individual genomes in six larger families, including one six-generation family with more than 30 members.

  - Leveraging the power of using whole family genome sequencing to identify genes that encode simple genetic diseases, ISB and its collaborators launched new genetics studies involving diseases such as congenital heart defects, Huntington's disease, and plans are underway for Alzheimer's, epilepsy, Parkinson's, and spinal muscular atrophy. The goal is to go one step further in family sequencing and actually find genes that modify the effects of well-known disease genes encoded in the diseases.

- As part of ISB's leading-edge research in proteomics, the Institute developed a set of brain, liver and lung-specific proteins / mass-spectrometry based blood plasma assays, as well as miRNA's in the blood that will be used as potential biomarkers to track the onset and progression of disease.

"Our first-ever family genome sequencing study illustrates the beginning of a new era in which the analysis of a family's genome can aid in the diagnosis and treatment of individual family members. We could soon find that our family's genome sequence will become a normal part of our medical records."

– David Galas, PhD - Senior Vice President of Strategic Partnerships

LAUNCHING THE P4 MEDICINE INSTITUTE
Linking the Lab to the Clinic

P4 MEDICINE INSTITUTE

"Together, ISB and Ohio State are well positioned to develop more specific, cost-effective treatments for patients with disease and to create new technologies and tools that will define wellness at a deep molecular level, empowering individuals to take an active role in their health care."

– Clay Marsh, MD, Executive Director, The Ohio State University Medical Center - Center for Personalized Health Care

ISB and Ohio State University are leading the way in bringing a new paradigm of health care to patients.

The P4 Medicine Institute (P4MI) was co-founded in 2010 by the Institute for Systems Biology and The Ohio State University to help catalyze the transformation of medicine from a reactive mode to a system that is Predictive, Preventive, Personalized and Participatory.

- P4MI's goal is to drive innovative approaches to disease prevention and maintenance of health and wellness by applying systems biology to medicine and care delivery.
- P4MI will recruit clinical centers, scientific research institutions and appropriate industrial partners to collaborate in a network of integrated demonstration projects in the United States and throughout the world.
- P4MI will also engage other healthcare stakeholders and thought leaders to accelerate the emergence of a P4 Medicine healthcare system that delivers better clinical care at a lower cost.

ISB and Ohio State University's Medical Center have launched two P4 Medicine demonstration projects: one will establish metrics for wellness and the other will apply P4 strategies to address heart failure. The projects will provide patients with a range of services that go beyond traditional genomic or "personalized" medicine by integrating many levels of hierarchical biological information – DNA, RNA, proteins, metabolites, networks, cells and tissues – to ultimately create predictive and actionable models for care delivery based on individual patient needs and novel forms of patient participation.

The projects will deploy cutting-edge clinical measurement techniques developed by ISB to generate the P4 cloud of personalized health data using genomic, proteomic and cellular analyses. These types of measurements and the enormous volume of personalized health data they generate are the core technological basis for P4 Medicine.

Photo courtesy of The Ohio State University Medical Center

ISB's unique approach to bringing its novel scientific technologies and tools to patients through the creation of P4MI will focus on transforming today's disease-based care to wellness-based care of the future.

Collaborate

We have developed a culture of inquiry and interaction...and an administrative structure that is designed to encourage our researchers to collaborate across the boundaries of their individual disciplines.

ISB'S CENTER FOR INQUIRY SCIENCE

TRANSFORMING SCIENCE EDUCATION
A National Model

"ISB is a unique and progressive example of how a research organization can effectively partner with school systems to advance science education for all students."

– Seattle civic leader Marty Smith in his nomination of the Center for Inquiry Science for the Golden Apple Award

ISB's passion and systemic approach emphasizes interconnectedness, integrative learning, and higher levels of achievement for all students.

K-12 science education has always been a priority for the Institute. ISB recognizes that all students graduating from high school need access to high-quality science education – not only to encourage future scientists and engineers, but also to develop a scientifically literate society. That's why it has pioneered a vision for learning that focuses on developing a deep understanding of science concepts and principles informed by contemporary science and educational research. This proven approach to science education, which is holistic rather than atomistic – supports the true needs of today's students while preparing them to keep pace with an increasingly complex global society.

A Shared Vision

Under the leadership of Dana Riley Black, PhD, director of the Center for Inquiry Science, the Institute has brought together the corporate, philanthropic, non-profit, government and higher education communities to align with school districts, teachers, administrators and students. Working together, they have enabled a transformation from traditional science education programs that supported only a select number of students to contemporary, leading-edge science education programs that are systemic.

A decade ago, ISB launched its science education program with five school districts in the Seattle area. Today, the Institute has established partnerships with almost every school district in the Puget Sound region whose student populations represent almost 40 percent of the state's total. And it continues to expand its partnerships to school districts across the state.

Results that Matter

Since the Center for Inquiry Science was launched in 2000, research of selected programs now shows that students whose teachers have participated in ISB's education programs have made statistically significant gains in science achievement (as measured by Washington State's assessment) ahead of the state average. Further, student achievement in schools with the highest levels of poverty show the greatest gains, with steady trends toward closing the achievement gap, exceeding a statewide comparison group.

"Working together with our partners, we have become a model for providing teachers with the tools they need to inspire students to want to learn science, technology, engineering and math."

– Dana Riley Black, PhD - Director of the Center for Inquiry Science

2010 Golden Apple Award

In October 2010 KCTS 9 television named the Center for Inquiry Science as the recipient of its 2010 Golden Apple Award. This prestigious award was established by KCTS 9 almost 20 years ago to honor educational programs and individuals that represent the best in Washington State education. By celebrating the contributions that outstanding individuals and programs make to the quality of education in Washington State, the Golden Apple Awards seek to provide models for others to emulate and to inspire a new generation of teachers.

KCTS 9 Golden Apple Awards
FOR EXCELLENCE IN EDUCATION

GOVERNANCE AND LEADERSHIP

2010 Board of Directors

***Louis G. Lange**, MD, PhD
Senior Adviser
Gilead

***Roger Perlmutter**, MD, PhD
Chairman of the Board
Executive Vice President, Research and Development
Amgen, Inc.

Mark Ashida
Managing Director
OVP Venture Partners

Bill Bowes
Co-Founder
U.S. Venture Partners

Thomas J. Cable
Board Member
Omeros Corporation

Chuck Hirsch
Founding Partner
MHz, LLC.

Leroy Hood, MD, PhD
Co-Founder and President
Institute for Systems Biology

Garry Menzel, PhD
Chief Operating Officer and
Executive Vice President of Finance
Regulus Therapeutics

Robert T. Nelsen
Co-founder and Managing Director
ARCH Venture Partners

George Rathmann, PhD
Director Emeritus
Chairman
Nuvelo, Inc.

David A. Sabey
President
Sabey Corporation & Sabey Construction

2010 Executive Management

Leroy Hood, MD, PhD
Co-Founder and President

Alan Aderem, PhD
Co-Founder and Executive Vice President, Director

John Aitchison, PhD
Associate Director

Joseph Nadeau, PhD
Director of Research and Academic Affairs

David Galas, PhD
Senior Vice President for Strategic Partnerships

James R. Ladd
Senior Vice President for Finance and Operations

Cathryn Campbell, JD, PhD
General Counsel

Faculty
Alan Aderem, PhD
Ruedi Aebersold, PhD
John Aitchison, PhD
Nitin Baliga, PhD
Aimée Dudley, PhD
David Galas, PhD
Tim Galitski, PhD
Leroy Hood, MD, PhD
Dan Martin, MD
Robert Moritz, PhD
Joseph Nadeau, PhD
Adrian Ozinsky, MD, PhD
Jeff Ranish, PhD
Ilya Shmulevich, PhD

Senior Research Scientists
Peter Askovich, PhD
John Boyle, PhD
Greg Carter, PhD
Eric Deutsch, PhD
Alan Diercks, PhD
Richard Gelinas, PhD
Mark Gilchrist, PhD
Gustavo Glusman, PhD
Liz Gold, MD
Nat Goodman, PhD
Richard Johnson, PhD
Andrew Keller, PhD
Kathleen Kennedy, PhD
Inyoul Lee, PhD
Simon Letarte, PhD
Ed Miao, PhD
Monica Orellana, PhD
Jacques Peschon, PhD
Shizhen Qin, PhD
Stephen Ramsey, PhD
David Reiss, PhD
Jared Roach, MD, PhD
Lee Rowen, PhD
Ramsey Saleem, PhD
Arian Smit, PhD
Jennifer Smith, PhD
Sabrina Spiezio, PhD
James Spotts, PhD
Vesteinn Thorsson, PhD
Qiang Tian, MD, PhD
Kai Wang, PhD
Julian Watts, PhD
Robert West, PhD
Wei Yan, PhD
Daniel Zak, PhD

Senior Software Engineers
Mi-Youn Brusniak, PhD
Lisa Iype, PhD
Sarah Killcoyne
Bill Longabaugh, MS
Hector Rovira
Paul Shannon

Senior IT Analyst
Kerry Deutsch, PhD

Senior Research Engineer
Chris Lausted, MS

*Louis G. Lange, MD, PhD elected as Chairman of the Board in October of 2010.

Our Donors

$100,000+
William K. Bowes, Jr. Foundation
Leroy Hood and Valerie Logan
Howard Hughes Medical Institute
Washington Research Foundation

$25,000 - $99,999
Frederick Frank and Mary Tanner
Kidder Mathews
Roger M. Perlmutter

$10,000 - $24,999
William and Barbara Edwards
Douglas O. Howe and L. Robin DuBrin
Louis G. Lange
LI-COR, Inc.

$2,500 - $9,999
Accelerator Corporation
Mark C. Ashida
Kim Klinke
in honor of Herbert W. and Barbara Hunt
Luxembourg ISB Partnership
Robert T. Nelsen
The Ohio State University Medical Center
Martin Selig
The Adam J. Weissman Foundation

$1,000 - $2,499
Ray and Edith Aspiri
Kasra R. Badiozamani
Thomas J. Cable
Sean T. Clisham
Renee Duprel
Laurence W. Herron
International Conference Services Ltd.
Gilbert Omenn and Martha Darling
PATH
PEMCO Foundation
The Procter & Gamble Company
Simon and Virginia Ramo
Georges C. St. Laurent, Jr.
Ronald C. Seubert
Thermo Fisher Scientific, Inc.
Aron and Sara Thompson
Peter Wilczak

$500 - $999
BP Foundation, Inc.
Daniel V. Byrne
Peter and Susan Cheney
Perkins+Will
Shawn J. Swift
Michele M. Vivona
Griffith Way

$250 - $499
Katherine Barnett
JoAnn Chrisman
Myron and Susan Hood
Jennifer Keys
Lyle and Nancy Middendorf
NFR Korea
Lorna C. and Louis W. Roebke
Erich C. Strauss

Up to $249
Valerie Alduen
James Bassingthwaighte
Anna Bran
Jennifer Dougherty
Al Endres
in rememberence of James Gould
Charles L. Hirsch
Kathlyn Huson
Rhoda and Robert Jensen
Anne Johnson
Mitchell and Hilde Kronenberg
Mike Losh
Damion Mullins
Thomas O'Leary
Shizhen Qin
William Spurlock
Alvin J. Thompson
Victoria VanBruinisse

Catalyze

"As a longstanding and enthusiastic member of the Board of Directors of ISB, I have had the privilege of seeing firsthand the world class research taking place here. After just ten years, ISB is now recognized around the world as one of the leading institutions dedicated to changing the future of medicine for the benefit of all.

By leaving a bequest in my will which will provide for the Institute, I am helping the incredible people at ISB to continue this groundbreaking work long into the future."

– Garry Menzel, PhD - ISB Board Member
Chief Operating Officer and Executive Vice President of Finance Regulus Therapeutics

FINANCIAL HIGHLIGHTS

Financially, 2010 was another good year for ISB, despite the continuing weak economy:

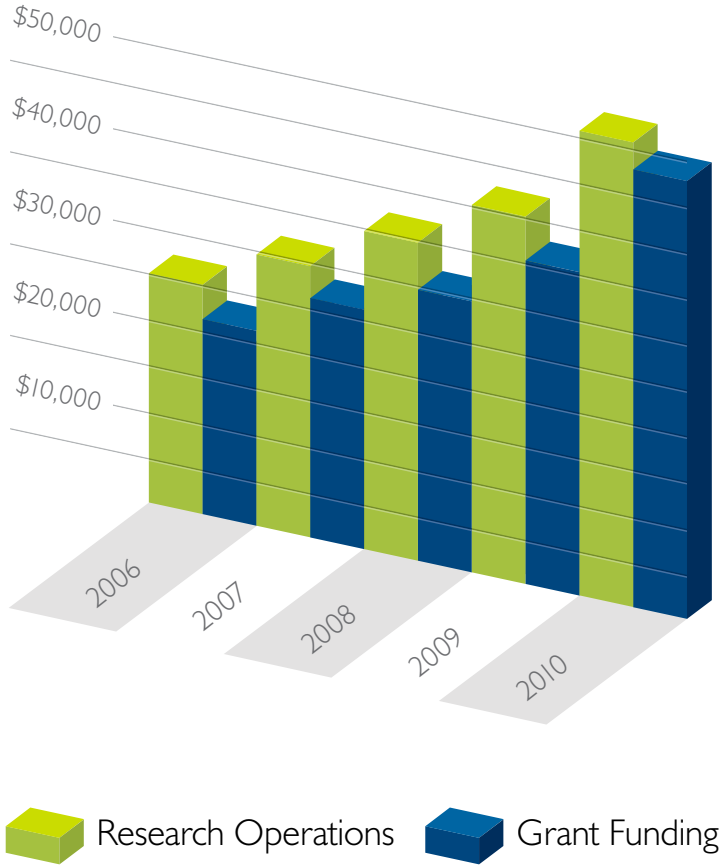
- Total revenue increased 31%, from $38.6 million to $50.4 million
- Revenue from grants and contracts increased by 36%, from $35.2 million to $47.8 million, led by an increase in income from our multi-year strategic partnership with the University of Luxembourg
- Research operations increased 26% from $40.7 million to $51.2 million
- Our balance sheet remains strong, with $21.9 million in net assets (equity) at year end, compared to $15.0 million at the prior year end

In early in 2011 we moved to a beautiful, and very well-equipped research building in Seattle's South Lake Union neighborhood. Our new building is much larger than our previous facilities, enabling us to once again have all our staff in one building with room to grow. The South Lake Union area has rapidly become the primary location for Seattle's biomedical research community, which enables more convenient collaboration with colleagues in nearby institutes.

As we look to the future, we expect our strategic partnership with the University of Luxembourg to continue providing opportunities for research at about the same level as in 2010. We also expect to continue forming strategic partnerships with organizations in the U.S. and abroad that value our areas of research expertise and the abilities of our faculty and staff. At the same time we have to be realistic – considering the state of the U.S. economy and budget deficits, it may not be realistic to expect continuing increases in U.S. government grants and contracts, despite our successful record. The margin of excellence funding from private philanthropy becomes even more essential to leveraging these grants and contracts.

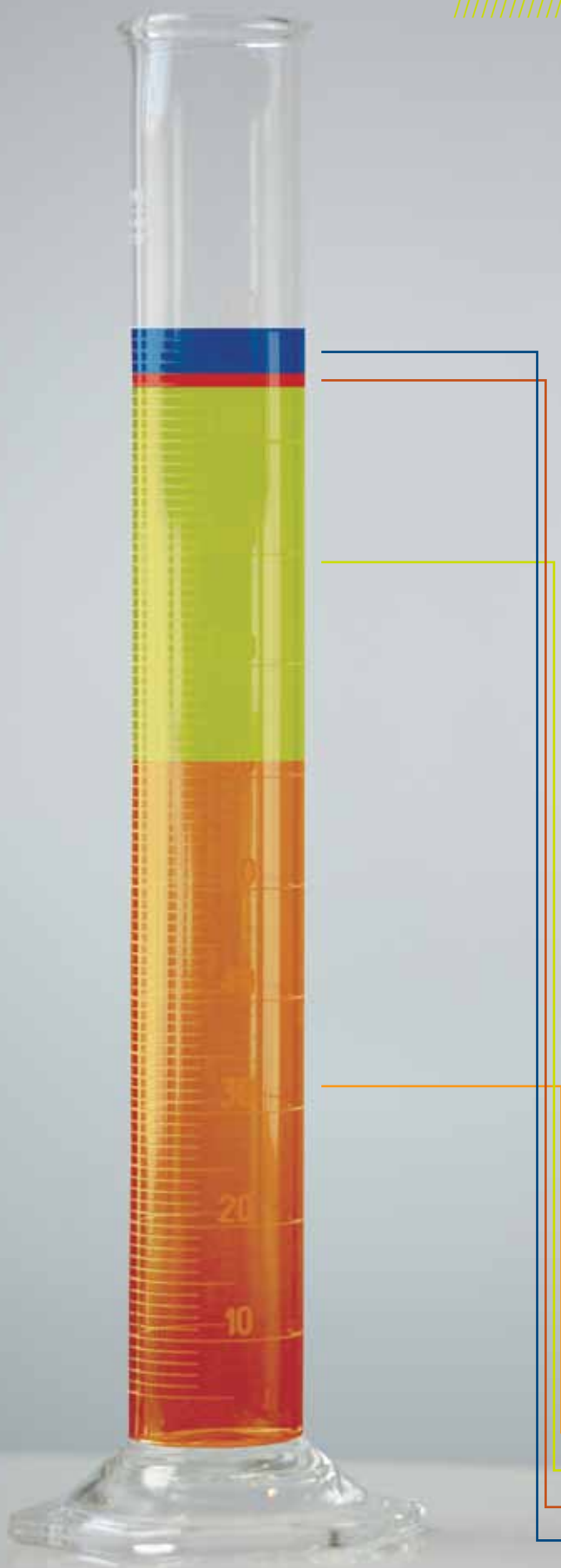
We look forward to the opportunities that continue to come to us, and to managing our finances and operations in the most productive ways possible.

Jim Ladd
Senior Vice President for Finance and Operations



FINANCIAL STATEMENT

For the Year Ended December 31, 2010 (Dollars in Thousands)



STATEMENT OF ACTIVITIES

REVENUES	$ AMOUNT
Grant & contract revenue	47,823
Contributions	518
Investment & other income	2,067
TOTAL REVENUES	**50,408**
EXPENDITURES	
Research & other direct costs	39,086
Management & general	11,739
Fundraising & other	327
TOTAL EXPENDITURES	**51,152**
CHANGE IN NET ASSETS	**(744)**

BALANCE SHEET

ASSETS	
Cash & investments	24,866
Other assets	14,158
Property & equiptment, net	17,161
TOTAL ASSETS	**56,185**
LIABILITIES	
Accounts payable & accrued expenses	17,523
Deferred revenues	7,402
Notes payable	9,387
TOTAL LIABILITIES	**34,312**
NET ASSETS	
Unrestricted net assets	4,764
Temporarily restricted net assets	8,437
Permanently restricted net assets	8,672
TOTAL NET ASSETS	**21,873**

2010 REVENUES

	% TOTAL
Grant and contract revenue (US)	61.4
Grant & contract revenue (foreign)	33.5
Contributions	1.0
Investments & other income	4.1

Innovate

ISB is catalyzing fundamental paradigm changes in how the life sciences and medicine are practiced globally — pioneering new knowledge, innovative technologies and computational tools, as well as creative ways of understanding, conducting and communicating science.

2010 ISB PUBLICATIONS

A

Akiyoshi, B., Sarangapani, K.K., Powers, A.F., Nelson, C.R., Reichow, S.L., Arellano-Santoyo, H., Gonen, T., Ranish, J.A., Asbury, C.L., and Biggins, S. (2010) ***Tension directly stabilizes reconstituted kinetochore-microtubule attachments.*** Nature 468: 576-9. PMID:21107429.

Amon, L.M., Law, W., Fitzgibbon, M.P., Gross, J.A., O'Briant, K., Peterson, A., Drescher, C., Martin, D.B., and McIntosh, M. (2010) ***Integrative proteomic analysis of serum and peritoneal fluids helps identify proteins that are up-regulated in serum of women with ovarian cancer.*** PLoS One 5: e11137. PMID:20559444.

Ao, P., Galas, D., Hood, L., Yin, L., and Zhu, X.M. (2010) ***Towards predictive stochastic dynamical modeling of cancer genesis and progression.*** Interdiscip Sci 2: 140-4. PMID:20640781.

Arpanaei, A., Winther-Jensen, B., Theodosiou, E., Kingshott, P., Hobley, T.J., and Thomas, O.R. (2010) ***Surface modification of chromatography adsorbents by low temperature low pressure plasma.*** J Chromatogr A 1217: 6905-16. PMID:20869062.

Auffray, C., Ideker, T., Galas, D.J., and Hood, L. (2010) ***The hallmarks of cancer revisited through systems biology and network modeling, in Cancer Systems Biology, Bioinformatics and Medicine: Research and Clinical Applications***, (F. Marcus and A. Cesario, Editors), Springer Science & Business Media B.V.

B

Bare, J.C., Koide, T., Reiss, D.J., Tenenbaum, D., and Baliga, N.S. (2010) ***Integration and visualization of systems biology data in context of the genome.*** BMC Bioinformatics 11: 382. PMID:20642854.

Basu, A., Cheung, K.C., Eddington, D.T., Gunther, A., Hansen, C., Huang, T.J., Juncker, D., Kaji, H., Khademhosseini, A., Khan, S.A., Klapperich, C., Love, J.C., Munson, M., Murthy, S., Ozcan, A., Ozinsky, A., Spotts, J.M., Squires, T., Takeuchi, S., Wang, W., and Williams, J. (2010) ***Contributors to the emerging investigators issue.*** Lab Chip 10: 2323-33. PMID:20717627.

Beck, C., Morbach, H., Beer, M., Stenzel, M., Tappe, D., Gattenlohner, S., Hofmann, U., Raab, P., and Girschick, H.J. (2010) ***Chronic nonbacterial osteomyelitis in childhood: prospective follow-up during the first year of anti-inflammatory treatment.*** Arthritis Res Ther 12: R74. PMID:20433730.

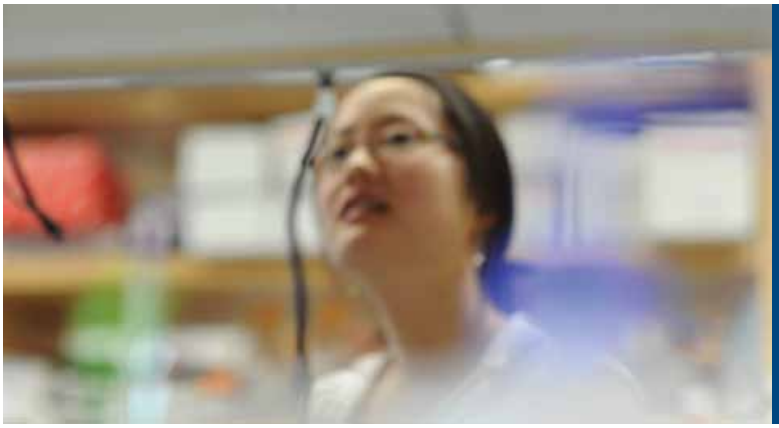
Berrington, W.R., Macdonald, M., Khadge, S., Sapkota, B.R., Janer, M., Hagge, D.A., Kaplan, G., and Hawn, T.R. (2010) ***Common polymorphisms in the NOD2 gene region are associated with leprosy and its reactive states.*** J Infect Dis 201: 1422-35. PMID:20350193.

Bodenmiller, B., Wanka, S., Kraft, C., Urban, J., Campbell, D., Pedrioli, P.G., Gerrits, B., Picotti, P., Lam, H., Vitek, O., Brusniak, M.Y., Roschitzki, B., Zhang, C., Shokat, K.M., Schlapbach, R., Colman-Lerner, A., Nolan, G.P., Nesvizhskii, A.I., Peter, M., Loewith, R., von Mering, C., and Aebersold, R. (2010) ***Phosphoproteomic analysis reveals interconnected system-wide responses to perturbations of kinases and phosphatases in yeast.*** Sci Signal 3: rs4. PMID:21177495.

Burdick, D.B., Cavnor, C.C., Handcock, J., Killcoyne, S., Lin, J., Marzolf, B., Ramsey, S.A., Rovira, H., Bressler, R., Shmulevich, I., and Boyle, J. (2010) ***SEQADAPT: an adaptable system for the tracking, storage and analysis of high throughput sequencing experiments.*** BMC Bioinformatics 11: 377. PMID:20630057.

C

Carter, G.W., Rush, C.G., Uygun, F., Sakhanenko, N.A., Galas, D.J., and Galitski, T. (2010) ***A systems-biology approach to modular genetic complexity.*** Chaos 20: 026102. PMID:20590331.



Cheng, L., Lu, W., Kulkarni, B., Pejovic, T., Yan, X., Chiang, J.H., Hood, L., Odunsi, K., and Lin, B. (2010) ***Analysis of chemotherapy response programs in ovarian cancers by the next-generation sequencing technologies.*** Gynecol Oncol 117: 159-69. PMID:20181382.

Christensen, G.B., Baffoe-Bonnie, A.B., George, A., Powell, I., Bailey-Wilson, J.E., Carpten, J.D., Giles, G.G., Hopper, J.L., Severi, G., English, D.R., Foulkes, W.D., Maehle, L., Moller, P., Eeles, R., Easton, D., Badzioch, M.D., Whittemore, A.S., Oakley-Girvan, I., Hsieh, C.L., Dimitrov, L., Xu, J., Stanford, J.L., Johanneson, B., Deutsch, K., McIntosh, L., Ostrander, E.A ., Wiley, K.E., Isaacs, S.D., Walsh, P.C., Isaacs, W.B., Thibodeau, S.N., McDonnell, S.K., Hebbring, S., Schaid, D.J., Lange, E.M., Cooney, K.A., Tammela, T.L., Schleutker, J., Paiss, T., Maier, C., Gronberg, H., Wiklund, F., Emanuelsson, M., Farnham, J.M., Cannon-Albright, L.A., and Camp, N.J. (2010) ***Genome-wide linkage analysis of 1,233 prostate cancer pedigrees from the International Consortium for Prostate Cancer Genetics using novel sumLINK and sumLOD analyses.*** Prostate 70: 735-44. PMID:20333727.

D

del Sol, A., Balling, R., Hood, L., and Galas, D. (2010) ***Diseases as network perturbations.*** Curr Opin Biotechnol 21: 566-71. PMID:20709523.

Deutsch, E.W. (2010) ***Mass spectrometer output file format mzML.*** Methods Mol Biol 604: 319-31. PMID:20013381.

2010 ISB PUBLICATIONS

Deutsch, E.W. (2010) ***The PeptideAtlas Project.*** Methods Mol Biol 604: 285-96. PMID:20013378.

Deutsch, E.W., Mendoza, L., Shteynberg, D., Farrah, T., Lam, H., Tasman, N., Sun, Z., Nilsson, E., Pratt, B., Prazen, B., Eng, J.K., Martin, D.B., Nesvizhskii, A.I., and Aebersold, R. (2010) ***A guided tour of the Trans-Proteomic Pipeline.*** Proteomics 10: 1150-9. PMID:20101611.

Deutsch, E.W., Shteynberg, D., Lam, H., Sun, Z., Eng, J.K., Carapito, C., von Haller, P.D., Tasman, N., Mendoza, L., Farrah, T., and Aebersold, R. (2010) ***Trans-Proteomic Pipeline supports and improves analysis of electron transfer dissociation data sets.*** Proteomics 10: 1190-5. PMID:20082347.

Dilworth, D.J., Saleem, R.A., Rogers, R.S., Mirzaei, H., Boyle, J., and Aitchison, J.D. (2010) ***QTIPS: a novel method of unsupervised determination of isotopic amino acid distribution in SILAC experiments.*** J Am Soc Mass Spectrom 21: 1417-22. PMID:20451407.

E

Eddy, J.A., Hood, L., Price, N.D., and Geman, D. (2010) ***Identifying tightly regulated and variably expressed networks by Differential Rank Conservation (DIRAC).*** PLoS Comput Biol 6: e1000792. PMID:20523739.

Erkkila, T., Lehmusvaara, S., Ruusuvuori, P., Visakorpi, T., Shmulevich, I., and Lahdesmaki, H. (2010) ***Probabilistic analysis of gene expression measurements from heterogeneous tissues.*** Bioinformatics 26: 2571-7. PMID:20631160.

F

Facciotti, M.T., Pang, W.L., Lo, F.Y., Whitehead, K., Koide, T., Masumura, K., Pan, M., Kaur, A., Larsen, D.J., Reiss, D.J., Hoang, L., Kalisiak, E., Northen, T., Trauger, S.A., Siuzdak, G., and Baliga, N.S. (2010) ***Large scale physiological readjustment during growth enables rapid, comprehensive and inexpensive systems analysis.*** BMC Syst Biol 4: 64. PMID:20470417.

Fitzgerald, L.M., McDonnell, S.K., Carlson, E.E., Langeberg, W., McIntosh, L.M., Deutsch, K., Ostrander, E.A., Schaid, D.J., and Stanford, J.L. (2010) ***Genome-wide linkage analyses of hereditary prostate cancer families with colon cancer provide further evidence for a susceptibility locus on 15q11-q14.*** Eur J Hum Genet 18: 1141-7. PMID:20407467.

Flamez, D., Roland, I., Berton, A., Kutlu, B., Dufrane, D., Beckers, M.C., De Waele, E., Rooman, I., Bouwens, L., Clark, A., Lonneux, M., Jamar, J.F., Goldman, S., Marechal, D., Goodman, N., Gianello, P., Van Huffel, C., Salmon, I., and Eizirik, D.L. (2010) ***A genomic-based approach identifies FXYD domain containing ion transport regulator 2 (FXYD2)gammaa as a pancreatic beta cell-specific biomarker.*** Diabetologia 53: 1372-83. PMID:20379810.

Foltz, G., Yoon, J., Lee, H., Ma, L., Tian, Q., Hood, L., and Madan, A. (2010) ***Epigenetic Regulation of Wnt Pathway Antagonists in Human Glioblastoma Multiforme.*** Genes & Cancer 1: 81.

G

Galas, D.J., Nykter, M., Carter, G.W., Price, N.D., and Shmulevich, I. (2010) ***Biological Information as Set-Based Complexity.*** IEEE transactions on information theory 56: 667-677.

Gehlenborg, N., O'Donoghue, S.I., Baliga, N.S., Goesmann, A., Hibbs, M.A., Kitano, H., Kohlbacher, O., Neuweger, H., Schneider, R., Tenenbaum, D., and Gavin, A.C. (2010) ***Visualization of omics data for systems biology.*** Nat Methods 7: S56-68. PMID:20195258.

Gilchrist, M., Henderson, W.R., Jr., Morotti, A., Johnson, C.D., Nachman, A., Schmitz, F., Smith, K.D., and Aderem, A. (2010) ***A key role for ATF3 in regulating mast cell survival and mediator release.*** Blood 115: 4734-41. PMID:20203264.

Glusman, G., Marzolf, B., Wang, K., Cho, J.-H., Kutlu, B., and Tian, Q. (2010) ***Bioinformatics strategies for understanding gene expression in human pluripotent cells, in Human Stem Cell Technology and Biology: A Research Guide and Laboratory Manual,*** (G.S. Stein, Editor), Wiley-Blackwell.

H-I

Handcock, J., Deutsch, E.W., and Boyle, J. (2010) ***mspecLINE: bridging knowledge of human disease with the proteome.*** BMC Med Genomics 3: 7. PMID:20219133.

Himeda, C.L., Ranish, J.A., Pearson, R.C., Crossley, M., and Hauschka, S.D. (2010) ***KLF3 regulates muscle-specific gene expression and synergizes with serum response factor on KLF binding sites.*** Mol Cell Biol 30: 3430-43. PMID:20404088.

Holstein Sherwood, C.A., Gafken, P.R., and Martin, D.B. (2010) ***Collision Energy Optimization of b- and y-Ions for Multiple Reaction Monitoring Mass Spectrometry.*** J Proteome Res. PMID:20968307.

Johanneson, B., McDonnell, S.K., Karyadi, D.M., Quignon, P., McIntosh, L., Riska, S.M., Fitzgerald, L.M., Johnson, G., Deutsch, K., Williams, G., Tillmans, L.S., Stanford, J.L., Schaid, D.J., Thibodeau, S.N., and Ostrander, E.A. (2010) ***Family-based association analysis of 42 hereditary prostate cancer families identifies the Apolipoprotein L3 region on chromosome 22q12 as a risk locus.*** Hum Mol Genet 19: 3852-62. PMID:20631155.

Jung, S., Marelli, M., Rachubinski, R.A., Goodlett, D.R., and Aitchison, J.D. (2010) ***Dynamic changes in the subcellular distribution of Gpd1p in response to cell stress.*** J Biol Chem 285: 6739-49. PMID:20026609.

K-L

Kaur, A., Van, P.T., Busch, C.R., Robinson, C.K., Pan, M., Pang, W.L., Reiss, D.J., DiRuggiero, J., and Baliga, N.S. (2010) ***Coordination of frontline defense mechanisms under severe oxidative stress.*** Mol Syst Biol 6: 393. PMID:20664639.

For the second year in a row, *The Scientist* named ISB as one of the top 10 places to work in academia in the United States.

Lam, H., Deutsch, E.W., and Aebersold, R. (2010) ***Artificial decoy spectral libraries for false discovery rate estimation in spectral library searching in proteomics.*** J Proteome Res 9: 605-10. PMID:19916561.

Lee, H.J., Suk, J.E., Patrick, C., Bae, E.J., Cho, J.H., Rho, S., Hwang, D., Masliah, E., and Lee, S.J. (2010) ***Direct transfer of alpha-synuclein from neuron to astroglia causes inflammatory responses in synucleinopathies.*** J Biol Chem 285: 9262-72. PMID:20071342.

Lee, L.W., Zhang, S., Etheridge, A., Ma, L., Martin, D., Galas, D., and Wang, K. (2010) ***Complexity of the microRNA repertoire revealed by next-generation sequencing.*** RNA 16: 2170-80. PMID:20876832.

Lin, B., Madan, A., Yoon, J.G., Fang, X., Yan, X., Kim, T.K., Hwang, D., Hood, L., and Foltz, G. (2010) ***Massively parallel signature sequencing and bioinformatics analysis identifies up-regulation of TGFBI and SOX4 in human glioblastoma.*** PLoS One 5: e10210. PMID:20419098.

M

Mansson, M., Phipps, R.K., Gram, L., Munro, M.H., Larsen, T.O., and Nielsen, K.F. (2010) ***Explorative solid-phase extraction (E-SPE) for accelerated microbial natural product discovery, dereplication, and purification.*** J Nat Prod 73: 1126-32. PMID:20509666.

Maziarz, M., Janer, M., Roach, J.C., Hagopian, W., Palmer, J.P., Deutsch, K., Sanjeevi, C.B., Kockum, I., Breslow, N., and Lernmark, A. (2010) ***The association between the PTPN22 1858C>T variant and type 1 diabetes depends on HLA risk and GAD65 autoantibodies.*** Genes Immun 11: 406-15. PMID:20445565.

Miao, E.A., Leaf, I.A., Treuting, P.M., Mao, D.P., Dors, M., Sarkar, A., Warren, S.E., Wewers, M.D., and Aderem, A. (2010) ***Caspase-1-induced pyroptosis is an innate immune effector mechanism against intracellular bacteria.*** Nat Immunol 11: 1136-42. PMID:21057511

Miao, E.A., Mao, D.P., Yudkovsky, N., Bonneau, R., Lorang, C.G., Warren, S.E., Leaf, I.A., and Aderem, A. (2010) ***Innate immune detection of the type III secretion apparatus through the NLRC4 inflammasome.*** Proc Natl Acad Sci U S A 107: 3076-80. PMID:20133635.

Miao, E.A. and Warren, S.E. (2010) ***Innate immune detection of bacterial virulence factors via the NLRC4 inflammasome.*** J Clin Immunol 30: 502-6. PMID:20349122.

Mirzaei, H., Rogers, R.S., Grimes, B., Eng, J., Aderem, A., and Aebersold, R. (2010) ***Characterizing the connectivity of poly-ubiquitin chains by selected reaction monitoring mass spectrometry.*** Mol Biosyst 6: 2004-14. PMID:20694217.

Mo, F., Mo, Q., Chen, Y., Goodlett, D.R., Hood, L., Omenn, G.S., Li, S., and Lin, B. (2010) ***WaveletQuant, an improved quantification software based on wavelet signal threshold de-noising for labeled quantitative proteomic analysis.*** BMC Bioinformatics 11: 219. PMID:20429928.

Munson, M.S., Spotts, J.M., Niemisto, A., Selinummi, J., Kralj, J.G., Salit, M.L., and Ozinsky, A. (2010) ***Image-based feedback control for real-time sorting of microspheres in a microfluidic device.*** Lab Chip 10: 2402-10. PMID:20593069.

N-P

Ng, S.B., Buckingham, K.J., Lee, C., Bigham, A.W., Tabor, H.K., Dent, K.M., Huff, C.D., Shannon, P.T., Jabs, E.W., Nickerson, D.A., Shendure, J., and Bamshad, M.J. (2010) ***Exome sequencing identifies the cause of a mendelian disorder.*** Nat Genet 42: 30-5. PMID:19915526.

2010 ISB PUBLICATIONS

Ouellet, E., Lausted, C., Lin, T., Yang, C.W., Hood, L., and Lagally, E.T. (2010) ***Parallel microfluidic surface plasmon resonance imaging arrays.*** Lab Chip 10: 581-8. PMID:20162233.

Pagan, H.J., Smith, J.D., Hubley, R.M., and Ray, D.A. (2010) ***PiggyBac-ing on a primate genome: novel elements, recent activity and horizontal transfer.*** Genome Biol Evol 2: 293-303. PMID:20624734.

Panchalingam, K.M., Paramchuk, W.J., Chiang, C.Y., Shah, N., Madan, A., Hood, L., Foltz, G., and Behie, L.A. (2010) ***Bioprocessing of human glioblastoma brain cancer tissue.*** Tissue Eng Part A 16: 1169-77. PMID:20021271.

Picotti, P., Rinner, O., Stallmach, R., Dautel, F., Farrah, T., Domon, B., Wenschuh, H., and Aebersold, R. (2010) ***High-throughput generation of selected reaction-monitoring assays for proteins and proteomes.*** Nat Methods 7: 43-6. PMID:19966807.

R

Rajan, J.V., Warren, S.E., Miao, E.A., and Aderem, A. (2010) ***Activation of the NLRP3 inflammasome by intracellular poly I:C.*** FEBS Lett. PMID:20971108.

Ramsey, S.A., Gold, E.S., and Aderem, A. (2010) ***A systems biology approach to understanding atherosclerosis.*** EMBO Mol Med 2: 79-89. PMID:20201031.

Ramsey, S.A., Knijnenburg, T.A., Kennedy, K.A., Zak, D.E., Gilchrist, M., Gold, E.S., Johnson, C.D., Lampano, A.E., Litvak, V., Navarro, G., Stolyar, T., Aderem, A., and Shmulevich, I. (2010) ***Genome-wide histone acetylation data improve prediction of mammalian transcription factor binding sites.*** Bioinformatics 26: 2071-5. PMID:20663846.

Roach, J.C., Glusman, G., Smit, A.F., Huff, C.D., Hubley, R., Shannon, P.T., Rowen, L., Pant, K.P., Goodman, N., Bamshad, M., Shendure, J., Drmanac, R., Jorde, L.B., Hood, L., and Galas, D.J. (2010) ***Analysis of genetic inheritance in a family quartet by whole-genome sequencing.*** Science 328: 636-9. PMID:20220176.

Ruusuvuori, P., Aijo, T., Chowdhury, S., Garmendia-Torres, C., Selinummi, J., Birbaumer, M., Dudley, A.M., Pelkmans, L., and Yli-Harja, O. (2010) ***Evaluation of methods for detection of fluorescence labeled subcellular objects in microscope images.*** BMC Bioinformatics 11: 248. PMID:20465797.

S

Sakhanenko, N.A. and Galas, D.J. (2010) ***Markov Logic Networks in the Analysis of Genetic Data.*** J Comput Biol. PMID:20958249.

Saleem, R.A. and Aitchison, J.D. (2010) S***ystems cell biology of the mitotic spindle.*** J Cell Biol 188: 7-9. PMID:20065087.

Saleem, R.A., Long-O'Donnell, R., Dilworth, D.J., Armstrong, A.M., Jamakhandi, A.P., Wan, Y., Knijnenburg, T.A., Niemisto, A., Boyle, J., Rachubinski, R.A., Shmulevich, I., and Aitchison, J.D. (2010) ***Genome-wide analysis of effectors of peroxisome biogenesis.*** PLoS One 5. PMID:20694151.

Saleem, R.A., Rogers, R.S., Ratushny, A.V., Dilworth, D.J., Shannon, P.T., Shteynberg, D., Wan, Y., Moritz, R.L., Nesvizhskii, A.I., Rachubinski, R.A., and Aitchison, J.D. (2010) ***Integrated phosphoproteomics analysis of a signaling network governing nutrient response and peroxisome induction.*** Mol Cell Proteomics 9: 2076-88. PMID:20395639.

Schmid, A.K., Pan, M., Sharma, K., and Baliga, N.S. (2010) ***Two transcription factors are necessary for iron homeostasis in a salt-dwelling archaeon.*** Nucleic Acids Res. PMID:21109526.

Sekedat, M.D., Fenyo, D., Rogers, R.S., Tackett, A.J., Aitchison, J.D., and Chait, B.T. (2010) ***GINS motion reveals replication fork progression is remarkably uniform throughout the yeast genome.*** Mol Syst Biol 6: 353. PMID:20212525.

Shimada, T., Park, B.G., Wolf, A.J., Brikos, C., Goodridge, H.S., Becker, C.A., Reyes, C.N., Miao, E.A., Aderem, A., Gotz, F., Liu, G.Y., and Underhill, D.M. (2010) ***Staphylococcus aureus evades lysozyme-based peptidoglycan digestion that links phagocytosis, inflammasome activation, and IL-1beta secretion.*** Cell Host Microbe 7: 38-49. PMID:20114027.

Sigmon, I., Lee, L.W., Chang, D.K., Krusberski, N., Cohen, D., Eng, J.K., and Martin, D.B. (2010) ***ChromEval: a software application for the rapid evaluation of HPLC system performance in proteomic applications.*** Anal Chem 82: 5060-8. PMID:20503988.

Sipova, H., Zhang, S., Dudley, A.M., Galas, D., Wang, K., and Homola, J. (2010) ***Surface plasmon resonance biosensor for rapid label-free detection of microribonucleic acid at subfemtomole level.*** Anal Chem 82: 10110-5. PMID:21090631.

T-V

Tenenbaum, D., Bare, J.C., and Baliga, N.S. (2010) GTC: ***A web server for integrating systems biology data with web tools and desktop applications.*** Source Code Biol Med 5: 7. PMID:20626906.

Van de Vosse, D.W., Wan, Y., Wozniak, R.W., and Aitchison, J.D. (2010) ***Role of the nuclear envelope in genome organization and gene expression.*** Wiley Interdiscip Rev Syst Biol Med. PMID:21171043.

Vencio, E.F., Pascal, L.E., Page, L.S., Denyer, G., Wang, A.J., Ruohola-Baker, H., Zhang, S., Wang, K., Galas, D.J., and Liu, A.Y. (2010) ***Embryonal carcinoma cell induction of miRNA and mRNA changes in co-cultured prostate stromal fibromuscular cells.*** J Cell Physiol. PMID:20945389

Vinh, D.B., Ko, D.C., Rachubinski, R.A., Aitchison, J.D., and Miller, S.I. (2010) ***Expression of the Salmonella spp. virulence factor SifA in yeast alters Rho1 activity on peroxisomes.*** Mol Biol Cell 21: 3567-77. PMID:20739463.

W

Wan, Y., Chiang, J.H., Lin, C.H., Arens, C.E., Saleem, R.A., Smith, J.J., and Aitchison, J.D. (2010) ***Histone chaperone Chz1p regulates H2B ubiquitination and subtelomeric anti-silencing.*** Nucleic Acids Res 38: 1431-40. PMID:20008511.

Wang, K., Lee, I., Carlson, G., Hood, L., and Galas, D. (2010) ***Systems biology and the discovery of diagnostic biomarkers.*** Dis Markers 28: 199-207. PMID:20534905.

Wang, K., Zhang, S., Weber, J., Baxter, D., and Galas, D.J. (2010) ***Export of microRNAs and microRNA-protective protein by mammalian cells.*** Nucleic Acids Res. PMID:20615901.

Warren, S.E., Armstrong, A., Hamilton, M.K., Mao, D.P., Leaf, I.A., Miao, E.A., and Aderem, A. (2010) ***Cutting edge: Cytosolic bacterial DNA activates the inflammasome via Aim2.*** J Immunol 185: 818-21. PMID:20562263.

Warren, W.C., Clayton, D.F., Ellegren, H., Arnold, A.P., Hillier, L.W., Kunstner, A., Searle, S., White, S., Vilella, A.J., Fairley, S., Heger, A., Kong, L., Ponting, C.P., Jarvis, E.D., Mello, C.V., Minx, P., Lovell, P., Velho, T.A., Ferris, M., Balakrishnan, C.N., Sinha, S., Blatti, C., London, S.E., Li, Y., Lin, Y.C., George, J., Sweedler, J., Southey, B., Gunaratne, P., Watson, M., Nam, K., Backstrom, N., Smeds, L., Nabholz, B., Itoh, Y., Whitney, O., Pfenning, A.R., Howard, J., Volker, M., Skinner, B.M., Griffin, D.K., Ye, L., McLaren, W.M., Flicek, P., Quesada, V., Velasco, G., Lopez-Otin, C., Puente, X.S., Olender, T., Lancet, D., Smit, A.F., Hubley, R., Konkel, M.K., Walker, J.A., Batzer, M.A., Gu, W., Pollock, D.D., Chen, L., Cheng, Z., Eichler, E.E., Stapley, J., Slate, J., Ekblom, R., Birkhead, T., Burke, T., Burt, D., Scharff, C., Adam, I., Richard, H., Sultan, M., Soldatov, A., Lehrach, H., Edwards, S.V., Yang, S.P., Li, X., Graves, T., Fulton, L., Nelson, J., Chinwalla, A., Hou, S., Mardis, E.R., and Wilson, R.K. (2010) ***The genome of a songbird.*** Nature 464: 757-62. PMID:20360741.

Weber, J.A., Baxter, D.H., Zhang, S., Huang, D.Y., How Huang, K., Jen Lee, M., Galas, D.J., and Wang, K. (2010) ***The MicroRNA Spectrum in 12 Body Fluids.*** Clin Chem 56: 1733-41. PMID:20847327.

Weber, J.A., Baxter, D.H., Zhang, S., Huang, D.Y., Huang, K.H., Lee, M.J., Galas, D.J., and Wang, K. (2010) ***The microRNA spectrum in 12 body fluids.*** Clin Chem 56: 1733-41. PMID:20847327

Y-Z

Yan, W., Luo, J., Robinson, M., Eng, J., Aebersold, R.H., and Ranish, J. (2010) ***Index-ion triggered MS2 Ion quantification: A novel proteomics approach for reproducible detection and quantification of targeted proteins in complex mixtures.*** Mol Cell Proteomics. PMID:21169564.

Yang, D., Ylipaa, A., Yang, J., Hunt, K., Pollock, R., Trent, J., Yli-Harja, O., Shmulevich, I., Nykter, M., and Zhang, W. (2010) ***An integrated study of aberrant gene copy number and gene expression in GIST and LMS.*** Technol Cancer Res Treat 9: 171-8. PMID:20218739.

Yin, X., Wolford, C.C., Chang, Y.S., McConoughey, S.J., Ramsey, S.A., Aderem, A., and Hai, T. (2010) ***ATF3, an adaptive-response gene, enhances TGF{beta} signaling and cancer-initiating cell features in breast cancer cells.*** J Cell Sci 123: 3558-65. PMID:20930144.

Youn, A., Reiss, D.J., and Stuetzle, W. (2010) ***Learning transcriptional networks from the integration of ChIP-chip and expression data in a non-parametric model.*** Bioinformatics 26: 1879-86. PMID:20525821.

ISB 2010 SYMPOSIUM SYSTEMS BIOLOGY AND GLOBAL HEALTH

Systems science at ISB is accelerating discovery in all aspects of human health and it will have enormous impact in the developing world.

While great strides have been made in improving health in the developing world, enormous challenges remain, especially in regard to infectious diseases, an increasing burden of chronic diseases, and improving maternal, newborn and child health.

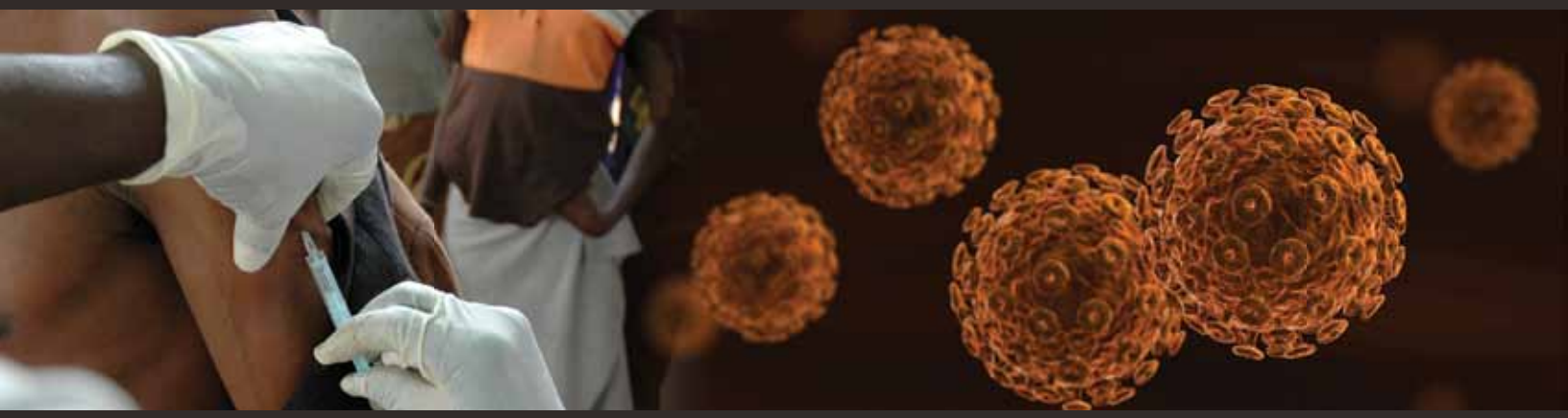
Seattle is home to world-leading institutes focused on global health – and through collaborative efforts, ISB is developing systems approaches to some of the most pressing problems in global health. ISB's science and technologies have the potential to unlock the mysteries of these diseases and conditions, which will accelerate progress in the development of diagnostics, therapeutics and prevention strategies that can successfully reduce the global disease burden.

How do we wade through terabytes of data to understand and validate the molecular networks underlying the body's response to infections?

How can we use this information to rationally design vaccines and drugs?

These and other fundamental questions related to closing the global health innovation gap were topics addressed at ISB's 2010 International Symposium on *Systems Biology and Global Health*. The event brought together some of the best minds in infectious diseases, vaccine development, gene therapy and other fields to showcase the new technologies and systems approaches that are making it possible to analyze complex biological networks, open new doors in research and create new opportunities for breakthroughs not possible until now.

9th INSTITUTE FOR SYSTEMS BIOLOGY International Symposium



Human Health

P4 Medicine in the Next Decade: Quantifying Wellness and Demystifying Disease

Imagine a day when a company will sequence your genome and your physician will combine that information with your medical records – including your molecular and cellular information, as well as the effects of environmental exposure – to predict your probability of getting a specific disease or, alternatively, what you should do to optimize your wellness.

You could find out that given your gene - environment interactions, you're the woman who is more likely to get ovarian cancer. That information could create a personalized roadmap for you and your doctor – to help ensure your future health and longevity.

We are moving toward a new era of medicine where we will quantify wellness and demystify disease. This will enable a dramatic shift in the health care system from a reactive to a proactive mode. It will enable the creation of a virtual cloud of billions of data points around each individual, which will require the development of analytic tools to translate this enormous data cloud into accurate predictions about health and disease.

In this new era, we will focus on health and wellness – with the consumer at the center of care. We will predict or even prevent disease and provide consumer-oriented services that advance well-being and more effectively promote healthy lifestyle changes. As we unravel the complexities of disease through stratification, researchers will be able to pinpoint specific types of diseases.

Institute for Systems Biology

www.systemsbiology.org

Institute for Systems Biology
401 Terry Avenue North
Seattle, WA 98109-5234

Find us on Facebook: www.facebook.com/ISB.USA