City of Hope

The 31st Annual

Beckman Symposium

November 10, 2022

Cooper Auditorium
Beckman Research Institute of City of Hope
Duarte, California

31st Annual Beckman Symposium

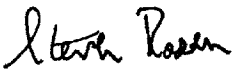
On behalf of Beckman Research Institute of City of Hope, welcome to the 31st Beckman Symposium, titled, "Integral Role of Quantitative Sciences in Medicine: From the Atomic Scale Through to Patients and Communities." The Beckman Symposia are dedicated to presenting the latest breakthroughs in the areas of basic, translational and clinical research. Beckman Research Institute of City of Hope, established in 1983, is the first of five Beckman Institutes that were created following a generous gift from the Arnold and Mabel Beckman Foundation. Over the past three decades, Beckman Research Institute of City of Hope has grown substantially to become a leader in innovative basic and translational research, focusing on cancer, diabetes and metabolism, HIV, and stem cell biology/regenerative medicine.

Beckman Research Institute of City of Hope is unique among the Beckman Institutes in that it has held a National Cancer Institute Cancer Center Support Grant for more than 30 years. City of Hope's National Cancer Institute-designated comprehensive cancer center is comprised of five research programs in the areas of basic, translational and prevention research: Molecular and Cellular Biology of Cancer, Developmental Cancer Therapeutics, Cancer Immunotherapeutics, Hematologic Malignancies, and Cancer Control and Population Sciences. These programs conduct activities across the entire Duarte, California, campus, facilitating interactions among researchers of all disciplines. Cancer center members who conduct laboratory research hold appointments as Beckman Research Institute faculty. These collaborative interactions between the cancer center and Beckman Research Institute provide tremendous opportunities for translation of laboratory discoveries directly into new therapies for patients. There are numerous clinical trials that build on the research discoveries of Beckman Research Institute investigators.

The Duarte, California, campus occupies 120 acres, with 64 buildings and more than 700,000 square feet of laboratory space devoted to biomedical research. Beckman Research Institute has over 30 state-of-the-art scientific shared (core) resources that support researchers across campus.

Thank you for your participation in this year's Beckman Symposium.

Sincerely yours,



Steven T. Rosen, M.D.
Provost and Chief Scientific Officer
Director, Comprehensive Cancer Center and Beckman Research Institute of City of Hope
Irell & Manella Cancer Center Director's Distinguished Chair
Morgan & Helen Chu Director's Chair of Beckman Research Institute

The History of Beckman Research Institute

The Arnold and Mabel Beckman Foundation, in April of 1983, awarded $10 million to City of Hope's research institute. This was the first major gift made by the foundation and set up the first of five Beckman Research Institutes. Arnold Beckman, Ph.D., during the formal dedication ceremony in January 1984, said: "We look on our contribution as an investment, probably one of the best investments of our lives. It may not pay dividends in dollars, but it will pay dividends that are far more valuable than dollars — the pride and satisfaction of being associated with an organization that is doing so much for the benefit of mankind." It is with his words in mind that Beckman Research Institute of City of Hope continues in its mission.

Funds from the foundation were earmarked for buildings, equipment and endowment. In addition, later donations from the Beckman Foundation have contributed to the construction of the Conrad Hilton, Shapiro and Kaplan-Black research buildings, Graff Medical and Scientific Library and, most recently, the Arnold and Mabel Beckman Center for Cancer Immunotherapeutics & Tumor Immunology, a 108,000-square-foot research facility.

In addition to the original gift, the foundation has also made annual donations that have provided valuable discretionary funds. Since 1991, Beckman monies have funded the annual Beckman Symposium, bringing world-renowned scientists to City of Hope, and the Beckman Fellows Program, which has helped to launch the careers of eight talented young scientists. During the current funding period, Beckman Foundation funds are being used for development of new state-of-the-art technologies and shared core facilities that enable leading-edge biomedical research at City of Hope.

The mission of the Arnold and Mabel Beckman Foundation, established in September 1977, is to support basic science research, medicine and education. "I accumulated my wealth by selling instruments to scientists," Beckman explained, "so I thought it would be appropriate to make contributions to science." For a quarter of a century, the Beckman Foundation has lived up to its mission by providing vital support to Beckman Research Institute of City of Hope. The new vision for Beckman Research Institute, supported by the foundation, is excellence in innovative biomedical research that impacts the treatment of cancer, diabetes and related diseases.

Schedule

7:30 to 8:20 a.m.	**Check-in and Breakfast**
8:20 to 8:30 a.m.	**Welcome** **David Horne, Ph.D.** Vice Provost and Associate Director, Beckman Research Institute of City of Hope Dr. & Mrs. Allen Y. Chao Chair in Developmental Cancer Therapeutics
	Challenges in Designing Next Generation Drugs: From Bench to Clinic Chaired by **Nagarajan Vaidehi, Ph.D.**
8:30 to 9:30 a.m.	**Following the Rabbit Into Chemical Space** **Brian K. Shoichet, Ph.D.** Professor, Pharmaceutical Chemistry University of California, San Francisco
9:30 to 10:30 a.m.	**From Polyfunctionality to Multipathogenicity With Intrinsic Disorder** **Vladimir N. Uversky, Ph.D.** Professor, Molecular Medicine USF Health Byrd Alzheimer's Research Institute Morsani College of Medicine University of South Florida
10:30 to 10:40 a.m	**Break**
	Translating Mathematical and Computational Oncology Models to Clinical Care Chaired by **Russell Rockne, Ph.D.**
10:40 to 11:40 a.m.	**Solving Brain Cancer: Every Patient Deserves Their Own Equation** **Kristin R. Swanson, Ph.D.** Vasek and Anna Varia Polak Professor, Cancer Research Professor, Radiation Oncology and Cancer Biology Mayo Clinic, Arizona Professor, Mathematical and Statistical Sciences Arizona State University

11:40 to Noon	**Panel Discussion I With the Speakers** Led by **Nagarajan Vaidehi, Ph.D.** **Russell Rockne, Ph.D.**
Noon to 1 p.m.	**LUNCH**
	Computational Systems Biology, Genomics, and Statistical Genetics: Mining Knowledge From Patient-Specific Heterogeneous Datasets Chaired by **Xiwei Wu, Ph.D.**
1 to 2 p.m.	**Multiscale - Multicellular Network Models for Data Integration and Precision Health** **Benedict N. Anchang, Ph.D.** Stadtman Tenure-Track Investigator, National Institute of Environmental Health Sciences National Cancer Institute
2 to 3 p.m.	**Deciphering Tissue Microenvironment by Integrative Analysis of Spatial Transcriptomics With Histology Images and Single Cells** **Mingyao Li, Ph.D.** Director, Biostatistics Gene Therapy Program Director, Statistical Center for Single-Cell and Spatial Genomics Chair, Graduate Program in Biostatistics University of Pennsylvania
3 to 4 p.m.	**The Human Brainome: Genome, Transcriptome, Proteome and Phenome Interaction in Human Cortex** **Amanda J. Myers, Ph.D.** Professor Principal Investigator, Laboratory for Functional Neurogenomics Co-appointments, Institute for Data Science and Computing, Division of Neuroscience, Department Human Genetics and Genomics, Center on Aging University of Miami

4 to 4:10 p.m.	**Break**
	Deriving Insights From Clinical Trials Using Bioinformatics and Data Science Chaired by **Joycelynne Palmer, Ph.D.**
4:10 to 5:10 p.m.	**Learning From Every Child: The Childhood Cancer Data Initiative** **Warren A. Kibbe, Ph.D.** Vice Chair and Professor of Biostatistics and Bioinformatics Chief, Division of Translational Biomedical Informatics Duke University
5:10 to 5:30 p.m.	**Panel Discussion II With the Speakers** Led by **James V. Lacey, Jr., Ph.D., M.P.H.** **Andrei S. Rodin, Ph.D.**
5:30 to 5:35 p.m.	**Closing Remarks** **Andrei S. Rodin, Ph.D.**

Following the Rabbit Into Chemical Space

Brian K. Shoichet, Ph.D.
Professor, Pharmaceutical Chemistry
University of California San Francisco

Recently, docking libraries have expanded from three million "in-stock" to over four billion diverse and stereogenic "tangible." It is easy to imagine that as we expand to ever larger libraries, the docking scoring functions, with all their approximations, will become overwhelmed by decoys. While there is some evidence that that can happen, if anything, affinities improve with library size. Meanwhile, plots of hit rates vs. score for the dopamine, and recently for the Sigma2 receptors, tested at scale, suggest that docking score remains a strong categorizer as libraries grow. Here we investigate why that may be and prospects for looking ahead into ever larger libraries, both by brute-force docking and by ML-based methods. Case studies seeking to discover new ligands with new pharmacologies for analgesia and depression targets will also be presented.

From Polyfunctionality to Multipathogenicity With Intrinsic Disorder

Vladimir N. Uversky, Ph.D.
Professor, Molecular Medicine
USF Health Byrd Alzheimer's Research Institute
Morsani College of Medicine
University of South Florida

Intrinsically disordered proteins (IDPs) lack stable tertiary and/or secondary structure under physiological conditions in vitro. They are highly abundant in nature and have functional repertoire which is very broad and complements functions of ordered proteins. Often, intrinsically disordered proteins are involved in regulation, signaling and control pathways. Functions of IDPs may arise from the specific disordered form, from inter-conversion of disordered forms, or from transitions between disordered and ordered as well as between ordered and disordered conformations. The choice between these conformations is determined by the peculiarities of the protein environment, and many IDPs possess an exceptional ability to fold in a template-dependent manner. These proteins are often key players in protein-protein interaction networks being highly abundant among hubs. Regions of mRNA which undergo alternative splicing code for disordered proteins more often than they code for structured proteins. This association of alternative splicing and intrinsic disorder helps proteins to avoid folding difficulties and provides a novel mechanism for developing tissue-specific protein interaction networks. IDPs are tightly controlled in the norm by various genetic and non-genetic mechanisms. Alteration in regulation of this disordered regulators are often detrimental to a cell and many IDPs are associated with a variety of human diseases such as cancer, cardiovascular disease, amyloidoses, neurodegenerative diseases, diabetes and others. Therefore, there is an intriguing interconnection between intrinsic disorder, cell signaling and human diseases. Pathogenic IDPs, such as α-synuclein, tau protein, p53, BRCA1 and many other disease-associated hub proteins represent attractive targets for drugs modulating protein-protein interactions. Several strategies have been elaborated for elucidating the mechanisms of blocking of the intrinsic disorder-based protein-protein interactions.

Solving Brain Cancer: Every Patient Deserves Their Own Equation

Kristin R. Swanson, Ph.D.
Vasek and Anna Varia Polak Professor, Cancer Research
Professor, Radiation Oncology and Cancer Biology
Mayo Clinic, Arizona
Professor, Mathematical and Statistical Sciences
Arizona State University

Glioblastoma is a uniquely challenging and aggressive cancer that is practically considered uniformly fatal. This aggressiveness is driven by heterogeneity between and within patients and the diffuse invasion of tumor cells deep into the normal appearing brain tissue surrounding the frank tumor abnormality. Mathematical neuro-oncology (MNO) is a burgeoning field that seeks to bring together individual patient data (like patient imaging, tissue biopsies etc.) to tune mathematical models that accurately predict and quantify response to treatments for each patient. These mathematical models use both mechanistic "weather forecasting" methods and artificial intelligence pattern recognition methods. Ultimately, these models form the basis of modern "precision medicine" approaches to tailor therapy in a patient-specific manner. These models can be used to overcome the limited ability of imaging to accurately detect tumor cells, improve prognostic predictions, stratify patients, and assess treatment response in silico in the construction of effective clinical trials and treatment protocols, thus accelerating the pace of clinical research. This talk will focus on the growing translation of MNO to clinical neuro-oncology highlighting burgeoning insights into sex differences in tumor incidence, outcomes, and response to therapy.

Multiscale — Multicellular Network Models for Data Integration and Precision Health

Benedict N. Anchang, Ph.D.
Stadtman Tenure-Track Investigator,
National Institute of Environmental Health Sciences
National Cancer Institute

Complex diseases such as cancer and infectious diseases are currently among the major causes of death in the US. The progression of these diseases is associated with multiple alterations in molecular pathways resulting in complex interactions at the cellular, tissue, organ and system levels confounded by time, space and environment. This challenges our ability to precisely diagnose and provide effective personalized treatment. We now can obtain highly resolved molecular phenotypes directly from individual cells from patient samples that can be used to define cell states, understand cellular networks, study developmental processes including, cellular responses to drugs or chemicals. In this talk, I will present an overview of how single-cell technologies and applications are being used to advance our knowledge of several heterogeneous biological processes during preclinical and clinical settings with the help of innovative machine learning, graphical and mechanistic models. Specifically, I will highlight recently published algorithms including PHENOtypic STAte MaP (PHENOSTAMP) based on neural networks, Dynamic Spanning Forest mixtures (DSFMix) and Multiscale Multicellular Quantitative Evaluator (MMQE) that are particularly optimized for visualizing, characterizing, benchmarking, and modeling normal and disease temporal biological processes in single-cell and multicellular systems.

Deciphering Tissue Microenvironment by Integrative Analysis of Spatial Transcriptomics With Histology Images and Single Cells

Mingyao Li, Ph.D.
Director, Biostatistics Gene Therapy Program
Director, Statistical Center for Single-Cell and Spatial Genomics
Chair, Graduate Program in Biostatistics
University of Pennsylvania

Recent developments in spatial transcriptomics technologies have enabled scientists to get an integrated understanding of cells in their morphological context. Applications of these technologies in diverse tissues and diseases have transformed our views of transcriptional complexity. Most published studies utilized tools developed for single-cell RNA-seq for data analysis. However, spatial transcriptomics data exhibit different properties from single-cell RNA-seq. To take full advantage of the added dimension on spatial location information in such data, new methods that are tailored for spatial transcriptomics are needed. Additionally, spatial transcriptomics data often have companion high-resolution histology images. Incorporating histological features in gene expression analysis is an underexplored area. In this talk, I will present several statistical and machine learning methods that we recently developed that aim to help decipher the microenvironment of tissue by integrative analysis of spatial transcriptomics data with histology images and single cells. I will show the applications of these methods in brain and cancer tissues.

The Human Brainome: Genome, Transcriptome, Proteome and Phenome Interaction in Human Cortex

Amanda J. Myers, Ph.D.
Professor
Principal Investigator, Laboratory for Functional Neurogenomics
Co-appointments, Institute for Data Science and Computing, Division of Neuroscience, Department Human Genetics and Genomics, Center on Aging
University of Miami

While there are currently over 30 replicated genes with mapped risk alleles for Late Onset Alzheimer's disease (LOAD), the Apolipoprotein E locus E4 haplotype is still the biggest driver of risk, with odds ratios for neuropathologically confirmed E44 carriers exceeding 30 (95% confidence interval 16.59-58.75). We sought to address whether the APOE E4 haplotype modifies expression globally through networks of expression to increase LOAD risk. We have used the data selected from a cohort of ~ 3000 human brain tissues (The Human Brainome) to build expression networks comparing APOE E4 carriers to non-carriers using scalable mixed-datatypes Bayesian Network (BN) modeling. Using this approach, we have found several novel targets for Late Onset Alzheimer's disease risk.

Learning From Every Child: The Childhood Cancer Data Initiative

Warren A. Kibbe, Ph.D.
Vice Chair and Professor of Biostatistics and Bioinformatics
Chief, Division of Translational Biomedical Informatics
Duke University

The NCI Childhood Cancer Data Initiative was announced by the Whitehouse and received its first allocation of funding in FY2020, with the goal of improving data sharing for pediatric cancers and to "learn from every child". I will present the current state of the project, where it is headed, and how to get involved.

The 2022 Beckman Symposium Integral Role of Quantitative Sciences in Medicine: From the Atomic Scale Through to Patients and Communities

Date: November 10, 2022
7:30 a.m. to 5:30 p.m.

Location: Cooper Auditorium
City of Hope
1500 E. Duarte Road
Duarte, CA 91010-3000

https://cityofhope.zoom.us/j/93011431822?pwd=TnJrTmFMMXpYdi95MmNBYlVkM0pNQT09

Password: 687940

The same Zoom link will be used for all sessions.

Please keep your microphone muted and camera off, unless the host asks for participants to unmute and/or share video to ask questions. Questions can be asked in the chat.

Registration: https://cityofhope.wufoo.com/forms/31st-beckman-symposium

Registration includes breakfast, lunch and afternoon snack.

Information: For more information during and after the event, please contact:

Wanda Fitzgerald
Email: wfitzger@coh.org

Angelica Quijada
Email: aquijada@coh.org

Maribel Ramirez
Email: maramirez@coh.org

Andrei Rodin
Email: arodin@coh.org

Website: https://www.cityofhope.org/research/beckman-research-institute/beckman-symposium

In compliance with the Americans with Disabilities Act, all reasonable efforts will be made to accommodate persons with disabilities at the meeting. If you have any special dietary or accommodation needs, please notify the program coordinator listed above prior to the symposium.

This advance notification will help us serve you better.

This is the 31st Beckman Symposium to be held at Beckman Research Institute of City of Hope. Supported by funds from the Beckman Endowment, the Beckman Symposia are arranged annually by the research staff organization of City of Hope.

This year's symposium was organized by:

Andrei Rodin, Ph.D. (organizing committee chair)
Dr. Susumu Ohno Chair in Theoretical Biology
Professor, Department of Computational and Quantitative Medicine

Nagarajan Vaidehi, Ph.D.
Professor and Chair, Department of Computational and Quantitative Medicine

Russell Rockne, Ph.D.
Associate Professor, Department of Computational and Quantitative Medicine

Xiwei Wu, Ph.D.
Professor, Department of Computational and Quantitative Medicine

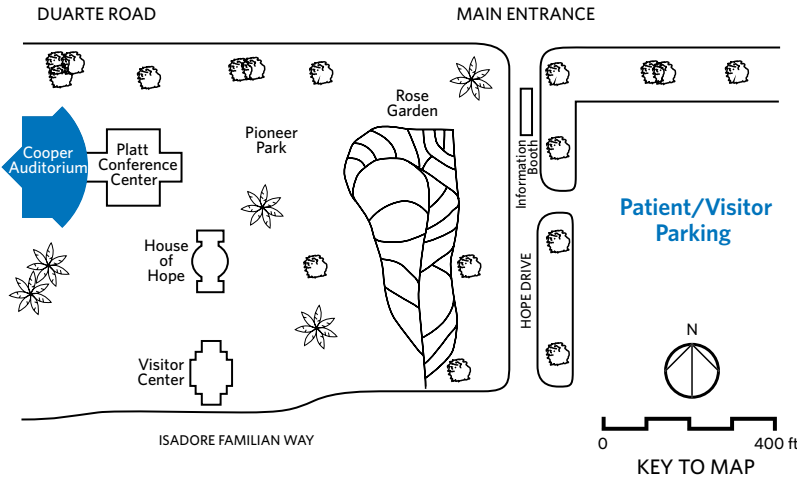
Joycelynne Palmer, Ph.D.
Professor, Department of Computational and Quantitative Medicine

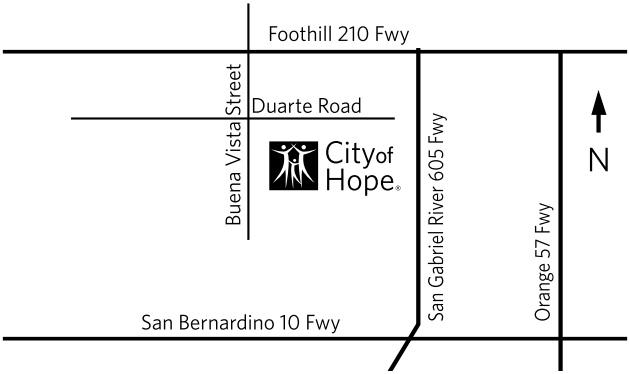
James V. Lacey, Jr., Ph.D., M.P.H.
Professor, Department of Computational and Quantitative Medicine

Faculty of the Department of Computational and Quantitative Medicine City of Hope

Supported by:

The Irell & Manella Graduate School of Biological Sciences Office





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