7th INSTITUTE FOR SYSTEMS BIOLOGY International Symposium

SYSTEMS BIOLOGY & ENGINEERING

APRIL 2008 SUN 20 MON 21

PROGRAM

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7th INSTITUTE FOR SYSTEMS BIOLOGY International Symposium

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Symposium Welcome

Sunday - 1:00 pm

Dear colleagues:

On behalf of the Institute for Systems Biology (ISB) and our co-host, the College of Engineering at the University of Washington, we welcome you to our seventh annual international symposium on *Systems Biology and Engineering*.

The 21st century presents an enormous challenge for biology—namely how do we deal with the bewildering complexity of biological systems. Systems biology has provided insights about how we have to understand biology in terms of the systems that encode its special features—development of organisms, the physiological response of the organism to its environment and even the response of the organism to disease.

The systems approach to biology and medicine requires that the leading-edge challenge of these disciplines drive the development of powerful new synthetic, sequencing, measurement and visualization technologies. In turn the generation of large data sets from these technologies mandates that new computational and mathematical techniques be generated to handle, store, mine, integrate and finally model these data. These powerful tools come from various realms of engineering—the objective of this symposium is to explore the interface between biology and engineering. We will explore new visualization and imaging techniques, new single-cell analyses approaches and the new synthetic biology—the creation of the building block of life on a scale that will let us think about synthesizing critical components of life. At the same time we will provide glimpses into the frontiers of biology in these various areas.

The 21st century will be the century of biology and medicine. We are delighted to have you join us for a birds-eye view of *Systems Biology and Engineering*. We look forward to your participation in what we hope will be an exciting adventure into the future.

Sincerely,

Leroy Hood, President

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SUNDAY, APRIL 20, 2008

12:00 PM REGISTRATION

SYMPOSIUM OPENING

1:00 pm Welcoming Remarks: **Lee Hood, M.D., Ph.D.,** President of ISB

1:15 pm Opening Keynote: **Nathan Myhrvold, Ph.D.,** Intellectual Ventures, LLC

2:00 pm Break, 15 minutes

SESSION 1: BIOLOGICAL IMAGING

CHAIR: DEAN MATT O'DONNELL, UW COLLEGE OF ENGINEERING

2:15 pm **Mark Ellisman, Ph.D.,** University of California, San Diego
Multi-scale Imaging of the Nervous System: Where's the Dark Matter?

Richard Caprioli, Ph.D., Vanderbilt University
Molecular Imaging and Profiling of Tissues Sections Using Mass Spectrometry: Applications in Biological and Clinical Research

Break, 15 minutes

Shuming Nie, Ph.D., Emory University
Nanotechnology and Bioengineering for Personalized Medicine

Lucas Pelkmans, Ph.D., ETH Institute of Molecular Systems Biology
Revealing and Predicting Single-cell Heterogeneity Signatures in Human Cell Populations Applied to Virus Entry and Endocytosis

5:30 pm Break, 15 minutes

5:45 pm Session 1 Speaker Panel

6:30 pm Session 1 Closed

RECEPTION & POSTER SESSION

7:00 pm Reception and Poster Session at Hotel Deca

MONDAY, APRIL 21, 2008

7:30 AM CONTINENTAL BREAKFAST

SESSION 2: SINGLE-CELL AND SINGLE-MOLECULE EXPERIMENTATION

CHAIR: BABAK AMIR PARVIZ, UW COLLEGE OF ENGINEERING

8:00 am **Adrian Ozinsky, M.D., Ph.D.,** Institute for Systems Biology
Imaging, Analysis and Manipulation of Single Cells

David Walt, Ph.D., Tufts University
Using Optical Arrays to Study Single Enzyme Molecules and Single Cells in Large Populations

Break, 15 minutes

Deirdre Meldrum, Ph.D., Arizona State University
Life-on-a-Chip: Single-cell Technologies for Health and the Environment

10:45 am Session 2 Speaker Panel

11:30 am Break, 1 hour – Lunch and ISB Tours

SESSION 3: SYNTHETIC BIOLOGY

CHAIR: AIMÉE DUDLEY, ISB

12:30 pm **Jay Keasling, Ph.D.,** University of California, Berkeley
Synthetic Biology in Pursuit of Low-cost, Effective, Anti-Malarial Drugs

Michael Elowitz, Ph.D., California Institute of Technology
Dynamics and Noise in Cell Fate Decisions

Break, 30 minutes

Drew Endy, Ph.D., Massachusetts Institute of Technology
Technologies for Engineering Biology

3:15 pm Session 3 Speaker Panel

4:00 pm Break, 15 minutes

SYMPOSIUM CLOSING

4:15 pm Closing Keynote: **Bill Gates,** Bill & Melinda Gates Foundation, Microsoft

5:00 pm Closing Remarks: **Alan Aderem, Ph.D.,** Director of ISB

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Keynote Address

Sunday

NATHAN MYHRVOLD, PH.D.

CEO and Founder of Intellectual Ventures, LLC

Dr. Nathan Myhrvold is chief executive officer and founder of Intellectual Ventures, a private firm focused on the funding, creation and commercialization of inventions. Before Intellectual Ventures, Myhrvold spent 14 years at Microsoft Corporation where he retired in May 2000 from his position as chief technology officer.

Prior to his role as CTO of Microsoft, Dr. Myhrvold held various positions within the company and was responsible for founding Microsoft Research and numerous technology groups that resulted in many of Microsoft's core, leading products. Before joining Microsoft in 1986, Myhrvold was founder and president of Dynamical Systems. Prior to that he was a postdoctoral fellow in the department of applied mathematics and theoretical physics at Cambridge University and worked with Professor Stephen Hawking on research in cosmology, quantum field theory in curved space time and quantum theories of gravitation.

Dr. Myhrvold holds a doctorate in theoretical and mathematical physics and a master's degree in mathematical economics from Princeton University. He also has a master's degree in geophysics and space physics and a bachelor's degree in mathematics, both from the University of California Los Angeles. He is an avid inventor with more than 20 issued patents and nearly 200 patents pending. He has published scientific papers in journals including Science, Nature, Paleobiology and the Physical Review. His paper "Cyberpaleontology - Supersonic Sauropods," co-authored with Dr. Philip Currie, was added to the Smithsonian Institution's 1998 Innovation collection and was one of the 1998 finalists for the Computerworld Smithsonian Innovation Awards.

Closing Keynote

Monday

BILL GATES

Co-chair of the Bill and Melinda Gates Foundation
Chairman of Microsoft Corporation

William "Bill" H. Gates III is co-chair of the Bill and Melinda Gates Foundation, and chairman of Microsoft Corporation—the worldwide leader in software services and solutions. He is also the founder of Corbis, one of the world's largest resources of art and photography, and a director of Berkshire Hathaway Inc.

Bill Gates has written two books, "Business @ the Speed of Thought" (published in 25 languages and available in over 60 countries), and "The Road Ahead." The proceeds of both books go to non-profit organizations supporting the use of technology in education and skills development.

Together, Bill and Melinda Gates shape and approve foundation strategies, review results, advocate for the foundation's issues, and help set the overall direction of the organization. They meet with local, national, and international grantees and partners to further the foundation's goal of improving equity in the United States and around the world. They also use many public appearances, including speeches, interviews, and articles, to focus attention on these issues.

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RICHARD M. CAPRIOLI, Ph.D. SUNDAY – SESSION 1

Vanderbilt University School of Medicine

Dr. Richard M. Caprioli is the Stanley Cohen Professor of Biochemistry and Director of the Mass Spectrometry Research Center at Vanderbilt University School of Medicine. Professor Caprioli is interested in the use of mass spectrometry for the analysis of compounds in biological systems. Current work includes the use of electrospray and laser desorption ionization methods with biological tissues and samples. Applications have focused on the development of this instrumentation and associated methodologies to achieve ultra-high sensitivity detection of endogenous compounds (e.g., neuropeptides) in live animal systems.

Dr. Caprioli has been a member of the American Society for Mass Spectrometry since 1975; he served two years each as President of the Society and Vice-President for Programs. He is a member of the American Society for Biochemistry and Molecular Biology, the American Association for Cancer Research, and the American Chemical Society. He has published over 300 scientific papers, including three books. In 2003, Dr. Caprioli received the Thomson Medal Award from the International Mass Spectrometry Society "for outstanding achievements in mass spectrometry and for distinguished service to international mass spectrometry." He received the Field and Franklin Award from the American Chemical Society in April 2006 for Outstanding Achievement in Mass Spectrometry.

MARK ELLISMAN, Ph.D. SUNDAY – SESSION 1

University of California, San Diego

Dr. Mark H. Ellisman established *National Center for Microscopy and Imaging Research* in 1988 to achieve greater understanding of the structure and function of the nervous system by developing 3D light and electron microscopy methods. Dr. Ellisman is also a founding fellow of the American Institute of Medical and Biological Engineering. Since 1996, he has been serving as the founding director of the UCSD Center for Research in Biological Systems (CRBS). He is also the interdisciplinary coordinator for the National Partnership for Advanced Computing Infrastructure (NPACI) and leads NPACI's Neuroscience thrust. In 2001, he founded the Biomedical Informatics Research Network (BIRN), an NIH program that provides a multiscale imaging infrastructure linking major neuroimaging centers around the country. The following year, Dr. Ellisman was appointed to the National Advisory Council of the NIH National Center for Research Resources (NCRR) and to the Physics Division Review Committee of the Department of Energy, Los Alamos National Laboratory.

Dr. Ellisman´s research promotes the development and application of advanced imaging technologies to obtain new information about cell structure and function, structural correlates of nerve impulse conduction and axonal transport, cellular interactions during nervous system regeneration, cellular mechanisms regulating transient changes in cytoplasmic calcium and aging in the central nervous system.

Speakers

MICHAEL ELOWITZ, Ph.D. MONDAY – SESSION 3

California Institute of Technology

Dr. Michael Elowitz completed his B.A. in physics at the University of California, Berkeley and his M.A. and Ph.D. in physics at Princeton University. He then did research at both Princeton and Rockefeller University before becoming an assistant professor at California Institute of Technology. His current research is focused on how living cells respond to their environment, communicate with one another and develop into multicellular organisms. Elowitz´s lab is interested in how these tasks are accomplished using the network of interacting genes and proteins contained in the cell. He is equally interested in the opposite question of how novel networks can be engineered within cells to implement alternative cellular behaviors.

One example of this approach is the Repressilator, a synthetic oscillatory network constructed in the bacteria Escherichia coli (Elowitz & Leibler, 2000). The Repressilator is designed to cause oscillations in the level of gene expression over time in individual cells. It consists of a negative feedback loop of three transcriptional repressors. When combined with a green fluorescent reporter gene, the Repressilator causes growing E. coli cells to flash periodically, or twinkle, demonstrating that oscillations can be genetically programmed. Interestingly, these programmed oscillations are far less regular than those of natural cellular clocks, such as the circadian clock that operates in many organisms. Elowitz´s research interests focus on how natural biological clocks behave so reliably, and conversely, in understanding what, if anything, limits the accuracy of synthetic genetic clocks.

DREW ENDY, Ph.D. MONDAY – SESSION 3

Massachusetts Institute of Technology

Dr. Drew Endy is helping to start the new Department of Biological Engineering at MIT. He is a co-founder of Codon Devices, Inc. and president of the BioBricks Foundation, a not-for-profit organization promoting open access to biological technologies. He also started and leads the organization of the International Meeting on Synthetic Biology conference series, and advises various government and private organizations on matters related to the ongoing development of biological technologies.

At MIT, Dr. Endy´s lab research has resulted in (a) the first example of refactoring the genome of a natural biological system, (b) an abstraction hierarchy for engineering genetic devices, including a common signal carrier for transcription-based devices, and (c) experiments suggesting that the behavior of natural molecular biological systems is determinable, and perhaps not so stochastic. His two future research interests are implementing reliable behavior in engineered biological devices, and developing a practical framework for designing reproducing machines whose designs are readily understandable by humans.

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JAY KEASLING, Ph.D. MONDAY – SESSION 3

University of California, Berkeley

Dr. Jay Keasling received his B.S. in chemistry and biology from the University of Nebraska in 1986; his Ph. D. in chemical engineering from the University of Michigan in 1991; and did post-doctoral work in biochemistry at Stanford University from 1991-1992. Keasling joined the Department of Chemical Engineering at the University of California, Berkeley as an assistant professor in 1992, where he is currently a professor. Keasling is also a professor in the Department of Bioengineering at Berkeley, a faculty scientist and director of the Physical Biosciences Division at the Lawrence Berkeley National Laboratory, and director of the Berkeley Center for Synthetic Biology.

Dr. Keasling's research focuses on engineering microorganisms for environmentally friendly synthesis of small molecules or degradation of environmental contaminants. Keasling's laboratory has engineered bacteria and yeast to produce polymers and a precursor to the anti-malarial drug artemisinin and soil microorganisms to accumulate uranium and to degrade nerve agents.

DEIRDRE MELDRUM, Ph.D. MONDAY – SESSION 2

Arizona State University

Dr. Deirdre R. Meldrum received a B.S in civil engineering from the University of Washington in 1983 a master's degree in electrical engineering from Rensselaer Polytechnic Institute, Troy, N.Y. in 1985, and a Ph.D. in electrical engineering from Stanford University in 1993. In 1996, she was awarded a Presidential Early Career Award for Scientists and Engineers "for recognition of innovative research utilizing a broad set of interdisciplinary approaches to advance DNA sequencing technology." In 2001, Meldrum was awarded a National Institutes of Health Center of Excellence in Genomics Science, which led to the establishment of the Microscale Life Sciences Center. The center brings together researchers in electrical engineering, chemical engineering, chemistry, materials science and engineering, laboratory medicine, microbiology and cancer biology from Arizona State University, University of Washington, the Fred Hutchinson Cancer Research Center, and Brandeis University to work on developing microscale devices to provide genetic information.

Meldrum is a member of the National Advisory Council for Human Genome Research U.S. Department of Health and Human Services. She is a Fellow of the American Association for the Advancement of Science and a Fellow of the Institute of Electrical and Electronics Engineers.

SHUMING NIE, Ph.D. SUNDAY – SESSION 1

Emory University

Dr. Shuming Nie is the Wallace H. Coulter Distinguished Chair Professor in Biomedical Engineering at Emory University and the Georgia Institute of Technology, with joint appointments in chemistry, materials science and engineering and hematology and oncology. He is the principal investigator and director of the Emory-Georgia Tech Nanotechnology Center for Personalized and Predictive Oncology, one of the eight national centers funded by the National Cancer Institute (NIH/NCI). His research interest is broadly in biomolecular engineering and nanotechnology, with a focus on bioconjugated nanoparticles for cancer molecular imaging, molecular profiling, pharmacogenomics and targeted therapy.

During the last 10 years, Professor Nie has published nearly 100 scholarly papers, filed 20 patents/inventions and has delivered more than 350 invited talks and keynote lectures. In recognition of his work, Professor Nie has received many awards and honors including the Merck Award (2007), Elected Fellow of the American Institute of Biological and Medical Engineering (2006), the Cheung Kong Professorship (The Ministry of Education of China, 2006), the Rank Prize in Opto-electronics (London, UK, 2005), the Georgia Distinguished Cancer Scholar Award (Georgia Cancer Coalition, 2002-2007), the Beckman Young Investigator Award, the National Collegiate Inventors Award and the NSFC Overseas Young Scholar Award.

ADRIAN OZINSKY, M.D., Ph.D. MONDAY – SESSION 2

Institute for Systems Biology

Dr. Adrian Ozinsky joined the ISB faculty in 2005. He is an immunologist with a strong background in cell biology, molecular biology and biochemistry. He is interested in deciphering how immune cells coordinate defenses during infections. What are the mechanisms used by white blood cells, such as macrophages, to detect, engulf and kill microbes, and how are these events coupled to the initiation of inflammation?

Dr. Ozinsky has made major contributions to establish that innate immune cells utilize the members of the Toll-like receptor (TLR) family to identify pathogens and coordinate protective immune defenses in order to limit infections. These studies have revealed how TLRs participate in the perception of a variety of microbes, including organisms as diverse as Gram-positive bacteria, Gram-negative bacteria, mycobacteria, yeasts and parasites. This wide range of pathogens is perceived through the recognition of select microbial components, including combinations of sugars, proteins, lipids and nucleic acids that represent molecular patterns that are unique to pathogens.

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Speakers

LUCAS PELKMANS, Ph.D. SUNDAY – SESSION 1

ETH Institute of Molecular Systems Biology

Dr. Lucas Pelkmans worked towards his Ph.D. degree at the Institute of Biochemistry of the ETH in Zürich. His thesis was awarded with the ETH medal. He then spent two years as an EMBO long-term fellow and Marie Curie fellow at the Max Planck Institute for Molecular Cell Biology and Genetics in Dresden, Germany. In February 2005 he was awarded with an independent research professorship from the Swiss National science Foundation (SNF), and in August 2005 he was awarded 'European Young Investigator' (EURYI).

During his Ph.D. work, Dr. Pelkmans discovered, by following the infectious entry of Simian Virus 40, an alternative endocytic route that is ligand-activated and involves caveolae and a new type of endocytic organelle that he named caveosomes. He also revealed that this involves a signal transduction event activated by the ligand which leads to a cycle of cortical actin depolymerization/polymerization and recruitment of the endocytic machinery to sites of internalization.

DAVID WALT, Ph.D. MONDAY – SESSION 2

Tufts University

Dr. David R. Walt is Robinson Professor of Chemistry at Tufts University and a Howard Hughes Medical Institute professor. He received a B.S. in chemistry from the University of Michigan and a Ph.D. in chemical biology from SUNY at Stony Brook. After postdoctoral studies at MIT, he joined the chemistry faculty at Tufts and served as Chemistry Department Chairman from 1989 to 1996.

Dr. Walt serves on many government advisory panels and boards and serves on the editorial advisory board for numerous journals. From 1996-2003 he was executive editor of Applied Biochemistry and Biotechnology. Dr. Walt is the scientific founder and a director of Illumina Inc. and Quanterix Corp. He has received numerous national and international awards and honors for his fundamental and applied work in the field of optical sensors and arrays and is a fellow of the American Association for the Advancement of Science. Dr. Walt has published over 200 papers, holds over fifty patents and has given hundreds of invited scientific presentations.

NOTES:

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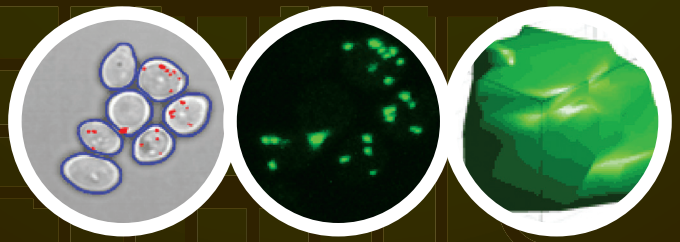
SYSTEMS BIOLOGY AND ENGINEERING AT ISB

The Institute for Systems Biology (ISB) was co-founded in 2000 by Leroy Hood, Alan Aderem, and Ruedi Aebersold. In eight years it has grown to more than 200 staff members, including 13 faculty members and their laboratory groups. Building a systems biology research institute requires a strategy that integrates biology, technology, computation and medicine to catalyze the development of predictive, preventive and personalized medicine. Because a systems approach to disease and immunity requires the seamless integration of these disciplines, ISB has developed a philosophy, an environment and an administrative structure that is designed to break down traditional organizational and disciplinary barriers. Researchers collaborate across the boundaries of their disciplines and reach outside organizational boundaries to share and leverage knowledge and expertise with partners in academia and industry.

Engineering is a central element of systems biology. Biological questions of great (or very small) scale and complexity drive the development of new technologies that open up new scientific possibilities. Moreover, concepts and analytical methods from engineering are finding direct applications in biology. Systems biology embraces the integration of biology and engineering. ISB researchers are conducting leading research in the areas of biological imaging, single-cell and single-molecule experimentation and synthetic biology.

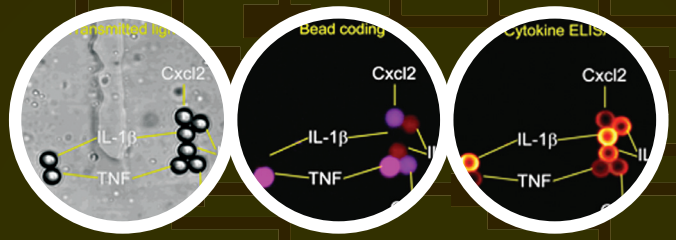
High-Throughput Image Analysis

High-throughput cellular imaging and microfluidic technologies are enabling phenotypic measurements on single cell and population-wide scales. The extraction of information from such imaging data is necessary for establishing the relationships between the behavior of molecular networks in cells and quantitative phenotypic features, which can subsequently be cast within a predictive framework. ISB researchers are developing image processing and analysis methods to count cells and subcellular objects, to statistically describe their shapes and to track the location of objects over time such as a protein within a cell or the interactions of two cells. To effectively manage such large data sets, software engineers are developing software tools for rapid and flexible customization of analysis pipelines, annotation of the analyzed results and analysis of the data in an integrated fashion with other systems measurements.



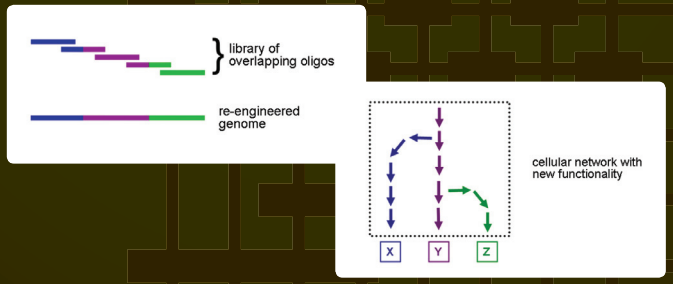
Measuring Biological Processes with Single-cell Resolution

Though the cell is a fundamental unit of biological organization, few experimental measurements are made with single-cell resolution. At ISB, several research programs utilize microfluidic devices to dynamically perturb and observe single cells and to capture ever-present cellular heterogeneity. The sub-nanoliter fluidic processing capability of the devices provide for the exposure of cells to well defined chemical stimuli and the continuous monitoring of cellular response through phenotype and fluorescence reporters. We also are addressing the analytical challenge of quantifying protein and mRNA abundance from single cells. The integration of measurements enabled by microfluidics technology will address questions of signaling kinetics, dynamics and heterogeneity.



Synthetic Biology

The ultimate test of our understanding of a system is our ability to accurately predict its response to novel perturbations. For biological systems, this includes large scale re-engineering of genes and genomes to significantly change the functional capacity of the network. ISB researchers, in collaboration with their academic and industrial partners, are developing synthetic biology approaches that will enable rapid re-engineering of model organisms. These technologies include platforms for large-scale gene synthesis, highly multiplexed mutagenesis and codon optimization. When integrated with a systems level analysis, these methods hold great promise not only for testing our knowledge of the underlying principles and emergent properties of biological systems, but also for practical applications, such as bioremediation and biomolecule production.



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CENTERS OF EXCELLENCE AT ISB

Center for Systems Biology

Funded by the National Institute of General Medical Sciences (NIGMS), part of NIH, the Center for Systems Biology at ISB **(www.centerforsystemsbiology.org)** creates programs that span not only the associated disciplines of systems biology—biology, computer science, applied mathematics, physics and engineering—but also the traditional 'edges' that can exist between the research and educational/outreach programs. Resources and results from the work conducted at the Center are available to the community.

Center for Inquiry Science

The Center for Inquiry Science (CIS) is a team of science educators uniquely hosted by ISB. Drawing from and contributing to educational research, the Center for Inquiry Science's efforts support K-12 inquiry-based science education within the Puget Sound region across Washington State. The CIS offers a variety of services including development, facilitation and coordination of professional development and consultation for teachers and administrators.

STRATEGIC PARTNERSHIPS

The ISB is a scientific catalyst and a hub of strategic partnerships driving the impacts of systems biology.

Helicos BioSciences Corporation

ISB partners with Helicos BioSciences **(www.helicosbio.com),** a pioneer in high-speed, high-sensitivity sequencing providing us access to Helicos' True Single Molecule Sequencing (tSMSTM) technology and protocols for use in scientifically groundbreaking research projects. The tSMSTM technology enables researchers to rapidly and accurately sequence individual molecules of DNA and RNA and promises to provide both maximum efficiency and cost-savings. We have begun applying the capabilities of true single molecule sequencing technology in the area of cancer research. The tSMSTM technology will allow us to address questions in the field of oncology that have, up until this point, remained elusive.

NanoSystems Biology Alliance

ISB, Caltech and UCLA have partnered to form the NanoSystems Biology Alliance, which is dedicated to driving new in vitro and in vivo measurement technologies to meet the needs of systems medicine. One aspect of the alliance, the Nanotechnology/Cancer Center, is funded by the National Cancer Institute. The Center **(www.caltechcancer.org)** is organized to take advantage of the state-of-the-art in chemistry, materials and physics of nanotechnology science and engineering, the state-of-the-art in the systems biology approach to health and disease, and the state-of-the-art in the science, technology and clinical applications of cancer biology.

Seattle Proteome Center

The goal of the Seattle Proteome Center **(www.proteomecenter.org),** supported by the National Heart, Lung and Blood Institute, is to develop innovative proteomic technologies and apply them to biological questions. The Center's research focus is an array of new, systematic assays to comprehensively study the dynamics of cells in health and disease. Over the long term, the Center will apply these technologies to the biology of the macrophage, a cell of central importance in chronic inflammatory responses that lead to disabling human diseases including atherosclerosis chronic fibrotic lung diseases.

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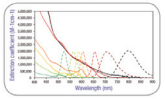

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