NIH NATIONAL CANCER INSTITUTE

6th Annual NCI CSSI Science Day

Center for Strategic Scientific Initiatives

June 7-8, 2018

Porter Neuroscience Research Center
NIH Main Campus, Bethesda, MD

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Porter Neuroscience Research Center
Building 35A
Room 640
NIH Main Campus, Bethesda, MD

For CSSI Information and Resources: https://cssi.cancer.gov

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Agenda

Thursday, June 7

8:00 a.m.	**Registration/Check In**
8:30 a.m.	**Welcome, CSSI Overview, and Introductory Presentations**

8:30 **Welcome Remarks and Overview of the NCI CSSI**
Sean Hanlon, Ph.D.
Office of the Director, CSSI, NCI, NIH

8:45 **Success Stories from Previous Science Days**
Norbert Tavares, Ph.D.
Office of the Director, CSSI, NCI, NIH

9:05 **Integrated Cancer Research and International Data Sharing: NCI, CPTAC, and Cancer Moonshot Proteogenomics Initiatives**
Henry Rodríguez, Ph.D., M.B.A.
Office of Cancer Clinical Proteomics Research, CSSI, NCI, NIH

9:25 **The Million Veteran Program: Driving Big Data Science**
Sumitra Muralidhar, Ph.D.
Office of Research and Development, Department of Veterans Affairs

9:35 a.m.	**Break**
9:50 a.m.	**Session 1: Leveraging Machine Learning and Artificial Intelligence in Harnessing Big Data**

9:50 **Session Introduction**
Eric Stahlberg, Ph.D. (Moderator)
Data Science & Information Technology Program,
Frederick National Laboratory for Cancer Research

9:55 **Knowledge-Rich Deep Learning for Precision Medicine**
Hoifung Poon, Ph.D.
Microsoft Research

10:20 **Deciphering Cancer through Imaging, Machine Learning, and Big Data**
Maryellen Giger, Ph.D.
University of Chicago

10:45 **AI, AI, AI: Multiple Opportunities for Artificial Intelligence in Digital Pathology**
Richard Levenson, M.D.
University of California, Davis

11:10 **Speaker Panel Q&A**

Thursday, June 7, Continued

11:35 a.m.	**Lunch (at attendees' expense)**
12:35 p.m.	**Session 2: Rigor & Reproducibility: Identifying Priorities for Standards Development**

12:35 **Session Introduction**
Paul Wagner, Ph.D. (Moderator)
Cancer Biomarkers Research Group, Division of Cancer Prevention, NCI, NIH

12:40 **The HPV Serology Standardization Initiative: Aims and Progress to Date**
Ligia Pinto, Ph.D.
HPV Serology Laboratory, Frederick National Laboratory for Cancer Research

1:05 **Coordinated Efforts to Develop a Robust Standards Infrastructure for Emerging Biotechnologies**
Sheng Lin-Gibson, Ph.D.
National Institute of Standards and Technology

1:30 **FDA, Standards and Innovation**
Živana Težak, Ph.D.
Office of In Vitro Diagnostic Device and Radiological Health, Center for Devices and Radiologic Health, Food and Drug Administration

1:55 **Speaker Panel Q&A**

2:20 p.m.	**Break & Group Picture**
2:40 p.m.	**Session 3: Frontiers for Interdisciplinary Science**

2:40 **Session Introduction**
Shannon Hughes, Ph.D. (Moderator)
Cancer Systems Biology Consortium, Division of Cancer Biology, NCI, NIH

2:45 **Engineered Chromatin to Support Epigenetic Research and Drug Development for Cancer**
Karmella Haynes, Ph.D.
Arizona State University

3:10 **Cancer Across Species and Disciplines: New Perspectives on Cancer Treatment**
Lisa Abegglen, Ph.D.
University of Utah

Thursday, June 7, Continued

3:35 **Deep Translational Research—Cancer Evolvability Mechanisms Discovered in Microbes**
Susan Rosenberg, Ph.D.
Baylor College of Medicine

4:00 **Speaker Panel Q&A**

4:25 p.m. Session Wrap Up and Reflection

4:25 Tony Dickherber, Ph.D.
Office of the Director, CSSI, NCI, NIH

4:35 p.m. Breakout Group Charge and Initial Group Meeting

4:35 **Breakout Activity Overview & Charge**
Paul Fearn Ph.D., M.B.A.
Surveillance Research Program, Division of Cancer Control & Population Sciences, NCI, NIH

4:50 **Introductory Meeting with Breakout Group**
Breakout groups meet in assigned breakout rooms

5:20 p.m. Adjournment, Day 1

Agenda

Friday, June 8

9:00 a.m. — **Welcome, Day 1 Recap, and Charge for Day 2 (Room 640)**

9:00 **Observations and Discussions from Day 1**
Tony Dickherber, Ph.D.
Office of the Director, CSSI, NCI, NIH

9:10 **Charge for Day 2**
Norbert Tavares, Ph.D.
Office of the Director, CSSI, NCI, NIH

9:15 a.m. — **Breakout Group Discussions**

Goal: Within the parameters of the future scenario provided, identify areas of need and opportunity in cancer research and technology, and the next steps to address or explore (next steps could include workshop, pilot project development, funding opportunity, etc.)

11:10 a.m. — **Break**

11:30 a.m. — **Breakout Group Reporting and Final Discussion**

11:30 **Breakout Group Reporting**
Representative(s) from each group

12:30 **Final Discussion and Wrap-up**
Norbert Tavares, Ph.D. and Tony Dickherber, Ph.D.
Office of the Director, CSSI, NCI, NIH

12:30 p.m. — **Adjournment, Day 2**

Speaker Biographies

Lisa Abegglen, Ph.D.

Lisa Abegglen is an Instructor in the Department of Pediatrics Hematology/Oncology Division at the University of Utah. She earned a BS in genetics from the University of Georgia and a PhD in immunology and molecular pathogenesis from Emory University. While the focus of her thesis and postdoc work was basic science, she possessed a strong desire to explore translational research. She accepted a position as a scientist in industry at Myrexis, Inc., where she led a team focused on developing kinase inhibitors to treat cancer for three years. She collaborated with multidisciplinary teams and became knowledgeable of the many stages of drug discovery and development. Her career shifted back to academia when she met Joshua Schiffman, MD, who shares her passion for improving patient outcomes through translational research. Dr. Schiffman is a pediatric oncologist and researcher at the University of Utah. Dr. Abegglen helps him lead a translational genomics laboratory at Huntsman Cancer Institute at the University of Utah. Their work to understand cancer risk in children led to a comparative oncology approach to also understand cancer risk across species, with the hope that cancer prone and cancer resistant species might reveal insights to help children with cancer. This comparative oncology approach lead to the discovery that cancer resistance in elephants is potentially related to additional copies of TP53 and that this amplification may contribute to increased apoptosis following DNA damage in elephant cells compared to humans. The current focus of their research is to characterize the function of these additional copies of TP53 in elephants and to translate this discovery into better treatments for cancer. In addition, Dr. Abegglen is leading efforts in the lab to work with the Arizona Cancer and Evolution (ACE) Center to identify additional mechanisms of cancer resistance across species.

Paul Fearn, Ph.D., M.B.A.

Paul Fearn joined the Surveillance Research Program as the Chief of the Surveillance Informatics Branch in 2016. He works with the SEER registries, the talented and hardworking team at SRP, and all of our collaborators to advance the application of natural language processing, machine learning, and other informatics tools and methods to support cancer surveillance. Previously, he was Director of Biomedical Informatics at Fred Hutchinson Cancer Research Center and a founding leader of the Hutch Integrated Data Repository and Archive (HIDRA). He has been the Informatics Manager for the Department of Surgery and the Office of Strategic Planning and Innovation at Memorial Sloan-Kettering Cancer Center (MSKCC), where he initiated and led the Caisis project, an open-source system that is currently used at multiple centers. Paul has a BA in Spanish from the University of Houston, biostatistics training from the University of Texas, School of Public Health in Houston, an MBA from the New York University Stern School of Business, and a PhD in Biomedical and Health Informatics from the University of Washington, School of Medicine. He has more than 20 years of experience in cancer research informatics at Baylor College of Medicine, MSKCC, Fred Hutch, and with the NCI SEER program.

Speaker Biographies

Maryellen L. Giger, Ph.D.

Maryellen L. Giger, Ph.D. is the A.N. Pritzker Professor of Radiology, Committee on Medical Physics, and the College at the University of Chicago. She is also the Vice-Chair of Radiology (Basic Science Research) and the immediate past Director of the CAMPEP-accredited Graduate Programs in Medical Physics/Chair of the Committee on Medical Physics at the University. For 30 years, she has conducted research on computer-aided diagnosis, including computer vision and machine learning, in the areas of breast cancer, lung cancer, prostate cancer, lupus, and bone diseases. She has also served on various NIH study sections, is a former president of the American Association of Physicists in Medicine, is the inaugural Editor-in-Chief of the *SPIE Journal of Medical Imaging*, and the current President of SPIE. She is a member of the National Academy of Engineering, a Fellow of AAPM, AIMBE, SPIE, and IEEE, a recipient of the AAPM William D. Coolidge Gold Medal and the EMBS Academic Career Achievement Award, and is a current Hagler Institute Fellow at Texas A&M University. She has more than 200 peer-reviewed publications (over 300 publications), has more than 30 patents and has mentored over 100 graduate students, residents, medical students, and undergraduate students. Her research in computational image-based analyses of breast cancer for risk assessment, diagnosis, prognosis, response to therapy, and biological discovery has yielded various translated components, and she is now using these image-based phenotypes in imaging genomics association studies.

Karmella Haynes, Ph.D.

Karmella Haynes is an Assistant Professor of Biomedical Engineering at Arizona State University. She earned her Ph.D. studying epigenetics and chromatin in Drosophila at Washington University, St. Louis. Postdoctoral fellowships at Davidson College and Harvard Medical School introduced her to synthetic biology. Today, her research aims to identify how the intrinsic properties of chromatin, the DNA-protein structure that packages eukaryotic genes, can be used to control cell development in tissues. Dr. Haynes received an NIH Young Faculty Award (K01) and an Arizona Biomedical Early Stage Investigator Award (AZ ESI). She is currently a Councilor of the Engineering Biology Research Consortium (EBRC), a SynBioLEAP alum, and Advisor and Judge Emeritus for the International Genetically Engineered Machines (iGEM) competition. She is a two-time featured guest on PRI's Science Friday.

Shannon Hughes, Ph.D.

Dr. Shannon Hughes joined the National Cancer Institute's Division of Cancer Biology in 2015 as a Program Director for the Cancer Systems Biology Consortium and the Physical Sciences in Oncology Network. Dr. Hughes' interest in cancer systems biology and physical oncology stems from her background in applying chemical and biomedical engineering principles to investigate cell signaling pathways involved in cell migration, invasion, and cancer metastasis. Following completion of her BS in Chemical Engineering from Iowa State University, Shannon spent three years as a process engineer working in the field of drug delivery at 3M in St. Paul, MN. Industrial research motivated her Ph.D. in Biomedical Engineering at Washington University in St. Louis where she studied the molecular mechanisms underlying bioactive sphingolipid-mediated endothelial cell migration. After moving to MIT, she obtained a DOD Breast Cancer Research Postdoctoral Fellowship to systematically investigate the role of the cytoskeleton in receptor tyrosine kinase-mediated breast cancer metastasis. Before coming to NCI, Shannon co-authored many research publications in both experimental and quantitative biology, mentored various undergraduate and graduate level students, and served as a lead technical research instructor in the Biological Engineering Department at MIT. She is currently managing the Cancer Systems Biology Consortium, NCI's main effort to tackle complex questions in cancer through the explicit integration of mathematical and computational approaches with experimental biology.

Speaker Biographies

Richard Levenson, M.D.

Richard Levenson, MD, FCAP, is Professor and Vice Chair for Strategic Technologies, Department of Pathology and Laboratory Medicine, UC Davis, where he develops novel imaging technologies. Board-certified in Anatomic Pathology, he received his MD at University of Michigan and pathology training at Washington University. A faculty position at Duke was followed by appointment at Carnegie Mellon University. He subsequently joined Cambridge Research & Instrumentation (now part of PerkinElmer), becoming VP of Research before returning to academia. He has helped develop multispectral microscopy systems and software for molecular pathology and diagnostics, multispectral and three-dimensional small-animal imaging systems, optical dynamic contrast techniques, orientation-independent birefringence microscopy, multiplexed ion-beam imaging, and most recently, real-time slide-free microscopy. He serves on multiple review panels, is section editor for Archives of Pathology and on the editorial board of Laboratory Investigation. Regrettably, he also successfully taught pigeons histopathology and radiology. He is co-founder of MUSE Microscopy, Inc.

Sheng Lin-Gibson, Ph.D.

Dr. Sheng Lin-Gibson is the Chief of the NIST Biosystems and Biomaterials Division and directs its Regenerative Medicine Programs. She serves as the Convener of ISO/TC 276: Biotechnology Working Group 3: Analytical Methods as well as the Chairperson for the U.S. Mirror Committee to ISO/TC 276. She leads and contributes to the development of several international standards particularly relevant to cell and gene therapy manufacturing and characterization. Dr. Lin-Gibson is the NIST lead for various joint NIST/SCB efforts to coordinate the development of standards for regenerative medicine. She co-chairs the Multi-Agency Tissue Engineering Science (MATES) Working Group, an ad hoc interagency group that ensures communication and coordination of US Federal Agencies. She is a NIST participant on the Technical Advisory Committee (TAC) of NIIMBL, a U.S. Manufacturing Institute aimed to accelerate biopharmaceutical manufacturing. Her research portfolio includes the measurement of cells, microbial systems, and biomaterials to provide data that underpins the development of science-based standards. She has coauthored over 60 peer-reviewed publications, served on numerous NSF, NIH, and NIST expert review panels, and is a recipient of three Department of Commerce Bronze Medals.

Sumitra Muralidhar, Ph.D.

Dr. Sumitra Muralidhar is the Program Director for VA's Million Veteran Program (MVP) in the Office of Research and Development (ORD). In this role, she oversees the development of policy and infrastructure for enrolling at least one million Veterans in a longitudinal cohort collecting genetic, clinical, lifestyle and military exposure data for future research, as well as for data use and conduct of science. She served as ORD's liaison to the White House Precision Medicine Initiative under President Obama, and continues to represent ORD/MVP in the federal interagency group on precision medicine. She also serves as the designated federal officer for VA's Genomic Medicine Program Advisory Committee- a FACA Committee which advises the VA Secretary on the development and implementation of research and clinical arms within the Veterans Health Administration.

Speaker Biographies

Ligia Pinto, Ph.D.

Ligia Pinto is currently the Director of the Vaccine, Immunity and Cancer Program and Head of the HPV Immunology Laboratory at the Frederick National Laboratory for Cancer Research. In her current position, she directs a portfolio of clinical and preclinical studies in the area of HPV, cancer and vaccines, involving a team of scientists, postdoctoral fellows, research associates and students. She completed her PhD in 1995 at the Experimental Immunology Branch, National Institutes of Health, after several years of research on cellular immunology of HIV infection at the University of Lisbon, School of Medicine in Portugal. She continued her postdoctoral studies at NIH where she focused on investigating immunological alterations induced by HIV, HIV vaccine candidates and host protective immune responses controlling HIV replication and associated pathogenesis. In 2001, she joined the Frederick National Laboratory for Cancer Research to establish the HPV Immunology Laboratory. The work from her Laboratory has played a critical role in the understanding of the systemic and mucosal immune responses induced by the currently licensed HPV vaccines in clinical trials. In addition, her Laboratory has an interest in evaluating immune responses in the context of natural HPV infection. She has worked in the area of immunology of infectious diseases and vaccines for the last 30 years, with over 110 peer-reviewed publications and a number of distinguished awards.

Hoifung Poon, Ph.D.

Hoifung Poon is the Director of Precision Health NLP and leads Project Hanover at Microsoft Research, with the overarching goal of advancing machine reading for precision health, by combining probabilistic logic with deep learning. He has given tutorials on this topic at top AI conferences such as the Association for Computational Linguistics (ACL) and the Association for the Advancement of Artificial Intelligence (AAAI). His research spans a wide range of problems in machine learning and natural language processing (NLP), and his prior work has been recognized with Best Paper Awards from premier venues such as the North American Chapter of the Association for Computational Linguistics (NAACL), Empirical Methods in Natural Language Processing (EMNLP), and Uncertainty in AI (UAI). He received his PhD in Computer Science and Engineering from University of Washington, specializing in machine learning and NLP.

Susan Rosenberg, Ph.D.

Susan Rosenberg is the Ben F. Love Chair in Cancer Research and Professor in the Departments of Molecular and Human Genetics, Biochemistry, and Molecular Virology and Microbiology, and founded and leads the Cancer Evolvability Program in Dan L Duncan Comprehensive Cancer Center at Baylor College of Medicine, Houston. Her lab studies molecular mechanisms that promote genome stability and instability, and their impacts on evolution, infectious disease, and cancer. Her lab originated technologies for studying endogenous DNA damage in living bacterial and human cells, and discovered that cells that are maladapted to their environment increase genetic diversity and potentially their ability to evolve using mechanisms of mutagenesis activated by stress responses, now evident from bacteria to cancer. Rosenberg founded the Gordon Research Conference on Molecular Mechanisms in Evolution, has received an NIH Director's Pioneer Award, the Biosphere and Humanity Medal (Russian Academy of Medicine), the Eli Lily / National Cancer Institute of Canada William Rawls Prize, the Young Scientist Award of the Genetics Society of Canada, and Michael E. DeBakey MD Award for Excellence in Research. Dr. Rosenberg is a fellow (elected) of the American Association for the Advancement of Science, a fellow (elected) of the American Academy of Microbiology, served on the Senior Editorial Board of SCIENCE, and serves as a Council Delegate (elected) to, and member of the Committee on Council Affairs (elected) of the American Association for the Advancement of Science.

Speaker Biographies

Lynn Sorbara, Ph.D.

Dr. Lynn Sorbara earned her PhD from Albert Einstein College of Medicine in 1986. Her thesis research was in the areas of the mechanism of action of the drug, Taxol, and of multidrug resistance. After postdoctoral fellowships at the Rockefeller University and the Mount Sinai College of Medicine in Manhattan, she came to the NIH as a Senior Staff Fellow in the Diabetes Branch of NIDDK. From 1996 to 2007, she was the Technical Supervisor and Clinical Staff Scientist for the Molecular Diagnostics Unit of the Laboratory of Pathology at NCI. As the Technical Supervisor, she was responsible for the development, validation, and quality assurance for all of the diagnostic tests performed in this College of American Pathologists and CLIA certified laboratory. Since 2007, she has been a Program Director for the Cancer Biomarkers Research Group in the Division of Cancer Prevention of NCI.

In her current role, she oversees and manages cooperative agreement grants for the Biomarker Reference Laboratories and is the co-coordinator of the Lung Collaborative Group for the Early Detection Research Network. She is the DCP Program Representative for the Innovative Molecular Technologies Analysis and the SBIR Programs. She has a strong interest in developing Standard Operating Procedures for biomarker discovery/validation, and diagnostic assay development. Her grant portfolio includes biomarkers for liquid biopsy, early detection of hematopoietic malignancies, lung and upper aerodigestive cancers, new technologies and diagnostics tools for cancer research.

Eric Stahlberg, Ph.D.

Working closely with the National Cancer Institute Center for Biomedical Information and Information Technology (CBIIT) since 2014, Dr. Stahlberg currently leads several collaborative initiatives developing the capabilities and capacity to accelerate cancer research through expanded utilization of computational models, data science, and high-performance computing. He is program co-lead for the NCI-DOE collaboration for Joint Design of Advanced Computing Solutions for Cancer (JDACS4C) and provides key leadership in developing strategic collaborations, including with the Department of Energy. Working with DOE colleagues, he helped establish the new public-private consortium for Accelerating Therapeutics for Opportunities in Medicine (ATOM) which aims to accelerate pre-clinical drug development with new levels of data, computation, collaboration across industry, academia and government. Dr. Stahlberg received his BA from Wartburg College with majors in chemistry, computer science and mathematics, his Ph.D. in Chemistry from The Ohio State University and held a post-doctoral appointment working at Argonne National Laboratory where he worked to advance the use of large scale computing in scientific applications.

Živana Težak, Ph.D.

Živana Težak, Ph.D., is an Associate Director for Science and Technology, Personalized Medicine Staff, in the Office of In Vitro Diagnostic Device (IVD) Evaluation and Safety (OIR), at the Center for Devices and Radiological Health, Food and Drug Administration (FDA). Prior to joining the FDA in 2004, Dr. Težak worked in biotechnology industry, holding research and development positions in a bioinformatics and array developer company. After receiving her Ph.D. from Florida State University, Dr. Težak was a research fellow at the University of Pittsburgh Medical Center and Children's National Medical Center, Research Center for Genetic Medicine, working on neuromuscular disorders, human genetics, gene therapy and high-throughput screening technologies. In her current position at the FDA, Dr. Težak has been leading efforts to develop flexible regulatory policies for novel technology based clinical diagnostic tests, such as next generation sequencing, in order to enable their smoother translation into the clinic.

The Million Veteran Program: Driving Big Data Science

Sumitra Muralidhar, Ph.D.
Office of Research and Development, Department of Veterans Affairs

Abstract:
An overview of the program and core infrastructure, updates on the current status of enrollment and scientific projects, plans for expanding access to the data, and partnerships will be presented.

Knowledge-Rich Deep Learning for Precision Medicine

Hoifung Poon, Ph.D.
Microsoft Research

Abstract:
The advent of big data promises to revolutionize medicine by making it more personalized and effective. But big data also presents a grand challenge of information overload, making it difficult to discern knowledge from data, and separate signal from noise. AI can play a key role in translating big data to optimal medical decisions. In particular, deep learning has emerged as a versatile tool for diverse tasks such as machine reading and patient outcome prediction. However, like other supervised methods, deep learning requires annotated examples, which are expensive and time-consuming to produce at scale.

In this talk, I'll present Project Hanover, where we overcome the annotation bottleneck by combining deep learning with probabilistic logic, and by exploiting indirect supervision from readily available resources such as ontologies and existing databases. This enables us to extract knowledge from millions of publications, reason efficiently with the resulting knowledge graph by learning neural embeddings of biomedical entities, and apply the learned embeddings as powerful features to personalized cancer drug combinations.

Abstracts

Deciphering Cancer through Imaging, Machine Learning, and Big Data

Maryellen L. Giger, Ph.D.
A. N. Pritzker Professor of Radiology / Medical Physics
The University of Chicago

Abstract:
Adapting the Precision Medicine Initiative into imaging research includes studies in both discovery and translation. Discovery is a multi-disciplinary data mining effort involving researchers such as radiologists, medical physicists, oncologists, computer scientists, engineers, and computational geneticists. Quantitative radiomic analyses are yielding novel image-based tumor characteristics, i.e., signatures that may ultimately contribute to the design of patient-specific breast cancer diagnostics and treatments. The role of quantitative radiomics continues to grow beyond computer-aided detection, with AI methods being developed to (a) quantitatively characterize the radiomic features of a suspicious region or tumor, e.g., those describing tumor morphology or function, (b) merge the relevant features into diagnostic, prognostic, or predictive image-based signatures, (c) estimate the probability of a particular disease state, (d) retrieve similar cases, (e) compare the tumor in question to thousands of other breast tumors, and (f) explore imaging genomics association studies between the image-based features/signatures and histological/genomic data. Advances in machine learning are allowing for these computer-extracted features (phenotypes), both from clinically-driven, hand-crafted feature extraction systems and deep learning methods, to characterize a patient's tumor via "virtual digital biopsies". Ultimately translation of discovered relationships will include applications to the clinical assessments of cancer risk, prognosis, response to therapy, and risk of recurrence.

AI, AI, AI: Multiple Opportunities for Artificial Intelligence in Digital Pathology

Richard Levenson, M.D.
University of California, Davis

Abstract:
Artificial intelligence (AI) promises to be a powerful, but unpredictable force affecting medicine in general and diagnostics in particular. The term, AI, has broad connotations and actually covers a large variety of approaches, technologies and application areas. Efforts to automate diagnostics are underway, and their promise and challenges are becoming somewhat well understood. Additional application areas that AI might affect include effects earlier in the data chain. One example is its remarkable potential for complementing computational optics. With AI, images emerging from current and future detection systems can be dramatically enhanced, possibly allowing less powerful devices to generate images currently requiring expensive optics and electronics. Additional points to consider: effect of AI on human-level expertise and training; medical-legal implications; and of course, the unknown unknowns.

The HPV Serology Standardization Initiative: Aims and Progress to Date

Ligia Pinto, Ph.D.

HPV Serology Laboratory, Frederick National Laboratory for Cancer Research

Abstract:

As protection against HPV infection is believed to be mediated by HPV-specific antibodies, HPV serology measurements are being proposed as endpoints in clinical trials of modified regimens of existing vaccines and follow-on products. However, there is a lack of standardized assays, procedures, and reagents accessible to the scientific community for assessment of immune responses to HPV prophylactic vaccines. The HPV Serology Laboratory at Frederick National Laboratory for Cancer Research, was established in January 2017 to address this challenge working with the National Cancer Institute (USA) and the Bill & Melinda Gates Foundation to lead standardization and harmonization efforts for HPV serological testing within HPV prophylactic vaccine trials. The main goal is to expedite serology assay standardization by developing a critical set of qualified immunoassay reagents, including secondary standards and HPV Virus-Like Particles (VLP) as well as validated assays that will be made available to the HPV scientific community. Furthermore, standard operating procedures for reagent production, immunoassay testing and qualification methods will be made accessible.

We are currently developing qualified HPV VLP for 9 HPV types included in currently licensed vaccines, HPV antibody secondary standards, serology-based proficiency panels, qualified serology assays, and testing guidelines. This work is being done in partnership with other HPV serology laboratories in the world. The achievement of these aims will enable comparisons of data across different HPV vaccines and different studies and, therefore, it will facilitate vaccine development and implementation of new vaccine indications and new vaccine candidates.

Coordinated Efforts to Develop a Robust Standards Infrastructure for Emerging Biotechnologies

Sheng Lin-Gibson, Ph.D.
National Institute of Standards and Technology

Abstract:
The development of standards for biotechnology and emerging areas of personalized/precision medicine is recognized as a high priority. Standards can serve many purposes, including accelerate and streamline the development of diagnostic tools and new treatment options, ensure the quality and consistency of processes and products, and facilitate their regulatory approval. More recently, standards are increasingly recognized as a means to assure the confidence of research results and data reproducibility. Yet, many knowledge gaps remain; a shared understanding is required for real progress towards the development of standards that advance biotechnology R&D to commercialization. While the general framework for a standards infrastructure may be similar across various disciplines of emerging biotechnologies, coordination and thoughtful considerations are needed for standards that are clear to the end users (no conflicts with existing standards) and broadly adopted. Recent progress as well as challenges and opportunities from ongoing standardization efforts will be discussed, particularly through the lens of recent international standardization efforts within ISO/TC276: Biotechnology. ISO/TC276 has several Working Groups and a large network of liaison organizations focused on 1) terminology to enable common understanding, 2) biobanking and bioresources intended to improve the quality of biological samples, 3) analytical methods aimed to improve measurement confidence and enable sound decision making from R&D to commercialization, 4) bioprocessing that focuses on improving the quality and consistency of via manufacturing control, and 5) data processing and interoperability to enable data comparability. Efforts are also under way to integrate physical standards/reference materials as critical components of the standards infrastructure for emerging areas of biotechnology. Finally, a robust standards infrastructure is incomplete without “pre-standardization work” to collect information from stakeholders and “post-standardization work” for dissemination and education.

FDA, Standards and Innovation

Živana Težak, Ph.D.
Office of In Vitro Diagnostic Device and Radiological Health, Center for Devices and Radiologic Health, Food and Drug Administration

Abstract:
FDA’s vision is to implement regulatory policies that accelerate translation of precision medicine technologies into treatments that benefit patients. Standards developed with the community, and updated as science and technology advance, can play a crucial role to accomplish this vision. The goal is to improve regulatory efficiency while encouraging safe and innovative product to reach the market faster. For example, when available, appropriate analytical standards for specific next generation sequencing (NGS) tests will aid in efficient test development, validation, provide transparency, and possibly even obviate steps in the regulatory process.

Engineered Chromatin to Support Epigenetic Research and Drug Development for Cancer

Karmella Haynes, Ph.D.
Arizona State University

Abstract:
Mounting evidence is showing that epigenetic co-repression of groups of genes distinguishes cancerous cells from healthy cells in many different tissue types. Chromatin, a system of nuclear proteins and nucleic acids, is a central genomic structure that packages genes into open (active) and closed (repressed) conformations. Small compounds and nucleic acids have been used to disrupt cancer-associated, hyper-repressed chromatin to simultaneously activate large sets of therapeutic genes. Another approach uses customizable fusion transcription factors (TF's) that contain a peptide motif (e.g., Gal4, TAL, ZF, etc.) or an RNA adapter (i.e., CRISPR) to target a specific promoter or enhancer near each target gene. Our work represents a unique approach to TF targeting: proteins that bind epigenetic marks on histones rather than DNA sequences. This approach enables efficient, broad macrogenomic engineering in cancer cells where hundreds of genes are misregulated as a cohort. We have developed the "Polycomb-based transcription factor" (PcTF), a fusion protein that reads histone modifications through a protein-protein interaction between its N-terminal Polycomb chromodomain (PCD) motif and trimethylated lysine 27 of histone H3 (H3K27me3). The C-terminal VP64 domain of PcTF recruits endogenous activators to silenced targets. We observed that dose-dependent, PcTF-mediated activation of target genes was accompanied by the loss of H3K27me3 and the accumulation of the activation-associated H3K4me3 mark over time. Expression of PcTF in triple negative breast cancer cells revealed that PcTF target genes include tumor suppressors. Therefore PcTF has significant implications for cancer treatment. We have implemented a cell-free to in-cell workflow to quickly identify more robust configurations of the modular PcTF fusion protein. Enzyme-linked immunosorbent assay (ELISA) and microspot array experiments showed that tandem PCD domains conferred enhanced and specific interaction with H3K27me3 in vitro. The double PCD fusion also showed enhanced target gene activation in a model cell line (HEK293). In conclusion, we have demonstrated a screening pipeline to support the design of TF's that bind chromatin (histones) and regulate target genes. We believe that peptides that specifically interact with epigenetic marks are on the verge of becoming the next generation of synthetic transcriptional regulators. The presentation will conclude with a discussion of challenges for the adoption of this technique by the broader community and clinical translation of the technology.

Cancer Across Species and Disciplines: New Perspectives on Cancer Treatment

Lisa Abegglen, Ph.D.
University of Utah

Abstract:
Through a number of collaborative and multidisciplinary research opportunities, we have developed an innovative approach to cancer treatment. The story begins with a focus on pediatric cancer and cancer predisposition syndromes. We were interested in developing functional assays to assess cancer risk in people with Li-Fraumeni syndrome (LFS). LFS is a cancer predisposition syndrome that results from loss of one functional allele of germline TP53 and leads to a lifetime cancer risk that approaches 100%. At the same time, Dr. Carlo Maley (evolutionary and computational biologist) and his team at UCSF and Arizona State University were collecting data on cancer across species. They confirmed that elephant mortality from cancer is much lower than expected (i.e., Peto's Paradox) and potentially related to a 20-fold increase in TP53 copy number. We initiated a collaboration with Dr. Maley, our local zoo, and Ringling Bros. and Barnum & Bailey Circus to measure p53 function in elephant cells. This work revealed that TP53 amplification was associated with increased p53-mediated, DNA damage-induced apoptosis of elephant cells compared to human cells. Our work on cancer resistance in elephants led to another collaborative project closer to home. At the University of Utah, Dr. Chris Gregg (neurobiologist and geneticists) and Dr. Elliott Ferris (bioinformatician) developed a method to identify regions of accelerated evolution in the genome by comparing the genomes of different animals with distinct phenotypic traits. They identified additional, potential genomic contributors to cancer resistance in elephants and we collaborated to functionally validate their results. As the primary focus of our lab is to use science to improve the lives of pediatric cancer patients, we were curious if it might be possible to develop a therapeutic based on the enhanced cancer resistance and DNA damage response in elephants. Our recent data suggests that EP53 can enhance and restore p53 function in in a wide range of human cancers and trigger p53-mediated cell death. In need of a drug development approach, we began collaborating with a chemical engineer and nanotechnology expert in Israel, Dr. Avi Schroeder, and a startup biotech company. Our research team also co-leads a project of the newly funded Arizona Cancer and Evolution (ACE) Center, part of NIH's Cancer Systems Biology Consortium, to explore functional DNA repair response across dozens of different animal species. We are still in the early stages of drug development based on all our findings, but our success up to now supports building bridges across not only scientific disciplines, but also across the community, to increase the rate and enhance the quality of discovery. Multidisciplinary research has the potential to lead to innovative approaches to cancer therapy by encouraging us to think outside of our scientific comfort zone.

Deep Translational Research—Cancer Evolvability Mechanisms Discovered in Microbes

Susan Rosenberg, Ph.D.
Baylor College of Medicine

Abstract:
The Cancer Evolvability Program in the Dan L. Duncan Comprehensive Cancer Center at Baylor College of Medicine (Houston) supports research to understand the fundamental molecular mechanisms that generate the variation that drives evolution, including evolution of cancers. These mechanisms are conserved across the tree of life, making any organism appropriate for their discovery. They are mostly unsolved, such that rates of fundamental discoveries continue apace. Our program members are doing deep translational research: addressing the mechanisms of generation of diversity critical in and relevant to cancer development, prevention, diagnosis, and therapy; starting in the world's most tractable organisms (bacteria, worms, yeasts) and human cells; then using results to query human cancer data bioinformatically (TCGA and other); translating to human cells, and aiming at preclinical then clinical assessment of the impacts of new evolvability paradigms and mechanisms for cancer biomarker and therapeutic strategies. Examples will be discussed.