



NATIONAL CANCER INSTITUTE



5th Annual NCI CSSI Science Day

Center for Strategic Scientific Initiatives

June 28-29, 2017

Porter Neuroscience Research Center
NIH Main Campus, Bethesda, MD



Agenda

Wednesday, June 28

- 9:00 a.m. – 10:05 a.m. Welcome and CSSI Overview and Highlights (Room 620/630)**
- 9:00 a.m. – 9:10 a.m. **Welcome Remarks and Overview of the NCI Center for Strategic Scientific Initiatives (CSSI)**
Sean Hanlon, Ph.D.
Office of the Director, CSSI, NCI
- 9:10 a.m. – 9:20 a.m. **Goals and Intent of Science Day**
Michelle Berny-Lang, Ph.D.
Office of the Director, CSSI, NCI
- 9:20 a.m. – 9:35 a.m. **Highlights from the Innovative Molecular Analysis Technologies (IMAT) Program**
Tony Dickherber, Ph.D.
Office of the Director, CSSI, NCI
- 9:35 a.m. – 9:50 a.m. **Highlights from the Office of Cancer Nanotechnology Research (OCNR)**
Stephanie Morris, Ph.D.
Office of Cancer Nanotechnology Research, CSSI, NCI
- 9:50 a.m. – 10:05 a.m. **Highlights from the Office of Cancer Clinical Proteomics Research (OCCPR)**
Christopher Kinsinger, Ph.D.
Office of Cancer Clinical Proteomics Research, CSSI, NCI
- 10:05 a.m. – 10:25 a.m. Break**
- 10:25 a.m. – 11:45 a.m. Session 1: Leveraging Health Data and Computational Approaches**
- 10:25 a.m. – 10:35 a.m. **Session Introduction**
Eric Stahlberg, Ph.D. (Moderator)
Data Science and Information Technology Program, Leidos Biomedical Research, Inc.
Frederick National Laboratory for Cancer Research
- 10:35 a.m. – 11:10 a.m. **Clinico-genomics: What Is It, and Why Do We Need It?**
Nathan Nussbaum, M.D.
Flatiron Health
- 11:10 a.m. – 11:45 a.m. **Towards Predictive Biology: High Performance Computing and the Cancer MoonshotSM**
Frederick Streitz, Ph.D.
Lawrence Livermore National Laboratory



Agenda

Wednesday, June 28, Continued

11:45 a.m. – 1:15 p.m. Lunch and Keynote Speaker

11:45 a.m. – 12:25 p.m.

Lunch on your own (Cafeteria)

12:25 p.m. – 1:15 p.m.

Keynote – Precision Pathology: Theranostics and Beyond

Michael Roehrl, M.D., Ph.D.

Memorial Sloan Kettering Cancer Center

1:15 p.m. – 2:40 p.m. Session 2: Prevention and Early Detection

1:15 p.m. – 1:25 p.m.

Session Introduction

Lynn Sorbara, Ph.D. (Moderator)

Cancer Biomarkers Research Group, Division of Cancer Prevention, NCI

1:25 p.m. – 2:05 p.m.

Clinical Applications of NanoVelcro Rare-Cell Assays for Detection and Characterization of Circulating Tumor Cells

Jie-Fu Chen, M.D.

Cedars-Sinai Medical Center

and

Edwin Posadas, M.D.

Cedars-Sinai Medical Center

2:05 p.m. – 2:40 p.m.

Nanocytological Biomarkers of Carcinogenesis: Implications for Screening and Therapy

Hemant Roy, M.D.

Boston University

2:40 p.m. – 3:00 p.m. Break

3:00 p.m. – 4:20 p.m. Session 3: Immunotherapy

3:00 p.m. – 3:10 p.m.

Session Introduction

Peter Ujhazy, M.D., Ph.D. (Moderator)

Translational Research Program, Division of Cancer Treatment and Diagnosis, NCI

3:10 p.m. – 3:45 p.m.

Genetic Engineering of Therapeutic T cells Using Synthetic Nanoparticles

Matthias Stephan, M.D., Ph.D.

Fred Hutchinson Cancer Research Center

3:45 p.m. – 4:20 p.m.

Viroimmunotherapy for Cancer

Richard Vile, Ph.D.

Mayo Clinic

Wednesday, June 28, Continued

4:20 p.m. – 4:30 p.m. Session Wrap Up and Reflection

Sean Hanlon, Ph.D.
Office of the Director, CSSI, NCI

4:30 p.m. – 5:30 p.m. Breakout Group Charge and Initial Group Meeting

4:30 p.m. – 5:00 p.m.

Breakout Activity Overview and Charge

Paul Fearn, Ph.D., M.B.A.
Surveillance Research Program, Division of Cancer Control and Population Sciences, NCI
and
Michelle Berny-Lang, Ph.D.
Office of the Director, CSSI, NCI

5:00 p.m. – 5:30 p.m.

Introductory Meeting with Breakout Group

5:30 p.m. Adjournment, Day 1

Thursday, June 29

9:00 a.m. – 9:15 a.m. Welcome and Charge for Day 2 (Room 620/630)

9:00 a.m. – 9:15 a.m.

Charge for Day 2

Michelle Berny-Lang, Ph.D.
Office of the Director, CSSI, NCI

9:15 a.m. – 11:10 a.m. Breakout Group Discussions

Goal: Within the future parameters provided, identify areas of need, development, and exploration in cancer technology (next steps could include workshop coordination, pilot project development, etc.)

11:10 a.m. – 11:30 a.m. Break

11:30 a.m. – 12:30 p.m. Breakout Group Reporting and Final Discussion

11:30 p.m. – 12:20 p.m.

Breakout Group Reporting

Representative(s) from each group

12:20 p.m. – 12:30 p.m.

Final Discussion and Wrap-up

12:30 p.m. Adjournment, Day 2



Speaker Biographies

Jie-Fu Chen, M.D.

Jie-Fu Chen, M.D. is a postdoctoral fellow in Dr. Edwin Posadas' laboratory. Dr. Chen received his M.D. degree from the National Taiwan University in 2013 and then started to work in a joint group between UCLA and Cedars-Sinai Medical Center (CSMC). He joined Dr. Posadas' laboratory in 2014, and his current field of study combines circulating tumor cell (CTC) isolation technology with next-generation sequencing and subsequent data analysis. Dr. Chen applied classic pathologic principles to CTCs, which appear as a predictive and prognostic biomarker in prostate cancer (PCa). He led a translational research project in which the discovery of vsnCTCs (i.e., very small nuclear CTCs) and their correlation with visceral metastases in PCa patients was made. Dr. Chen and his colleagues further advanced the understanding of vsnCTCs through the study of nuclear shape instability, which plays a critical role in the development of metastasis. His recent work also led to the successful translation of PCa Classification System (PCS), a tissue-based RNA classifier, in CTCs as an indicator of the underlying biology of the cancer. Finishing up his postdoctoral research at CSMC, Dr. Chen will soon begin his residency training at Department of Pathology & Immunology in Washington University in St. Louis, and continue to pursue the career of a physician scientist.

Nathan C. Nussbaum, M.D.

Nathan C. Nussbaum, M.D. is the Oncology Medical Director at Flatiron Health, a healthcare technology company focused on organizing the world's cancer data and making it actionable for providers, patients, researchers, and life sciences. At Flatiron, Dr. Nussbaum specializes in real-world evidence generation in oncology, and his work as an outcomes researcher spans a wide range of cancer types. Dr. Nussbaum earned a B.A. magna cum laude in history from Yale University and received his M.D. from the Johns Hopkins University School of Medicine. He completed residency training in internal medicine at the Hospital of the University of Pennsylvania, and medical oncology fellowship at Duke University, where he was also a fellow at the Duke Clinical Research Institute. He maintains a clinical practice at Bellevue Hospital's Cancer Center and has an appointment as a Clinical Instructor at NYU School of Medicine. He is board-certified in internal medicine and medical oncology. Before entering medicine, he worked in management consulting with Bain & Company.

Edwin M. Posadas, M.D.

Edwin M. Posadas, M.D. is the Director of the Translational Oncology Program and the Medical Director of the Urologic Oncology Program at the Samuel Oschin Comprehensive Cancer Institute and the Clinical Chief of the Division of Hematology Oncology of the Department of Medicine at Cedars-Sinai Medical Center (CSMC). Dr. Posadas was recruited to CSMC from the University of Chicago, where he was an assistant professor of medicine and surgery. While at Chicago, he received the Prostate Cancer Foundation's Stewart Rahr Young Investigator Award. Prior to that appointment, Dr. Posadas served as an assistant clinical investigator at the National Cancer Institute. He earned his undergraduate and medical degrees at Johns Hopkins University and served his residency at the University of Michigan Medical Center. Dr. Posadas has more than 15 years of experience in clinical oncology and translational research with interests in the treatment of advanced prostate cancer (PCa) and the biology of cancer metastasis, primarily through exploring the nature of circulating tumor cells (CTCs). Over the past five years, Dr. Posadas has initiated a variety of IRB-approved protocols for biospecimen collection, including a joint operation with the CSMC BioBank and other institutes, which have provided samples for multiple translational studies and this proposed study. Through a partnership with UCLA, Dr. Posadas and his team identified a subpopulation of CTCs named very-small-nuclear CTCs (vsnCTCs) defined by nuclear size criteria, and demonstrated a strong correlation with lethal progression event to visceral organs in prostate cancer patients.

Michael Roehrl, M.D., Ph.D.

Michael Roehrl, M.D., Ph.D. is Director of the newly created Precision Pathology Biobanking Center at Memorial Sloan Kettering Cancer Center. He is dually board-certified in Anatomic Pathology and Laboratory Medicine and practices subspecialty gastrointestinal pathology as Pathology faculty at MSKCC. Dr. Roehrl's research lab focuses on biomarker discovery in GI cancers and other solid tumors using a variety of biochemical, biophysical, and computational approaches, especially high-resolution mass spectrometry-based proteomics and integrated proteogenomics. Dr. Roehrl obtained his M.D. in Munich, Germany, and a Ph.D. in Biological Chemistry from Harvard University. He trained at Massachusetts General Hospital and was academic faculty in both Boston and Toronto before moving to New York.

Hemant Roy, M.D.

Hemant Roy, M.D. is the Ingelfinger Professor of Medicine and Chief of Gastroenterology at Boston University Medical School. His undergraduate degree was from Vanderbilt University in molecular biology summa cum laude and he received his M.D. with distinction from Northwestern University Medical School. His clinical training in internal medicine was completed at Beth Israel/Harvard Medical School and Gastroenterology fellowship at University of Chicago. Prior to moving to Boston in 2013, he served as an Associate Professor of Medicine at Northwestern University for the prior decade.

Dr. Roy's area of interest has been biomarkers for cancer risk stratification via detection of field carcinogenesis. For the last 15 years, he has worked closely with Dr. Vadim Backman on clinical and biological aspects of a suite of novel biophotonic techniques. The work has led to numerous publications, grants etc. He also has interest in early molecular events in colon carcinogenesis and in development of novel therapeutics agents. Dr. Roy serves on the Cancer Biomarker Study Section and has closely interacted with the Early Detection Research Network.

Matthias Stephan, M.D., Ph.D.

The laboratory of Matthias Stephan, M.D., Ph.D. in the Clinical Research Division at Fred Hutchinson Cancer Research Center works at the interface of materials science and immunology, designing synthetic materials that can be used as components of novel cancer immunotherapies. Because certain cells of our immune system can selectively destroy cancerous cells without damaging healthy tissue, engineering approaches grounded in immunology may hold the key to the discovery and development of safe and effective new cancer treatments. To this end, his group takes a materials science-centric engineering approach to create new therapies based in the controlled modulation of the immune system. During his postdoctoral training at the Massachusetts Institute of Technology, Dr. Stephan acquired first-hand skills in synthesizing and employing synthetic materials as a powerful approach to manipulate the function of immune cells. This skillset, coupled with his Ph.D. training in tumor immunology at Cornell University, allows him to design unconventional bioengineering approaches for safe and effective cancer immunotherapy.

His research efforts are currently focused on (1) the development of an implantable device to eradicate tumor left behind after surgery, and (2) the design of novel polymeric nanoparticles that can rapidly program tumor-recognizing capabilities into lymphocytes *in vivo*.

Frederick Streitz, Ph.D.

Frederick (Fred) Streitz, Ph.D. is the Chief Computational Scientist and Director of the High Performance Computing Innovation Center (HPCIC) at Lawrence Livermore National Laboratory (LLNL). He develops strategies and leads efforts to address the nation's forefront scientific problems through the application of supercomputing. As HPCIC Director, he helps guide LLNL's efforts to form strategic industrial, academic, and government collaborations that support and expand HPC resources, expertise and capability at the Lab. Dr. Streitz sits on review boards for Argonne and Oak Ridge National Labs, in addition to service on the Advanced Computing Round Table at the Council on Competitiveness and as a Subject Editor for the International Journal of High Performance Computing Applications. He is a Fellow of the American Physical Society and a two-time winner of the IEEE Gordon Bell Prize.

Fred joined LLNL in 1999 as a computational physicist after holding positions as a National Research Council Fellow at the Naval Research Laboratory and an Assistant Professor at Auburn University. He received a Bachelor of Science in physics from Harvey Mudd College in Claremont, California and a doctorate in physics from the Johns Hopkins University in Baltimore, Maryland.

Richard Vile, Ph.D.

Richard Vile, Ph.D., and his research team develop experimental cancer therapies, all based on stimulating antitumor immune responses. Dr. Vile's research combines in vivo and in vitro assays, but predominantly focuses in murine immune-competent models and syngeneic tumors. Although his team has a major interest in melanoma, they also have models of prostate cancer, glioma and brain metastases, and can be applied across tumor sites.

Oncolytic viruses (OV) have been one of Dr. Vile's key areas of research for several years, and his team previously demonstrated the critical role of the immune system in successful therapy with OV. In addition to making OV expressing cytokines and tumor-associated antigens, they have developed a novel approach in which the vesicular stomatitis virus (VSV) can be engineered to express a library of tumor antigens, resulting in exceptional treatment.

All of this work is intended to help patients with cancer. Dr. Vile's team deliberately focuses on developing therapies that can be rapidly taken to clinical trials. Accordingly, the team works closely with the Mayo Clinic team, as well as those at other U.S. hospitals and worldwide, and have been directly involved in clinical trials of several oncolytic viruses. An ongoing clinical trial for patients with hepatocellular carcinoma is being performed at Mayo Clinic in Arizona with a VSV the team designed to express interferon. Internationally, Dr. Vile's research lab has strong links with researchers in the UK and other countries, to test OV in patients with a range of cancers.

Clinico-genomics: What Is It, and Why Do We Need It?

Nathan Nussbaum, M.D.

Flatiron Health

Abstract:

In an era of abundant biological data, deep clinical phenotyping is crucial for deriving insights that matter to patients. The widespread adoption of Electronic Health Records (EHRs) enables access to large amounts of real-world longitudinal data; however, curation is necessary to assemble datasets that contain research-quality clinical evidence. Dr. Nussbaum will explore what happens when we are able to combine real-world clinical evidence from the patient's EHR with their genomic analysis. He will discuss insights and findings from the combined clinico-genomics datasets, discoveries previously only made possible through clinical trials or patient registries.

Towards Predictive Biology: High Performance Computing and the Cancer MoonshotSM

Frederick Streit, Ph.D.

Lawrence Livermore National Laboratory

Abstract:

The marriage of experimental science with simulation has been a fruitful one—the fusion of high performance computing (HPC)-based simulation and experimentation moves science forward faster than either discipline alone, rapidly testing hypotheses and identifying promising directions for future research. The emergence of machine learning at scale promises to bring a new type of thinking into the mix, incorporating data analytics techniques alongside traditional HPC to accompany experiment. I will discuss the convergence of machine learning, predictive simulation, and experiment in the context of one element of the Cancer MoonshotSM—a detailed investigation of Ras biology in realistic membranes.

This work is performed under the auspices of the U.S. Department of Energy by Lawrence Livermore National Laboratory under Contract DE-AC52-07NA27344.

Keynote – Precision Pathology: Theranostics and Beyond

Michael Roehrl, M.D., Ph.D.

Memorial Sloan Kettering Cancer Center

Abstract:

This talk will elaborate on the rapidly transforming role of Pathology as a central hub for the future of Precision Medicine and Personalized Health Care.

We will introduce the five major pillars of excellence in the new Precision Pathology Center at Memorial Sloan Kettering Cancer Center (MSKCC): (1) Science-driven biobanking for research and clinical trials; (2) Precision Pathology Informatics and Big Data Analytics; (3) new technologies and innovation incubator; (4) joint R&D with academic and private-sector partners; and (5) new Pathology Hub for next generation specimen-driven clinical trials and drug development.

Pathology is now evolving from a single time-point (“snapshot”) diagnostic paradigm to becoming a proactive key theranostic clinical discipline where diagnosis, therapeutic decision-making, continuous molecular response monitoring, and therapeutic escape detection are fully integrated.

Clinical Applications of NanoVelcro Rare-Cell Assays for Detection and Characterization of Circulating Tumor Cells

Jie-Fu Chen, M.D.

Cedars-Sinai Medical Center

and

Edwin Posadas, M.D.

Cedars-Sinai Medical Center

Abstract:

Circulating tumor cells (CTCs) are regarded as a liquid biopsy of a tumor, allowing non-invasive, repetitive, and systemic sampling of the disease. Although detecting and enumerating CTCs is of prognostic significance in metastatic cancer, it is conceivable that performing molecular and functional characterization on CTCs will reveal unprecedented insight into the pathogenic mechanisms driving lethal disease. Our nanomaterials-embedded cancer diagnostic platforms (i.e., NanoVelcro CTC Assays) introduce a unique rare-cell sorting method that enables detection, isolation, and characterization of CTCs in peripheral blood, providing an opportunity to noninvasively monitor the disease progression in individual cancer patients. Over the past decade, our joint research team has developed a series of NanoVelcro CTC Assays exploring the full potential of CTCs as a clinical biomarker, including CTC enumeration, phenotyping, genotyping and expression profiling. In this presentation, we will briefly introduce the development of four generations of NanoVelcro CTC Assays, and highlight their clinical applications focusing on predicting, detecting, and monitoring of lethal progression in prostate cancer. We envision that our integrated approach will pave the way for implementation of precision oncology.

Nanocytological Biomarkers of Carcinogenesis: Implications for Screening and Therapy

Hemant Roy, M.D.

Boston University

Abstract:

Cancers are characterized by a myriad of genetic and epigenetic alterations that lead to increased transcriptional activity. The molecular heterogeneity provides challenges for diagnostic tests for carcinogenesis. High order chromatin structure appears to be the final common denominator for diverse molecular events leading to carcinogenesis. This can be identified using a biophotonic platform including partial wave spectroscopic microscopy (PWS) which quantifies cell microarchitecture at length scales ranging from 10-100 nm.

Our group has implemented this in both a diagnostic and therapeutic implications. Diagnostically, we have leveraged it to detect risk of cancer through field carcinogenesis. This is the well established clinical and biological concept of condemned mucosa—the proposition that the genetic and environmental milieu that leads to focal neoplastic lesions should be detectable throughout the field of injury. The application of this concept is using PWS analysis of the microscopically normal rectal mucosa to predict advanced adenomas elsewhere in the colon with an 85% accuracy. In a similar vein, the buccal mucosa which is impacted by smoking can provide insight into lung cancer with similar accuracy. From a therapeutic perspective, biophotonically detected field carcinogenesis can be used to detect response to drugs that bend the risk curve (chemoprevention) which we have validated in double blinded trials. We have also developed a cell culture system to evaluate changes in higher order chromatin to show marked synergy with standard chemotherapeutic agents (termed chromatin protection therapy) as a novel platform for therapeutic agent development.

Genetic Engineering of Therapeutic T cells Using Synthetic Nanoparticles

Matthias Stephan, M.D., Ph.D.

Fred Hutchinson Cancer Research Center

Abstract:

Technologies and approaches from the physical sciences and engineering can act as enabling partners with biology to find solutions to difficult problems in medicine. In this talk, two examples illustrating work from our laboratory will be described. In the first segment, I will describe a strategy to genetically modify cultured immune cells for therapeutic applications, simply by mixing them with an mRNA-carrying nanoreagent. In the second part of my presentation, I will introduce a new nanoparticle reagent our group developed to program tumor-recognizing capabilities into circulating T cells, thus avoiding the need to manipulate them in the laboratory.

Viroimmunotherapy for Cancer

Richard Vile, Ph.D.

Mayo Clinic

Abstract:

The concept of immunosurveillance proposes that a patient's own immune system can fight, and reject, their cancer. Consistent with this notion, sporadic spontaneous tumor regressions have been reported, and pre-clinical studies have shown that immune based rejection of tumors is possible in multiple model systems. More recently, convincing evidence of genuine immune mediated tumor control has emerged from clinical trials using adoptive transfer of tumor specific T cells, and from the use of so-called immune checkpoint blockade (ICB). Therefore, it is now clear that the immune system can, under specific circumstances, be re-educated to recognize antigens on tumor cells, even though most tumor cells represent immunological 'self.' However, for optimal anti tumor immunotherapy to occur, it will be critical to activate the anti tumor T cell responses in ways which the immune system is naturally adapted to recognize. In this respect, we have been using oncolytic viruses to act as potent danger signals to the immune system with the goal of activating the presentation of tumor antigens to T cells. Although oncolytic viruses were first developed to infect and kill tumor cells directly, there is considerable evidence that viral infection stimulates the immune system such that antigens associated with the infection can now be recognized by T cells present in the immune repertoire. Therefore, oncolytic viruses which kill tumors directly also lead to the priming of anti tumor T cell responses. This presentation will review the evidence that the immune system can be used to treat tumors and how various different strategies have been developed to optimize the breaking of immune tolerance to self or near self tumor associated antigens.

Arriving at the National Institutes of Health (NIH) Campus

The 5th Annual NCI CSSI Science Day will be held at the Porter Neuroscience Research Center, Building 35A, Conference Room 620/630, located on the NIH Campus, 9000 Rockville Pike, Bethesda, MD 20892.

Pedestrian visitors (arriving on foot, by Metro, or parking on campus) must enter through the NIH Gateway Center (Building 66). The NIH Gateway Center is located adjacent to the Medical Center Metro Station at the NIH Gateway Drive entrance off of Rockville Pike/Wisconsin Avenue (Route 355).

All visitors who wish to park on campus must use the Visitor Parking Garage (MLP 11), which is off of NIH Gateway Drive.

Driving and Parking

Driving a personal vehicle is discouraged as parking is generally quite limited on campus. Visitors arriving by car must use the NIH Gateway Drive entrance off Rockville Pike/Wisconsin Avenue. For directions, please visit <http://www.ors.od.nih.gov/maps/Pages/Gateway-Center-Map.aspx>.

Once through the entrance, stay in the left lane and park in the **Visitor Parking Garage - MLP 11** (Multi-Level Parking Garage 11). All visitors who wish to park on campus must use MLP 11. MLP 11 is open for entrance from 6:00 a.m. – 9:00 p.m. and exit from 6:00 a.m.–11:00 p.m., Monday through Friday. Parking rates are \$2 per hour for the first 3 hours and \$12 for 4 to 12 hours.

After parking in MLP 11, proceed to the NIH Gateway Center to be processed through security. It is a 10-15 minute walk from the Gateway Center to the Porter Center or simply use the campus shuttle service that originates at the Gateway Center.

Metro

The nearest Metro is the **Medical Center Station** of the Red Line of the Metro System. Please refer to the Metro Map at <https://www.wmata.com/schedules/maps/>. Follow Metro bus and train maps and schedules to navigate to the Medical Center Station.

Exit at the Medical Center Station to gain access to the NIH campus via The Gateway Center. The Gateway Center is immediately in front of the escalators that serve as the primary entrance and exit to Medical Center Station. Proceed to the Gateway Center to be processed through security.

