National Institutes of Health

American Association for Cancer Research

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NIH-AACR Cancer, Autoimmunity, and Immunology Conference

March 23-24, 2020

Julie R. Brahmer, MD, Codirector, Upper Aerodigestive Clinical Research Program, Bloomberg-Kimmel Institute for Cancer Immunotherapy, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University
Elad Sharon, MD, MPH, Senior Investigator, National Cancer Institute
Connie Sommers, PhD, Program Director, National Cancer Institute
Howard Young, PhD, Senior Investigator, National Cancer Institute
Ravi Madan, MD, Clinical Director, Genitourinary Malignancies Branch, National Cancer Institute
Katarzyna (Kasia) Bourcier, PhD, Program Director, National Cancer Institute
Marie Mancini, PhD, Program Director, National Institute of Arthritis and Musculoskeletal and Skin Diseases
Annette Rothermel, PhD, Section Chief, National Institute of Allergy and Infectious Diseases
Lisa Spain, PhD, Program Director, National Institute of Diabetes and Digestive and Kidney Diseases

AGENDA: MARCH 23, 2020

INTRODUCTION

9:00 AM **Welcome and opening remarks**
Hugh Auchincloss, MD, National Institute of Allergy and Infectious Diseases

KEYNOTE ADDRESS

9:15 AM **Understanding the immunopathogenesis of irAEs and the prospects for targeted therapy**
Leonard H. Calabrese, DO, FACR, Cleveland Clinic

SESSION I: RHEUMATIC TOXICITIES
SESSION MODERATOR: LEONARD H. CALABRESE, DO, FACR

9:45 AM **Rheumatologic immune-related adverse events: Not our classic autoimmune diseases**
Laura C. Cappelli, MD, MHS, MS, Johns Hopkins University

10:00 AM **Rheumatic toxicities associated with immune checkpoint inhibitors: The severity of myositis**
Yves Allenbach, MD, PhD, Sorbonne Université

10:15 AM **Seeing is believing: Imaging modalities in rheumatologic immune-related adverse events**
Sarthak Gupta, MD, National Institute of Arthritis and Musculoskeletal and Skin Diseases

10:30 AM **PANEL DISCUSSION**

11:00 AM **BREAK**

SESSION II: INFECTIOUS DISEASES
SESSION MODERATOR: VIRGINIA SHEIKH, MD, MHS

11:30 AM **Effects of immune checkpoint blockade on HIV latency**
Rafick-Pierre Sékaly, PhD, Case Western Reserve University

11:45 AM **Preclinical TB work in Macaques**
Dan Barber, PhD, National Institute of Allergy and Infectious Diseases

12:00 PM	**PD-1 inhibitors for the treatment of progressive multifocal leukoencephalopathy** **Irene Cortese, MD,** National Institute of Neurological Disorders and Stroke
12:15 PM	**PANEL DISCUSSION**
12:45 PM	**LUNCH BREAK**
	SESSION III: ROLE OF THE MICROBIOME **SESSION MODERATOR: GIORGIO TRINCHIERI, MD**
2:00 PM	**The role of the gut-tumor axis in tumorigenesis** **Florencia McAllister, MD,** MD Anderson Cancer Center
2:15 PM	**Treatment of refractory melanoma patients with fecal microbiota transplants and immunotherapy** **Gal Markel, MD, PhD,** Sheba Medical Center
2:30 PM	**Manipulating the microbiome to treat inflammatory cardiomyopathy** **Burkhard Ludewig, DVM,** Kantonsspital St. Gallen
2:45 PM	**PANEL DISCUSSION**
	SESSION IV: PREDICTIVE BIOMARKERS **SESSION MODERATOR: DOUGLAS B. JOHNSON, MD**
3:15 PM	**Characterizing toxicities of immune checkpoint inhibitors** **Douglas B. Johnson, MD,** Vanderbilt-Ingram Cancer Center
3:30 PM	**Defining the features of T cell responses to tumor and self-antigens as predictors of response to checkpoint inhibitor therapy** **Jane Buckner, MD,** Benaroya Research Institute
3:45 PM	**Statistical considerations for evaluating biomarkers for irAEs** **Lisa Meier McShane, PhD,** National Cancer Institute
4:00 PM	**PANEL DISCUSSION**
4:30 PM	**ADJOURN DAY 1**

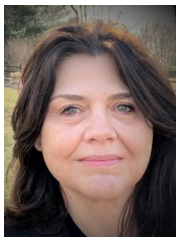
NIH-AACR Cancer, Autoimmunity, and Immunology Conference

AGENDA: MARCH 24, 2020	
INTRODUCTION	
9:00 AM	**Welcome** **Norman E. "Ned" Sharpless, MD,** National Cancer Institute
KEYNOTE ADDRESS	
9:10 AM	**Immune checkpoint blockade in cancer therapy: At the interface between anti-tumor and anti-self immunity** **Suzanne L. Topalian, MD,** Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University
9:45 AM	**BREAK**
SESSION V: IRAES RESULTING FROM COMBINATION THERAPIES SESSION MODERATOR: JULIE BRAHMER, MD	
10:05 AM	**Differentiation of dermatologic irAEs for patients on combination therapies: A consultant's perspective** **Mario E. Lacouture, MD**, Memorial Sloan-Kettering Cancer Center
10:20 AM	**Differentiating between irAEs and other AEs in combination therapies** **Lilian L. Siu, MD,** Princess Margaret Cancer Centre
10:35 AM	**irAEs from RT + ICI** **Silvia Formenti, MD,** Weill Cornell Medicine
10:50 AM	**PANEL DISCUSSION**
11:30 AM	**LUNCH BREAK**
SESSION VI: NONTRADITIONAL NONCLINICAL MODELS SESSION MODERATOR: KRISTINA HOWARD, DVM, PHD	
12:45 PM	**Wild mouse microbiota in preclinical research** **Barbara Rehermann, MD,** National Institute of Diabetes and Digestive and Kidney Diseases
1:00 PM	**Programmable bacteria for cancer** **Tal Danino, PhD,** Columbia University
1:15 PM	**A better HCC model for immunotherapy, in woodchucks?** **Minhyung Kim, MD,** Roswell Park Comprehensive Cancer Center
1:30 PM	**CANINE: A comparative genomics, oncology, and immunotherapy consortium** **Melissa Renee Chambers, DVM, MD,** University of Alabama at Birmingham
1:45 PM	**PANEL DISCUSSION**

SESSION VII: MULTIDISCIPLINARY TREATMENT MODELS SESSION MODERATOR: NICOLE R. LEBOEUF, MD, MPH	
2:15 PM	**Severe Immunotherapy Complications (SIC) Service: A model integrating clinical care and clinical-translational research** **Kerry Reynolds, MD,** Massachusetts General Hospital Cancer Center, and **Alexandra-Chloé Villani, PhD,** Massachusetts General Hospital, Harvard Medical School, Broad Institute
2:35 PM	**A multidisciplinary immune-related toxicity team and prospective clinical trials for irAEs** **Jarushka Naidoo, MBBCh,** Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University
2:50 PM	**Management of immune checkpoint inhibitor-related GI toxicity** **Yinghong "Mimi" Wang, MD, PhD, MS,** MD Anderson Cancer Center
3:05 PM	**Alliance A151804: Establishment of a national biorepository to advance studies of immune-related adverse events** **David Kozono, MD, PhD,** Dana-Farber Cancer Institute
3:20 PM	**PANEL DISCUSSION**
4:00 PM	**WRAP-UP AND ADJOURN**

Conference Organizing Committee

Katarzyna (Kasia) Bourcier, PhD, *National Institute of Allergy and Infectious Diseases*



Dr. Kasia Bourcier obtained a PhD in Biomedical Sciences from the Medical University of Warsaw, Poland studying neuroimmune interactions in mouse models of neurological diseases. Dr. Bourcier then joined the Center for Neurologic Diseases (CND) at Brigham and Women's Hospital, Harvard Medical School where her major research interests were related to characterization of antigen specific T-cell responses in Multiple Sclerosis and HTLV-I associated myelopathy/tropical spastic paraparesis patients. To extend the pursuit of research in monitoring the immune system, Dr. Bourcier took the role of Associate Director of the Clinical Immunology Laboratory in CND and managed the development and implementation of mechanism of action studies for clinical trials. In 2004 she joined the Immune Tolerance Network (ITN), University of California, San Francisco, to lead a group overseeing performance of centralized Core Laboratories and implementation of standardized, cutting edge assays for monitoring patients enrolled in ITN's clinical trials. In 2011 she joined the Autoimmunity and Mucosal Immunology Branch at the Division of Allergy, Immunology and Transplantation at NIAID, NIH. Since October 2019, she is a Program Director in the Immuno-Oncology Branch where her programmatic interests include new developments empowering the immune system to fight cancer, specifically cell-based cancer therapies, mechanisms governing development of immune related adverse events induced by checkpoint inhibitor therapies and development of new cutting-edge technologies to study the immune system.

Julie Brahmer, MD, MSc, *Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University*

Julie R. Brahmer, MD, MSc, is the codirector of the Upper Aerodigestive Cancer Program within the Bloomberg-Kimmel Institute for Cancer Immunotherapy at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins. She was recently appointed as Co-Program Leader of the Cancer Immunology Program. In addition to serving as Co-Program Leader of the Cancer Immunology Program, she also directs the Kimmel Cancer Center on the Johns Hopkins Bayview campus. She is co-principal investigator of the Johns Hopkins' National Clinical Trials Network and helps direct all oncology cooperative group activities on the Johns Hopkins campuses. Dr. Brahmer is an international leader in lung cancer clinical trials research with particular expertise in drug development for thoracic malignancies and immunotherapy.

Dr. Brahmer received her undergraduate degree in Chemistry and Philosophy in 1989 from the Creighton University in Omaha, Nebraska and went on to receive her medical degree from the University of Nebraska Medical Center, College of Medicine in 1993. Completing her internship and residency in Internal Medicine at the University of Utah, she later became the Chief Medical Resident until moving to Baltimore to complete her fellowship in Medical Oncology at the Kimmel Cancer Center at Johns Hopkins.

Dr. Brahmer's research interests include leading early phase immunotherapy trials of anti-PD-1 antibodies, international phase III studies of immunotherapies in lung cancer and investigator-initiated trials evaluating epigenetic therapies in combination with immunotherapies. She is a member of the Johns Hopkins Kimmel Cancer Center immunotherapy related toxicity management team and co-leads ASCO, NCCN, and SITC toxicity guideline development for these national and international organizations.

Ravi Madan, MD, *National Cancer Institute*

Dr. Madan is an Assistant Clinical Investigator at the National Cancer Institute (NCI), conducting clinical research in therapeutic cancer vaccines and genitourinary malignancies. Dr. Madan received his MD from the UMDNJ-New Jersey Medical School in 2001 and completed his internal medicine residency at UMDNJ-University Hospital in June 2004. He joined the NCI Medical Oncology Branch as an oncology/hematology fellow in 2005. He currently holds a joint appointment in the Medical Oncology Branch and the Laboratory of Tumor Immunology and Biology. His research interests are focused on immune stimulating therapeutic cancer vaccines and novel therapies in the treatment of prostate cancer.

Marie Mancini, PhD, *National Institute of Arthritis and Musculoskeletal and Skin Diseases*

Dr. Marie Mancini is the Program Director of the Systemic Autoimmune Diseases Biology Program in the Division of Extramural Research at the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS). Her programmatic interests include basic and translational studies on rheumatic autoimmune diseases, such as lupus and inflammatory myositis; intersection of cancer immunotherapies and autoimmune diseases; and training and career development of early-stage investigators and physician-scientists. Prior to joining the NIAMS in 2007, Dr. Mancini was a Research Scientist at MedImmune, Inc., where she focused on pre-clinical studies for several disease targets in the areas of autoimmunity, inflammation, and respiratory diseases. Dr. Mancini earned her doctorate in 2000 in Immunology and completed a post-doctoral fellowship at the Johns Hopkins University School of Medicine, where she studied the cell biology of programmed cell death. Prior to full-time graduate studies, Dr. Mancini worked as a Biologist at the Surgery Branch of the National Cancer Institute, after obtaining a B.S. in Biology from Georgetown University.

Annette Rothermel, PhD, *National Institute of Allergy and Infectious Diseases*

Dr. Annette Rothermel is the Chief of the Autoimmunity and Primary Immunodeficiency Diseases Section in the Division of Allergy, Immunology, and Transplantation at the National Institute of Allergy and Infectious Diseases (NIAID). Her programmatic interests include the role of the immune response in autoimmunity, mucosal immunology, and cancer immunotherapy-associated autoimmunity. Prior to joining the NIAID in 2003, Dr. Rothermel was Research Faculty at Yale University, and a Senior Scientist at the R.W. Johnson Pharmaceutical Research Institute where she focused on immunoregulation and development of protein therapeutics for immune-mediated diseases. Dr. Rothermel earned her doctorate in 1985 in Immunology/Microbiology at Thomas Jefferson University and completed a post-doctoral fellowship at the Research Institute of Scripps Clinic focusing on regulatory T cells.

Elad Sharon, MD, MPH, *National Cancer Institute*

Elad Sharon, MD, MPH, joined the NCI Cancer Therapy Evaluation Program (CTEP) in December 2011 as a Senior Investigator in the Investigational Drug Branch, where he works with academia and industry to develop promising new cancer therapies. His portfolio includes antibody-drug conjugates, immune checkpoint inhibitors and other agents. Dr. Sharon co-directs immunotherapy trials at CTEP and serves as an attending physician in NCI's Developmental Therapeutics Clinic. As part of his work in immunotherapy drug development, he has made a major effort to advance the understanding of immune-related adverse events, including the establishment of the Alliance-NIH irAE Biorepository. In addition, Dr. Sharon is the co-Principal Investigator of the AIM-NIVO trial, evaluating the use of nivolumab for patients with pre-existing autoimmune disease. With the advent of Cancer Moonshot, Dr. Sharon has served as the co-chair of the Adult Immunotherapy Implementation Team to help the NCI accelerate cancer care innovation.

Dr. Sharon is on program committees for several major oncology meetings. He has chaired the NIH-AACR Joint Conference on Cancer, Autoimmunity, and Immunology. He has also served on the committee and chaired several ASCO pre-annual

meeting seminars on the Economics of Cancer Care. Dr. Sharon works on patterns of care projects with NCI's Healthcare Delivery Research Program using SEER data and with NCI's Surveillance Research Program to evaluate emerging practice patterns. He has worked with several providers of data to evaluate real world evidence for use in drug development and patient safety analyses, through collaborations with the FDA, Friends of Cancer Research, and other stakeholders in the field.

Dr. Sharon received his MD from Baylor College of Medicine in Houston, Texas in 2003. He completed his internal medicine residency at Emory University in 2006 and his Hematology/Oncology Fellowship at the NIH in 2011, while obtaining a Master of Public Health degree at the Harvard University in 2009. His fellowship research focused on clinical trials in mesothelioma. During his fellowship at the NCI, he had previously worked as a guest at the Brookings Institution. He serves as an associate editor of JNCI Cancer Spectrum and on the editorial board of JCO Clinical Cancer Informatics.

Connie Sommers, PhD, *National Cancer Institute*

Dr. Connie Sommers is a Program Director in the ImmunoOncology Branch, Developmental Therapeutics Program, Division of Cancer Treatment and Diagnosis. She introduced the concept of EMT (epithelial-mesenchymal transition) in breast cancer during her time at the National Cancer Institute (NCI) Medicine Branch and at Georgetown University School of Medicine (PhD). She transitioned to studying developmental immunology during her postdoctoral studies at the National Institute of Child Health and Human Development and was a Staff Scientist at NCI for 17 years as an expert on genetic mouse modeling to study T cell signaling. She is happy to be able to utilize her backgrounds in cancer research and in basic immunology in her current position. Her programmatic research interests include: checkpoint inhibitor immunotherapy, adoptive cellular immunotherapies, preclinical models of immunotherapy, canine immunotherapy, the role of the microbiome in immunotherapy, and combination cancer therapies.

Lisa Spain, PhD, *National Institute of Diabetes and Digestive and Kidney Diseases*

Dr. Spain serves as director of the Immunobiology of Type 1 Diabetes and Autoimmune Endocrine Diseases Program. Her portfolio includes basic and clinical research on the pathogenic mechanisms of autoimmunity in type 1 diabetes and autoimmune thyroid diseases.

She is the Project Scientist for Type 1 Diabetes TrialNet—an international consortium for the conduct of clinical trials for the prevention and reversal of type 1 diabetes. Her special interest is in facilitating biomarker discovery.

Dr. Spain is also the Program Director for K01, K08, K12, K23, K24, K25, R03 mentored investigator programs for the division. She provides advice and assistance to applicants, participate in funding decisions, and is involved in program evaluations as needed.

Howard Young, PhD, *National Cancer Institute*

Dr. Howard Young obtained his PhD in microbiology at the University of Washington and carried out postdoctoral research at the National Cancer Institute under Drs. Edward Scolnick and Wade Parks. He was a member of the Laboratory of Molecular Immunoregulation at NCI from 1983 to 1989 prior to joining the Laboratory of Experimental Immunology in 1989. He was President of the International Society for Interferon and Cytokine Research (2004-2005) and served as Chair of the Immunology Division of the American Society for Microbiology. He has also served as Chair of the NIH Cytokine Interest Group and Co-Chair and then Chair of the NIH Immunology Interest Group. He is a three-time recipient of the NIH Director's Award for Mentoring (2000, 2006, 2018) and in 2006 he received the National Public Service Award.

Keynote Lecturers

Leonard H. Calabrese, DO, FACR, *Cleveland Clinic*

Leonard Calabrese is a Professor of Medicine, Vice Chair of the Cleveland Clinic's Department of Rheumatic and Immunologic Diseases and the Co-director of the Centre for Vasculitis Care and Research. He also serves as Director of the RJ Fasenmyer Centre for Clinical Immunology at the Cleveland Clinic. He also holds appointments in the Department of Infectious Diseases and the Wellness Institute.

He has particular interest in vascular inflammatory disease of the central nervous system, primary and secondary immunodeficiency states and the intersection of infections and autoimmunity. Over the course of his academic research career, Professor Calabrese has authored over 400 publications including book chapters and peer-reviewed journal articles.

Suzanne L. Topalian, MD, *Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University*

Dr. Topalian is a physician-scientist whose studies of anti-tumor immunity have been foundational in developing cancer immunotherapy. She received her medical and scientific training at Tufts University School of Medicine, Thomas Jefferson University Hospital, and the National Cancer Institute. She joined the Johns Hopkins Kimmel Cancer Center in 2006 as the inaugural director of its Melanoma Program. Her current research focuses on manipulating "immune checkpoints" such as PD-1 in cancer therapy, discovering biomarkers predicting response and resistance, and developing new strategies such as pre-surgical anti-PD-1 administration and effective treatment combinations. Dr. Topalian's work is widely recognized: she was named one of *Nature's 10* in 2014, and received the Karnofsky Award from ASCO in 2015, the Taubman Prize in 2016, and the NCI's Rosalind E. Franklin Award in 2018, for landmark discoveries in cancer immunotherapy. Dr. Topalian was elected to the National Academy of Medicine in 2017. Her work has opened new avenues of scientific investigation and has established immunotherapy as a pillar of oncology.

Conference Speakers and Panelists

Yves Allenbach, MD, PhD, *Sorbonne Université*

Yves Allenbach is an Associate Professor in the Department of Internal Medicine and Clinical Immunology at Sorbonne University, Paris, France. He also holds positions in the National Reference Center for Myositis and the Myology Center for Research.

He is an international expert in the field of auto-immune myopathies. Based on a translational approach the research interests are the diagnosis/classification/follow-up of myositis, the pathophysiology (in vitro and in vivo models) and the development innovative therapy for myositis.

With the development of immune checkpoint inhibitors (ICI), and the emergence of severe immune-related adverse events, he was interested in ICI-induced myositis. He initiated and leads now a clinical network I6TOX in Pitié Salpêtrière Hospital gathering several specialists (Oncology, Cardiology, Immunology, Neurology, Rheumatology, Internal medicine) and researchers. This working group focuses on severe immunotoxicity to increase their recognition and management. In parallel, Dr. Allenbach started several research projects on ICI-induced myositis: a National Registry to collect clinical data, a translational research project on ICI-induced myositis physiopathology.

Hugh Auchincloss, MD, *National Institute of Allergy and Infectious Diseases*

Hugh Auchincloss, MD, serves as NIAID Principal Deputy Director. In this capacity, Dr. Auchincloss is responsible for the following:

- Providing leadership for all NIAID research planning and implementation activities, including helping to prepare and support a strategic vision for NIAID;
- Overseeing an extensive portfolio of basic, clinical, and applied research, as well as product development for biodefense, HIV/AIDS, infectious diseases, and immune-mediated disorders.

His recent leadership activities include spearheading the development of the Institute's strategic plan and chairing the NIAID Research Initiative Committee, an internal governance group that has designed and implemented a more efficient approach to planning, developing, and approving NIAID initiatives. Currently, Dr. Auchincloss is leading an NIAID initiative to design and implement changes in the Institute's clinical research infrastructure, which will be flexible and available for domestic and international clinical research on HIV/AIDS and other infectious diseases. Additionally, Dr. Auchincloss is part of an NIAID senior leadership group responsible for reviewing all aspects of HIV/AIDS research policy, including the evaluation of "test and treat" strategies, analysis of results of pre-exposure prophylaxis (PrEP) clinical trials (including microbicide trials), and coordination of future HIV/AIDS vaccine clinical trials.

Dr. Auchincloss is active on many federal and NIH-wide committees, including the Trans-Federal Task Force on Optimizing Biocontainment Oversight, the National Security Strategy/Office of Science and Technology Policy on Optimizing Biological Select Agents and Toxins Working Group, and the National Biodefense Science Board. He recently was appointed as co-chair of the International Clinical Research Subcommittee of the NIH Global Health Research Working Group and as a member of the NIH Institute and Center Directors Clinical and Translational Science Awards Advisory Board. He also serves as the NIH point of contact for the Emergency Use Authorization program.

Dr. Auchincloss earned bachelor's degrees in political science and economics and a master's degree in economics from Yale University. He received his medical degree from Harvard Medical School in 1976.

Prior to his 2006 appointment at NIAID, Dr. Auchincloss was a transplant surgeon and professor of surgery at Harvard Medical School. For more than 17 years he operated a laboratory in transplantation immunology at Massachusetts General Hospital in Boston. In 1998, he founded the Juvenile Diabetes Research Foundation Center for Islet Transplantation and served as its director until 2003. He subsequently served as Chief Operating Officer of the NIAID Immune Tolerance Network.

In 2005, Dr. Auchincloss was elected president of the American Society of Transplantation. He has authored numerous scientific articles and texts and serves on the editorial boards of several major scientific publications.

Dan Barber, PhD, *National Institute of Allergy and Infectious Diseases*

Dr. Barber obtained his BS from Rider University and his PhD from Emory University in the department of microbiology and immunology. In 2006, he joined the Laboratory of Parasitic Diseases as a postdoctoral fellow in the Immunobiology Section. In 2012, Dr. Barber was awarded a position as an Earl Stadtman Tenure-Track Investigator in the Laboratory of Parasitic Diseases.

Jane Buckner, MD, *Benaroya Research Institute*

Dr. Buckner received her bachelor's degree in chemistry from Carleton College, magna cum laude. She attended Johns Hopkins School of Medicine, and after receiving her MD, she completed her residency training in Internal Medicine at the University of Minnesota. Dr. Buckner went on to complete a fellowship in rheumatology at the University of Washington. As a fellow she was honored with the American College of Rheumatology's Senior Rheumatology Scholar Award. After completing her medical training, Dr. Buckner continued her research training as a postdoctoral fellow in the laboratory of Dr. Gerald Nepom. In 1999, she was the recipient of the ACR Arthritis Investigator Award. Since 1999, Dr. Buckner has been an investigator at the Benaroya Research Institute (BRI). She became the Director of the Translational Research Program at BRI in 2005, was named Associate Director of BRI in January 2012 and was appointed President of BRI in January 2016.

Dr. Buckner continues to care for rheumatology patients at the Virginia Mason Medical Center, and she is an affiliate professor of medicine in the Division of Rheumatology at the University of Washington, an affiliate professor of immunology in the UW School of Medicine, an affiliate of the UW Diabetes Research Center, an active member of the Type 1 Diabetes TrialNet Biomarker and Mechanisms Panel, and a member of the Brehm Coalition.

Dr. Buckner's laboratory is focused on identifying the underlying mechanisms by which regulation of the adaptive immune response fails or is overcome in the setting of human autoimmunity. The diseases studied in Dr. Buckner's laboratory include type 1 diabetes (T1D), multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosus and relapsing polychondritis. Her laboratory is currently examining the question of how autoreactive T and B cells escape regulation in these diseases and the closely related question of whether the development or function of regulatory T cells is impaired in autoimmunity. Her group uses the genetics of autoimmunity to identify pathways that contribute to the failure of tolerance in these diseases.

Through BRI's commitment to groundbreaking research, Dr. Buckner serves as a principal investigator (PI) in a new partnership with the Allen Institute for Immunology, profiling healthy immune systems to serve as a foundation for existing and future disease research programs. She is also a PI in a new collaborative research effort with the Parker Institute for Cancer Immunotherapy, JDRF and The Leona M. and Harry B. Helmsley Charitable Trust to understand, predict and prevent insulin-dependent diabetes following checkpoint therapy for cancer. In addition, Dr. Buckner founded and oversees BRI's large biorepository, which collects biological samples from both healthy individuals and individuals with autoimmune diseases and serves as an invaluable resource for scientists to accelerate their understanding of human autoimmune disease.

Laura C. Cappelli, MD, MHS, MS, *Johns Hopkins University*

Dr. Laura C. Cappelli is an Assistant Professor of Medicine at the Johns Hopkins University School of Medicine, Division of Rheumatology, and a faculty member of the Johns Hopkins Arthritis Center. She earned her MD from Johns Hopkins. She completed her residency in internal medicine and fellowship in rheumatology at the Johns Hopkins Hospital. Dr. Cappelli earned an MHS in Clinical Investigation at the Johns Hopkins Bloomberg School of Public Health. Her primary research focus is rheumatologic adverse effects of cancer immunotherapy including the clinical characteristics, epidemiology, impact on patients, and biologic mechanisms of these adverse events. Her work involves collaborations with oncologists and laboratory investigators in rheumatology and oncology. Dr. Cappelli also co-chairs the Immune Related Toxicity Team at Johns Hopkins. In addition, she studies rheumatoid arthritis, focusing on patients with seronegative disease and on the use of autoantibodies as biomarkers.

Melissa Renee Chambers, DVM, MD, *University of Alabama at Birmingham*

Dr. Chambers attended Auburn University College of Veterinary Medicine and University of Alabama at Birmingham (UAB) School of Medicine. She completed the Halsted Surgical fellowship at Johns Hopkins Hospital in Baltimore, MD and neurosurgical residency at Vanderbilt in Nashville, TN. She is a professor in the Department of Neurosurgery at UAB. As a veterinarian and board-certified neurosurgeon, Dr. Chambers is a strong proponent of the One Health Initiative, an effort to improve animal and public health worldwide and strengthen medicine by working together. She is founder of the Alabama Comparative Oncology Network, principal investigator of the regional Southeastern Comparative Oncology Network, and founding member of the NCI Comparative Brain Tumor Consortium at the Center for Cancer Research, each a collaboration of veterinary & medical scientists and clinicians working together to identify genetic targets for treatment of disease through comparative genomics.

“CANINE” is a multi-institutional consortium to test an innovative immuno-therapeutic approach in dogs that spontaneously and sporadically develop malignant glial brain tumors that resemble in most important aspects, high-grade malignant gliomas in humans. The current multi-center study is designed to advance research and improve outcomes for both people and pets with brain tumors and will analyze samples, data and response to treatment. Each dog enrolled in the trial will help the next and hopefully translate to improved outcomes in the future.

Irene Cortese, MD, *National Institute of Neurological Disorders and Stroke*

Dr. Cortese is the director of the Neuroimmunology Clinic at NIH. She earned her medical and neurology residency from the Universita di Roma Tor Vergata, Rome, Italy. She then came to NIH for a research fellowship in neuroimmunology in the Neuroimmunology Branch in Roland Martin’s lab. After completion fellowship, Dr. Cortese elected to repeat her neurology training in the U.S. to obtain US board certification. She completed both Neurology residency and combined Clinical Neurophysiology Fellowship at Johns Hopkins Hospital and Clinical Neuroimmunology Fellowship at NIH. In 2008 she joined the NIH faculty as a staff clinician, and was named Director of the Neuroimmunology Clinic in 2013. Over her career, her research focus has been Multiple Sclerosis and related immune medicated diseases of the central nervous system, and in more recent years, in collaboration with Dr. Avi Nath, she has established a PML clinical program at NIH.

Tal Danino, PhD, *Columbia University*

Tal Danino is an Assistant Professor in the Department of Biomedical Engineering at Columbia University. His lab focuses on engineering bacteria for biomedical applications, with a particular emphasis on been developing bacteria as a cancer therapy. Originally from Los Angeles, Tal received a PhD in Bioengineering from UCSD and was a postdoctoral fellow at MIT. He is the recipient of awards including the NSF CAREER Award, Era of Hope Scholar Award, TED Fellow, and NIH Pathway to Independence Award. He directs the Synthetic Biological Systems Laboratory and is a member of the Herbert Irving Comprehensive Cancer Center and Data Science Institute.

Silvia Formenti, MD, *Weill Cornell Medicine*

Dr. Silvia Formenti is Chair of the Department of Radiation Oncology and Associate Director of Radiation Oncology at the Sandra and Edward Meyer Cancer Center at Weill Cornell Medicine, and Radiation Oncologist-in-Chief at New York-Presbyterian/Weill Cornell Medical Center. She is also the Sandra and Edward Meyer Professor of Cancer Research at Weill Cornell Medicine.

Dr. Formenti received her medical degree in Italy from the University of Milan. She is board certified in medical oncology, radiology and radiation oncology. A recognized leader in radiation oncology and breast cancer research, Dr. Formenti's groundbreaking work has transformed the paradigm in radiation biology, demonstrating the efficacy of combining radiotherapy with immunotherapy to control cancer cell growth in solid tumors. In combination with immune checkpoint blockade, focal radiotherapy can be used to recruit patients' immune systems to reject their individual tumor, resulting in a form of personalized immunotherapy, specific for each individual patient. She has translated preclinical work into clinical trials in metastatic solid tumors like breast and lung cancer, and in brain metastases. She is currently leading six investigator-initiated clinical trials of immunotherapy and radiotherapy. A prolific researcher, Dr. Formenti has published more than 250 papers recognized by high-impact journals including Nature Medicine, JAMA, Lancet Oncology and the Journal of Clinical Oncology. In 2019, she was honored to receive the ASTRO Gold Medal.

Sarthak Gupta, MD, *National Institute of Arthritis and Musculoskeletal and Skin Diseases*

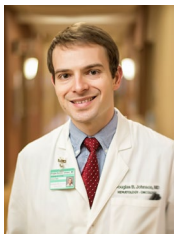
Dr Sarthak Gupta is an Assistant Research Physician in the Systemic Autoimmunity Branch in Intramural NIAMS. He received his medical degree in India and completed a residency in Internal Medicine at SUNY at Buffalo. He then moved to NIH to pursue a fellowship in adult rheumatology where he also served as the chief fellow for the training program. He conducts translational research in autoimmune diseases and has published extensively in leading rheumatology and immunology journals and is recipient of multiple awards and grants. He is an investigator on several ongoing clinical trials using novel therapies in systemic autoimmune diseases. Dr. Gupta is also an active clinician and a core faculty for the rheumatology training program at NIAMS.

Dr Gupta collaborates extensively with oncologists in intramural NCI and has reported on imaging findings in immune checkpoint inhibitor induced adverse events and also helped develop the AIM-NIVO trial, a multicenter trial assessing the role of nivolumab in cancer patients with underlying autoimmunity.

Kristina Howard, DVM, PhD, *U.S. Food and Drug Administration*

Kristina Howard is a scientist who directs research studies in the Division of Applied Regulatory Science, Center for Drug Evaluation and Research of the United States Food and Drug Administration. Her research focuses on evaluating the ability of humanized mouse models to better predict the safety of small and large molecule drug products in humans. She received her veterinary degree from the Virginia-Maryland Regional College of Veterinary Medicine and her doctorate degree in immunology from North Carolina State University. Prior to joining the FDA, she worked with a wide variety of animal models in research focused on immunotoxicity, viral pathogenesis and vaccine development.

Douglas B. Johnson, MD, *Vanderbilt-Ingram Cancer Center*



Douglas Johnson, MD, MSCI received his MD from the University of Alabama School of Medicine and completed internal medicine residency at Duke University before coming to Vanderbilt for hematology/oncology fellowship. He has been on faculty at Vanderbilt since 2014 as an Assistant Professor of Medicine and is now the director of the melanoma clinical and research program.

Dr. Johnson's research focuses on optimizing and extending the use of novel immune and targeted therapies in melanoma, to identify markers of response and resistance, to understand and more effectively manage the side effects of these new therapies, and to develop new treatment options for melanoma. He is the local and national principal investigator for numerous clinical trials and his research is funded by individual philanthropy, National Cancer Institute, the American Society of Clinical Oncology, the National Comprehensive Cancer Network, and the Melanoma Research Foundation. He also has national leadership positions, including membership in the NCCN Melanoma Guidelines Committee.

Minhyung Kim, MD, *Roswell Park Comprehensive Cancer Center*

Dr. Kim practiced medicine as a surgeon in South Korea. Dr. Kim has been interested in medical research ever since he was a surgery resident, so he decided to move to the US in 2011. Dr. Kim began this endeavor as a visiting scientist performing basic/translational research at Roswell Park Comprehensive Cancer Center. Since joining Roswell Park, Dr. Kim has developed a research program in regional cancer therapies. His special interests in research are "Application of animal models for better understating in immune response after immunotherapy", "Lymphocyte trafficking in cancer immunotherapy", and "Investigation of immune modulation effects of adrenergic receptors".

David Kozono, MD, PhD, *Dana-Farber Cancer Institute*

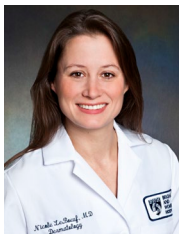
David Kozono, MD, PhD, is a Senior Physician in Dana-Farber's Lowe Center for Thoracic Oncology and Assistant Professor of Radiation Oncology at Harvard Medical School. His clinical and research focus is on precision radiotherapy and combination therapies for lung cancer. He serves as the Executive Officer for the Respiratory Committee and Co-Chair of the Immuno-Oncology Committee in the Alliance for Clinical Trials in Oncology. He completed his undergraduate studies at the University of California Berkeley. He received his MD and PhD at Johns Hopkins University School of Medicine, where in the laboratory of Nobel laureate Dr. Peter Agre he and his colleagues characterized the molecular structure and function of the aquaporin water channels. He then completed his internship in internal medicine at Brigham and Women's Hospital and residency in the Harvard Radiation Oncology Program. His research in lung cancer has been supported by the American Society for Radiation Oncology (ASTRO) Junior Faculty Award, the LUNGevity Foundation Career Development Award and the National Cancer Institute (NCI) K08 Award.

Mario E. Lacouture, MD, *Memorial Sloan-Kettering Cancer Center*

Dr. Lacouture is a Professor and the director of the Oncodermatology Program in the Dermatology Service, Department of Medicine, at Memorial Sloan Kettering Cancer Center in New York City. He did his postdoctoral work at Brigham and Women's Hospital in Boston, MA, an internship in General Surgery at Cleveland Clinic and residency in dermatology at The University of Chicago, IL. He received his MD degree from Javeriana University in Bogota, Colombia, where he grew up. His research interests span the disciplines of dermatologic conditions in cancer patients, and those that arise as a consequence of chemotherapy and/or radiotherapy or stem cell transplants. Dr. Lacouture is currently the Principal Investigator for "The CHANCE Trial", A Longitudinal Study of Chemotherapy-Induced Hair Changes and Alopecia, Skin Aging and Nail Changes in Women with Non-Metastatic Breast Cancer and a NIH funded study to identify the mechanisms of immune-related cutaneous adverse events. In addition, Dr Lacouture is the PI for various therapeutic trials in oncodermatology. Dr. Lacouture is a well-known lecturer in the US and abroad on dermatologic conditions as a result of cancer therapies. He founded a clinical program that encompasses patient care,

education, and research on dermatologic care in cancer patients and survivors. He is currently Co-Chair of the Skin Toxicity Study Group and the Board of the Multinational Association of Supportive Care in Cancer and is on the advisory board of Cancer.Net and Bridges, the Newsletter for Cancer Survivors. In 2012, CancerCare named Dr Lacouture as Physician of the Year for his contributions to the education of people living with cancer and in 2020 he was awarded the Everett C. Fox Memorial Lectureship by the American Academy of Dermatology for his innovative work in oncodermatology. Dr Lacouture has published over 240 articles in peer-reviewed journals and is the author of *Dr Lacouture's Skin Care Guide for People Living With Cancer* and Editor of the textbook *Dermatologic Principles and Practice in Oncology*.

Nicole R. LeBoeuf, MD, MPH, *Dana-Farber Cancer Institute*



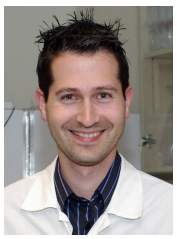
Dr. LeBoeuf received her medical from the University of Massachusetts Medical School in 2006. She completed her residency in Dermatology at Columbia University followed by a fellowship in Cutaneous Oncology at Brigham and Women's/Dana-Farber Cancer Center at Harvard. Dr. LeBoeuf joined the faculty in the Department of Dermatology and Center for Cutaneous Oncology at Dana-Farber and Brigham and Women's in 2012 and earned a Masters in Public Health from the Harvard TH Chan School of Public Health in 2015. In addition to directing the Cutaneous Oncology and Medical Dermatology Fellowship programs, Dr. LeBoeuf established and directs the Program in Skin Toxicities from Anticancer Therapies at the Dana-Farber/Brigham and Women's Cancer Center. She leads clinical trials in cutaneous lymphoma and rare skin malignancies as well as interventional studies for the prevention or management of side effects from cancer treatment. Her research focuses on using novel imaging and computational methods to understand the immunologic mechanisms of side effects to cancer therapeutics and implementing therapies or other interventions to mitigate them.

Burkhard Ludewig, DVM, *Kantonsspital St. Gallen*

Burkhard Ludewig is currently acting as the head of the Medical Research Center and the Institute of Immunobiology at the Kantonsspital St. Gallen, Switzerland. His research interests are focused on the interaction of viruses with the innate and adaptive immune system. Furthermore, his laboratory has established transgenic mouse model for in vivo stromal cell targeting. He is affiliated with the Life Science Faculty of the University of Zürich and serves as an affiliated PI of the Zürich Life Science Graduate School. Further academic activities include teaching of biology students of the ETH Zürich and the University of Zürich in immunology, and supervising PhD students from the Life Science Zürich Graduate School.

Prof. Ludewig graduated in 1992 at the Faculty of Veterinary Medicine of the Free University (FU) Berlin, Germany, and received a Doctorate in Veterinary Medicine in 1995 at the FU Berlin following a three year experimental work at the Robert-Koch Institute, Berlin. Following two short postdoctoral positions at the Robert-Koch Institute and the Hebrew University of Jerusalem, he joined the Institute of Experimental Immunology at the University of Zürich in 1997 as a recipient of the postdoctoral fellowship from the Deutsche Forschungsgemeinschaft. In 2002, Prof. Ludewig accepted the position as head of the Institute of Immunology at the Cantonal Hospital St. Gallen in Eastern Switzerland. Currently, he serves as a member of the editorial boards of the Journal of Immunology and the European Journal of Immunology.

Gal Markel, MD, PhD, *Sheba Medical Center*



Gal Markel is a trained medical oncologist, an Associate Professor of Immunology at Tel Aviv University and the Chief Scientist of the Ella Lemelbaum Institute of Immuno-Oncology at Sheba Medical Center. He completed his PhD in Immunology in 2004 with highest honors, and his MD at 2005, both at the Hebrew University of Jerusalem, Israel. Gal is an internationally recognized expert in translational tumor immunology and clinical immuno-oncology; he is the author of 110 peer-reviewed papers and the inventor of more than 20 patents. His main research focuses on tumor mechanisms of immune resistance, and how to exploit them to develop novel immunotherapies.

Gal was a co-founder of BoneTone Communications, which was acquired by DSPG in 2011 and the founder and CSO of cCAM Biotherapeutics, which was acquired by Merck & Co in 2015. He is the founder and CSO of 4C Biomed Inc. Gal is a

highly active speaker and has given numerous international talks, including TED MED, and has won many national and international awards.

Florencia McAllister, MD, *MD Anderson Cancer Center*

Florencia McAllister, MD, is a physician-scientist who leads a basic and translational Immunology laboratory with the goal of making discoveries that can result in effective cancer early detection, immunoprevention and immunotherapy. McAllister has received Immunology post-graduate training with Jay Kolls, MD, at the University of Pittsburgh, where she made several discoveries in T Helpers17 (TH17) cells biology, including the characterization of the lung epithelial IL-17 signaling pathway, the dissection of the role of IL-17 pathway in cystic fibrosis, the understanding of the function of IL-22 in innate immunity. Upon completion of her Internal Medicine in Pittsburgh, McAllister pursued a combined clinical training in Medical Oncology and Clinical Pharmacology at Johns Hopkins University, where she undertook postdoctoral research studies in Cancer Biology and Tumor Immunology in the laboratories of Steven Leach and Drew Pardoll, discovering the key role of TH17 cells in the initiation and progression of pancreatic cancer. In 2012 McAllister was the recipient of the Pancreatic Cancer Action Network (PanCAN)- AACR Samuel Stroum Fellowship and was awarded the Young Investigator Award from the Conquer Cancer Foundation.

McAllister began her research lab at MD Anderson Cancer Center in the fall of 2014. Her lab focuses on understanding the role of the immune system in immunosurveillance and immunoevasion. More recently, the laboratory has developed an interest on dissecting the role of bacterial products in modulating cancer immune responses. McAllister has received the PanCAN-AACR Career Development Award in 2014 and a Translational Award in 2016. She is currently the recipient of a K12-Career Development Award from NCI, a V Foundation Research Scholar and received the Bernard Lee Schwartz Designated Research Scholar Award from the American Gastrointestinal Association.

McAllister is an attending in Gastrointestinal Medical Oncology and leads a multi-disciplinary Pancreatic Cancer High-Risk Clinic in which patients with higher genetic susceptibility for pancreatic cancer undergo surveillance and elect to participate in a cohort with prospective biospecimens and data collection with the ultimate goal of validating novel biomarkers of risk and early detection of pancreatic cancer.

Lisa Meier McShane, PhD, *National Cancer Institute*

Lisa Meier McShane, PhD, is an Associate Director for the Division of Cancer Treatment and Diagnosis (DCTD), U.S. National Cancer Institute, National Institutes of Health. She heads the Biometric Research Program (BRP), comprising statisticians, bioinformaticians, and computational biologists in Biostatistics and Computational and Systems Biology Branches. She is an internationally recognized expert on development of tumor markers for prognosis, therapy selection, and disease monitoring; omics-based predictors for clinical use; and reporting guidelines for health research studies. Dr. McShane holds a PhD in Statistics from Cornell University and is a Fellow of the American Statistical Association. Her statistical research interests include biomarker-driven clinical trial design, analysis of high-dimensional omics data, multiple comparisons methods, surrogate endpoints, and biomarker assay analytical performance assessment. She co-led efforts to develop "Reporting guidelines for tumor marker prognostic studies (REMARK)" and "Criteria for the use of omics-based predictors in clinical trials." She has coauthored numerous statistical and biomedical papers and the book *Statistical Design and Analysis of DNA Microarray Investigations*.

Dr. McShane serves on the Scientific Advisory Board for *Science Translational Medicine* and Editorial Board for *BMC Medicine*. She has served on American Society of Clinical Oncology committees that developed guidelines for *HER2* and hormone receptor testing in breast cancer, *EGFR* mutation testing in lung cancer, and biomarkers in early stage breast cancer. She has served as a member of the Institute of Medicine *Committee for Management of the Air Force Health Study Data and Specimens*, the *Consensus Committee on Management of the Air Force Health Study Data and Specimens-Report to Congress*, and the *Committee on the State of the Science in Ovarian Cancer Research*.

Jaruska Naidoo, MBBCh, *Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University*

Dr. Jarushka Naidoo is an Assistant Professor of Oncology at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, in Baltimore, MD. She completed Internal Medicine and Medical Oncology training through the Royal College of Physicians of Ireland, after which she was awarded an advanced fellowship at Memorial Sloan Kettering Cancer Center (New York), from the Irish Society of Medical Oncology. Her research interests include: immunotherapy, novel immunotherapeutic combinations, toxicities of immunotherapy and lung cancer. In the field of immune-related toxicity, she has published a number of seminal studies, including the first comprehensive analysis of pneumonitis with anti-PD-1/PD-L1 agents (J Clin Oncol 2016), the first analysis of patients with autoimmune bullous pemphigoid (Cancer Immunol Res 2017) and inflammmatory arthritis (Oncologist 2018) from anti-PD-1/PD-L1. She serves on national immune-toxicity guidelines for NCCN and SITC, is the chair of the Johns Hopkins Immune-related Toxicity Team, and the Chair of the NRG Immunotherapy subcommittee.

Barbara Rehermann, MD, *National Institute of Diabetes and Digestive and Kidney Diseases*

Dr. Barbara Rehermann is Chief of the Immunology Section, Liver Diseases Branch, NIDDK at the National Institutes of Health in Bethesda, Maryland. She received an MD degree and the venia legendi for Immunology from Medizinische Hochschule, Hannover, Germany, and als completed a clinical residency and fellowship in the Department of Gastroenterology, Hepatology and Endocrinology at the same university, and a postdoctoral research fellowship at The Scripps Research Institute, La Jolla, CA. Her scientific interests include innate and adaptive immunology, the gut-liver axis and the microbiome. By learning from naturally co-evolved microbiota, she is trying to increase the translational research value of the laboratory mouse. She is currently associate editor of the Journal of Hepatology, editor for The Journal of Clinical Investigation and an editorial board member for Gastroenterology, Hepatology, and Journal of Infectious Diseases. Dr. Rehermann's publications are cited over 13,000 times.

Kerry Reynolds, MD, *Massachusetts General Hospital Cancer Center*

Dr. Kerry Reynolds is a physician at the Massachusetts General Hospital Cancer Center and Instructor of Medicine at Harvard Medical School. She currently serves as the Director of the Severe Immunotherapy Complications Service, in addition to being the Clinical Director for the inpatient cancer services at Mass General Cancer Center.

Dr. Reynolds specializes in the care of hospitalized patients. Under her leadership, the Massachusetts General Cancer Center's inpatient program evaluates and treats over 5,000 patients each year and serves as a core training experience for Harvard Medical School students, residents, and fellows each year.

Dr. Reynolds completed her residency and chief residency at Massachusetts General. Following fellowship training in Oncology at Dana-Farber/Partners Cancer Care, she joined the Harvard Medical School faculty in 2014. She is presently focused on efforts to uncover predictors for those patients who are at highest risk for adverse events associated with immunotherapy, to characterize the signs and symptoms of these events, and to understand the cellular and molecular blueprints that drive them—all with a goal of gaining knowledge that will allow the medical community to develop new therapeutics and improve the treatment of this unique patient population. She is the author of articles and textbook chapters on immunotherapy toxicity as well as the lead editor for "Facing Immunotherapy", a book for patients and care givers to guide them through their treatment journey.

Rafick-Pierre Sékaly, PhD, *Case Western Reserve University*

Dr. Sekaly is the Richard J. Fasenmyer Professor of Immunopathogenesis at the Case Western Reserve University School of Medicine, Director of the Center for Systems Immunology, and member of the Hematopoietic and Immune Cancer Biology Program at the Case Western Comprehensive Cancer Center. Dr. Sekaly's lab has been focused for the past 20 years on developing a better understanding of the human immune response to vaccines and to chronic viral infections, with a specific focus on cancer and HIV infection. Over the past 7 years, Dr. Sekaly and his team have implemented the use of system biology approaches to monitor the diversity of memory T cells and to identify the mechanisms underlying the diversity of memory T cell subsets. His group has also pioneered the application of systems biology approaches to the understanding of mechanisms of action of the licensed vaccines and adjuvants, and has shown for the first time the diversity of the mechanism that lead to the establishment and persistence of different memory T cell subsets. Dr. Sekaly's work has led to more than 342 peer-reviewed articles in scientific journals and more than 23 patents. He has been a principal investigator on numerous grants from the National Institutes of Health and foundations, including the Bill and Melinda Gates Foundation and the American Foundation for AIDS Research.

Norman E. "Ned" Sharpless, MD, *National Cancer Institute*

Norman E. "Ned" Sharpless, MD, was officially sworn in as the 15th director of the National Cancer Institute (NCI) on October 17, 2017. Prior to his appointment, Dr. Sharpless served as the director of the University of North Carolina (UNC) Lineberger Comprehensive Cancer Center, a position he held since January 2014.

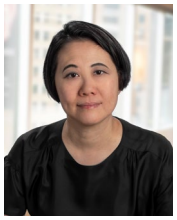
Dr. Sharpless was a Morehead Scholar at UNC–Chapel Hill and received his undergraduate degree in mathematics. He went on to pursue his medical degree from the UNC School of Medicine, graduating with honors and distinction in 1993. He then completed his internal medicine residency at the Massachusetts General Hospital and a hematology/oncology fellowship at Dana-Farber/Partners Cancer Care, both of Harvard Medical School in Boston. After 2 years on the faculty at Harvard Medical School, he joined the faculty of the UNC School of Medicine in the Departments of Medicine and Genetics in 2002. He became the Wellcome Professor of Cancer Research at UNC in 2012.

Dr. Sharpless is a member of the Association of American Physicians and the American Society for Clinical Investigation. He has authored more than 160 original scientific papers, reviews, and book chapters, and is an inventor on 10 patents. He cofounded two clinical-stage biotechnology companies: G1 Therapeutics and Sapere Bio (formerly HealthSpan Diagnostics). He served as Acting Commissioner for Food and Drugs at the US FDA for seven months in 2019, before returning to the NCI Directorship.

Virginia Sheikh, MD, MHS, *U.S. Food and Drug Administration*

Dr. Sheikh is a Medical Officer in the Division of Antivirals at FDA/CDER, where she has reviewed antiviral products intended for the treatment of HIV, hepatitis C, hepatitis B, cytomegalovirus, and various other viruses. Dr. Sheikh has represented the FDA at several HIV Cure-related meetings and is a member of the DHHS HIV Treatment Guidelines Panel. Prior to joining the FDA in 2016, Dr. Sheikh performed clinical research in the HIV Pathogenesis Section at NIAID where she focused on the immunopathogenesis and management of HIV/AIDS, immune reconstitution inflammatory syndrome (IRIS), and idiopathic CD4 lymphocytopenia (ICL). Dr. Sheikh earned her master's degree at Johns Hopkins School of Public Health (2000) and her medical degree at Eastern Virginia Medical School (2005). She trained in internal medicine at Columbia Presbyterian Hospital (2008) and in infectious diseases at the National Institutes of Allergy and Infectious Diseases (NIAID, 2011).

Lillian Siu, MD, *Princess Margaret Cancer Centre*



Dr. Siu is a senior medical oncologist at Princess Margaret Cancer Centre since 1998, and has been a Professor of Medicine at the University of Toronto since 2009. She is theMeli Director of the Phase I Program and Co-Director of the Bras and Family Drug Development Program at Princess Margaret Cancer Centre, and holds the BMO Chair in Precision Genomics (2016-2026). She is also the Clinical Lead for the Tumor Immunotherapy Program at Princess Margaret Cancer Centre. Dr. Siu served on the Board of Directors for the American Society of Clinical Oncology (ASCO) for a four-year term (2012-2016). She also served as a member of the Nomination Committee for the American Association for Cancer Research (AACR) (2014-2016). She currently serves on the AACR Board of Directors for a three-year term (2017-2020).

Dr. Siu's major research focus is in the area of new anticancer drug development, particularly with respect to phase I trials and head and neck malignancies. She is the Principal Investigator of a phase I cooperative agreement UM1 award sponsored by the United States National Cancer Institute. In addition to her active research in early phase clinical trials, she has been leading genomics initiatives and immuno-oncology trials at the Princess Margaret Cancer Centre. Together, the three programs of drug development, cancer genomics and tumor immunotherapy form a triad of synergy that supports the institution's core vision to deliver precision cancer medicine.

Internationally, Dr. Siu was the recipient of the US NCI Michaele C. Christian Award in Oncology Drug Development in 2010. She has been awarded the TAT 2020 Honorary Award for contributions in the development of anticancer drugs. Locally, she was awarded the University of Toronto Department of Medicine Eaton Scholar Researcher in 2016. She was the ASCO Conquer Cancer Foundation Grants Selection Committee Chair in 2009-10. She was Chairperson of the AACR Education Committee, Co-Chairperson of the Scientific Committee for the 2012 Annual Meeting and Co-Chairperson for the Clinical Trials Committee 2015-2017. Dr. Siu has published over 300 peer-reviewed manuscripts, and she is currently a scientific editor for *Cancer Discovery* and is on the editorial board for *JAMA Oncology*.

Giorgio Trinchieri, MD, *National Cancer Institute*

Dr. Trinchieri was most recently the Director of the Schering Plough Laboratory for Immunological Research in Dardilly, France, and an NIH Fogarty Scholar at the Laboratory for Parasitic Diseases, NIAID. Since August 2006, he has been the Director of the Cancer and Inflammation Program, and Chief of the Laboratory of Experimental Immunology. His research at the CCR focuses on the interplay between inflammation/innate resistance and adaptive immunity, and the role of pro-inflammatory cytokines in the regulation of hematopoiesis, innate resistance, and immunity. He discovered interleukin-12 while at the Wistar Institute in 1989 and for many years has been characterizing the molecular mechanisms of interleukin-12 production and action, and the role of this molecule in tumor immunity, infections, and autoimmunity.

Alexandra-Chloé Villani, PhD, *Massachusetts General Hospital, Harvard Medical School, Broad Institute*

Alexandra-Chloé Villani is an Assistant Professor of Medicine at Harvard Medical School and an Associate Member of the Broad Institute. She holds the positions of Principal Investigator at the Massachusetts General Hospital (MGH) Center for Cancer Research and at the MGH Center for Immunology and Inflammatory Diseases, where she is also the Director of the Single Cell Genomics Research Program. She received a BSc in Physiology and a PhD in Experimental Medicine from McGill University, where she worked on mapping new genetic loci contributing to inflammatory bowel disease susceptibility. She completed her postdoctoral training as a Banting Postdoctoral Fellow at the Broad Institute, where she developed new systems immunology and single-cell genomics strategies to define key components regulating human immune response that led to identifying novel human blood immune cell populations. Her findings contributed to highlighting the value of embarking on a comprehensive Human Cell Atlas initiative. The Villani Lab aims at achieving a higher resolution definition and functional characterization of cell subsets and rules governing human immune response regulation as a foundation for deciphering how immunity is dysregulated in diseases and for developing a comprehensive human immune lexicon that is key to promoting effective

bench-to-bedside translation of findings. The Villani Lab is using single-cell 'multi-omics' strategies, unbiased systems immunology approaches, and integrative computational frameworks empowering the study and modeling of the immune system as a function of "healthy" and inflammatory states, disease progression, and response to treatment. Dr. Villani is the recipient of several awards, including the MGH Transformative Innovation Award, and the NIH Director's New Innovator Award.

Yinghong "Mimi" Wang, MD, PhD, MS, *MD Anderson Cancer Center*

Dr. Wang has a strong academic background (MD, PhD, M.Sc.) and profound clinical experience from world renowned medical programs (Johns Hopkins, Cleveland Clinic) and specializes in Inflammatory Bowel Disease (IBD), fecal microbiota transplantation (FMT), and immunotherapy induced colitis. Prior to joining the University of Texas MD Anderson Cancer Center, she had 8 years of experience from a tertiary IBD practice at Cleveland Clinic taking care of patients with Crohn's Disease, and Ulcerative Colitis with or without serious complications, in addition to 2 years of clinic experience doing FMT for recurrent Clostridium difficile infection with eradication rate of over 95%.

After joining MD Anderson in December 2016, Dr. Wang quickly caught the unmet need of effectively managing immunotherapy induced GI toxicity and connected her unique expertise in IBD and FMT with this strong demand. She established new services of IBD and fecal transplantation at GI department. Her contributions have been quickly and broadly recognized by colleagues within the GI department and from various oncology departments. In addition to improving the clinical practice, Dr. Wang has made significant accomplishments in clinical research that include 40 published journal papers, 4 book chapters, and more than 50 conference presentations. She also leads the guideline writing for immunotherapy induced GI toxicity in three national oncology societies (SITC, ASCO, NCCN).

Accepted Poster Abstracts

The original agenda for the NIH-AACR Cancer, Autoimmunity, and Immunology Conference included a poster session. The below abstracts would have been presented at the conference as posters, and are now included as part of the digital program here.

Multi-omics: Differential expression of IFN-g results in distinctive mechanistic features linking chronic inflammation, gut dysbiosis, and autoimmune diseases

Heekyong R. Bae[1], Patrick S.C. Leung[2], Deborah L. Hodge[1], John M. Fenimore[1], Seon-Min Jeon[3], Vishal Thovarai[1], Amiran Dzutsev[1], Andrew A. Welcher[4], Michael Boedigheimer[4], Michael A. Damore[4], Myung-Sook Choi[3], Richard A. Fravell[5], Giorgio Trinchieri[1], M. Eric Gershwin[2], Howard A. Young[1]
[1]Laboratory of Experimental Immunology, Cancer and Inflammation Program, Center for Cancer Research, National Cancer Institute-Frederick, Frederick, MD; [2]Division of Rheumatology, Allergy and Clinical Immunology, University of California at Davis, Davis, CA; [3]Center for Food and Nutritional Genomics Research, Department of Food Science and Nutrition, Kyungpook National University, Daegu, Republic of Korea; [4]Amgen Inc., Thousand Oaks, CA; [5]Department of Immunology, Yale School of Medicine, New Haven, CT

Low grade, chronic inflammation is a critical risk factor for immunologic dysfunction including autoimmune diseases. However, the multiplicity of complex mechanisms and lack of relevant murine models limit our understanding of the precise role of chronic inflammation. To address these hurdles, we took advantage of multi-omics data and a unique murine model with a low but chronic expression of IFN-g, generated by replacement of the AU-rich element (ARE) in the 3' UTR region of IFN-g mRNA with random nucleotides. Herein, we demonstrate that low but differential expression of IFN-g in mice by homozygous or heterozygous ARE replacement triggers distinctive gut microbial alterations, of which alteration is female-biased with autoimmune-associated microbiota. Metabolomics data indicates that gut microbiota-dependent metabolites have more robust sex-differences than microbiome profiling, particularly those involved in fatty acid oxidation and nuclear receptor signaling. More importantly, homozygous ARE-Del mice have dramatic changes in tryptophan metabolism, bile acid and long-chain lipid metabolism, which interact with gut microbiota and nuclear receptor signaling similarly with sex-dependent metabolites. Consistent with these findings, nuclear receptor signaling, encompassing molecules such as PPARs, FXR, and LXRs, was detectable as a top canonical pathway in comparison of blood and tissue-specific gene expression between female homozygous vs heterozygous ARE-Del mice. Further analysis implies that dysregulated autophagy in macrophages is critical for breaking self-tolerance and gut homeostasis, while pathways interact with nuclear receptor signaling to regulate inflammatory responses. Overall, pathway-based integration of multi-omics data provides systemic and cellular insights about how chronic inflammation driven by IFN-g results in the development of autoimmune diseases with specific etiopathological features.

Inclusion of a Dap10 costimulatory domain enhances anti-tumor efficacy of chimeric PD1-expressing T cells in multiple types of solid tumors

Barber, Amorette
Department of Biological and Environmental Sciences, Longwood University, Farmville, VA, USA

Adoptive transfer of T cells is a promising anti-tumor therapy for many cancers. To enhance tumor recognition by T cells, chimeric antigen receptors (CAR) consisting of signaling domains fused to receptors that recognize tumor antigens can be expressed in T cells. One receptor that is a prospective target for a new chimeric antigen receptor is PD1 because the ligands for the PD1 receptor are expressed on many cancer types. Therefore, we developed a murine chimeric PD1 receptor (chPD1) consisting of the PD1 receptor extracellular domain and the activation domain of CD3 zeta. In addition, current chimeric antigen receptor therapies utilize various costimulatory domains to enhance anti-tumor efficacy. Therefore, we also compared the inclusion of CD28, Dap10, 4-1BB, GITR, ICOS, or OX40 costimulatory domains in the chPD1 receptor to determine which costimulatory domain induced optimal anti-tumor immunity. To determine if this novel CAR could potentially target a wide variety of tumors, the anti-tumor efficacy of chPD1 T cells against murine lymphoma, melanoma, kidney, pancreatic, liver, colon, breast, ovarian, prostate, and bladder cancer cell lines was measured. Of the eighteen cell lines tested, all expressed PD1 ligands on their cell surface, making them potential targets for chPD1 T cells. Regardless of the costimulatory domain in the CAR, all of the chPD1 T cells induced similar levels of T cell proliferation and tumor cell lysis. However, differences were observed in the cytokine secretion profiles depending on which costimulatory receptor was included in the CAR. While most of the chPD1 T cell receptor combinations secreted both pro-inflammatory (IFNγ, TNFα, IL-2, GM-CSF, IL-17, and IL-21) and anti-inflammatory cytokines (IL-10), chPD1 T cells containing a Dap10 costimulatory domain secreted high levels of proinflammatory cytokines but did not secrete a significant amount of anti-inflammatory cytokines. Furthermore, T cells expressing chPD1 receptors with a Dap10 domain also had the strongest anti-tumor efficacy *in vivo*. ChPD1 T cells did not survive for longer than 14 days in vivo, however treatment with chPD1 T cells induced long-lived protective host-anti-tumor immune responses in tumor-bearing mice. Therefore, adoptive transfer of chPD1 T cells could be a novel therapeutic strategy to treat multiple types of cancer and inclusion of the Dap10 costimulatory domain in chimeric antigen receptors may induce a preferential cytokine profile for anti-tumor therapies.

An unusual case of palmar-plantar erythrodysesthesia syndrome

Flewelling, Kayla R., Central Michigan University College of Medicine, Mt. Pleasant, MI, USA
Effiong, Utibe, M.D., MPH, MidMichigan Health, Mt. Pleasant, MI, USA

Introduction

Cabozantinib is a recently approved chemotherapeutic drug which is increasingly used to treat renal cell carcinoma and several other cancers. It acts as a chemotherapeutic agent through inhibition of tyrosine kinases. One potential side effect is a condition called palmar-plantar erythrodysesthesia syndrome (PPES). While the phase III clinical trial for cabozantinib demonstrated PPES occurring in 42% of participants, 95% of these cases occurred between two and six weeks. The median onset was 3.4 weeks.¹ This case is highly unusual because the patient developed PPES after 29 weeks of treatment.

Case Report

Our patient presented with sudden onset of painful, erythematous lesions on his palms and soles. He woke up at night feeling like he had just walked on hot coals. The lesions impeded his activities of daily living significantly, and he was diagnosed with grade three PPES. His cabozantinib chemotherapy was promptly discontinued with subsequent resolution of symptoms.

In some cases, a dose reduction or temporary discontinuation of a drug may be the preferred choice, but in severe cases of PPES, permanent cessation may be necessary. This was the case with our patient. The likelihood of this being a drug reaction was assessed using two methods, the Naranjo algorithm² and the World Health Organization - Uppsala Monitoring Centre causality criteria³. Both indicated cabozantinib as the probable cause.

Discussion

This case describes a patient with a significantly delayed onset of PPES, which occurred seven months after initiation of cabozantinib therapy. The aberrant timeline of PPES in this particular patient poses an interesting question regarding the immunological differences that may underlie such a delayed presentation of this cutaneous response. It also serves as a reminder to healthcare providers that adverse drug reactions can occur at any time. This highlights the need for vigilance for drug reactions in patients on chemotherapy, even those that may be statistically unlikely.

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Immunological features of immune-related adverse events during anti-PD-1 immune checkpoint inhibition in relapsed/refractory AML

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Immune checkpoint inhibition (ICI) against PD-1/PD-L1 has shown remarkable efficacy in many solid tumors. However, the PD-1 checkpoint is critical for peripheral tolerance, and endocrine toxicities are common immune-related adverse events (irAEs) of PD-1/PD-L1 inhibitors.

We characterized immune features in relapsed/refractory acute myeloid leukemia (AML) patients who developed irAEs during treatment with pembrolizumab and decitabine (NCT02996474). Two of 10 patients developed hypothyroidism, a known irAE. A third developed central diabetes insipidus, thought possibly related to pembrolizumab. We performed TCRb sequencing (ImmunoSEQ, Adaptive Biotechnologies) on genomic DNA from longitudinal blood and bone marrow samples; through TCRb sequencing, we identified several expanded CD8+ T cell clonotypes whose expansion coincided with irAE onset in the 3 AML irAE patients. To further explore genetic and proteomic signatures of these expanded clones in a representative AML hypothyroidism patient, we performed 10x Genomics 5' single-cell RNA / VDJ sequencing (scRNAseq) and cell surface protein profiling with oligo-conjugated antibodies (Biolegend) on FACS-purified CD3+ T cells from mononuclear cells; ultimately, we profiled 8578 T cells with scRNAseq. All expanded TCRb clonotypes of interest were captured and paired TCRa chains identified. Most clonotypes of interest expressed high levels of cell surface PD-1, HLA-DR, and CD27, with no CCR7 and moderate CD45RO, indicating an activated effector memory phenotype. These clonotypes had high *PDCD1* and *CD27* transcripts as well and an expression profile suggestive of activation, proliferation, and degranulation.

Our data suggests that treatment with pembrolizumab and decitabine can induce changes in the T cell repertoire, and that irAEs may be associated with detectable changes in the frequencies of select T cell clonotypes. Specifically, in a representative patient, we identified several T cell clonotypes that may have contributed to pembrolizumab-induced hypothyroidism that may have been previously peripherally silenced and then stimulated with treatment with pembrolizumab. We believe irAEs offer a model system for discerning mechanisms of action of PD-1/PD-L1 inhibitors on T cells.

Progression of lung cancer in patients with co-morbid autoimmune disease

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Introduction: There is increasing interest in treatment of lung cancer in patients with autoimmune disease, both from a clinical and immunologic perspective. More specifically, understanding the effect of autoimmune disease on lung cancer may help guide the use of immune therapy in this group. We aimed to characterize cancer progression of patients with autoimmune disease compared to national controls within the NIH Surveillance, Epidemiology, and End Results (SEER) database to better understand the effects of autoimmune disease on cancer prognosis.

Methods: We performed a retrospective review under an IRB-approved protocol within a single institution (Northwestern University) between 2003-2019. EDW query identified patients with ICD codes for lung cancer and one of the following autoimmune conditions: rheumatoid arthritis (RA), systemic lupus erythematous (SLE), systemic sclerosis, myositis, Sjogren's syndrome, mixed connective tissue disease, interstitial lung disease (ILD), pulmonary fibrosis, and interstitial pneumonia with autoimmune features. All cases were manually reviewed for biopsy-confirmed lung cancer and autoimmune diagnosis confirmed by a rheumatologist or pulmonologist. Collected data included whether patients received standard of care cancer treatment, and progression/death. Stage at treatment was classified as localized disease, regional disease if nodal involvement and distant if evidence of metastasis. 5-year overall survival (OS) and progression-free survival (PFS) as well as median times stratified by disease location were estimated via the Kaplan-Meier method.

Results: We identified 176 patients with lung cancer and underlying autoimmune disease. Most common autoimmune diagnoses were RA (n=97), ILD (n=54), systemic sclerosis (n=43), myositis (n=22), and SLE (n=15). Lung cancers identified were adenocarcinoma (n=99, 46%), squamous cell carcinoma (n=29, 13%), small cell lung cancer (n=17, 9%), non-small cell lung cancer not otherwise specified (n=13, 6%), and large cell lung cancer (n=3, 1%). Of our cohort, 53 did not receive standard of care lung cancer treatment (30%) and of these, 27 did not receive it due to frailty/co-morbid disease. OS for localized disease at 5 years was 80.52% (CI 67.48%, 88.75%), compared to 59.5 % (59.0, 60.1) at 5 years within the SEER database. For regional disease, OS at 5 years was 39.86% (18.05%, 61.01%), compared to 30.2% (29.8, 30.6) within SEER. Finally, for distant disease OS was 10.20% (0.39%, 20.29%), compared to 5.2% (5.0-5.3) in the SEER database.

Conclusions: Overall, patients with autoimmune disease and lung cancer received standard of care treatment and had equal to improved PFS and OS when compared to national controls. These outcomes raise questions about a unique immune physiology leading to a possible protective role in cancer progression. Future multi-center, prospective trials are needed to further characterize disease progression and clinical implications of immune function on lung cancer treatment.

Bacteroides fragilis, a potential pathogen of breast cancer

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Background: Last decade established significant contributions of microbiome to organ specific cancers. A few recent studies suggested the existence of distinct breast microbiota and a shift in microbial community composition in diseased breast compared to normal breast. However, their functional impact and underlying mechanisms are unknown. Present study was designed to examine the contribution of pro-carcinogenic bacteria in breast cancer initiation, growth and progression.

Results: Utilizing extensive data mining and metagenomic analyses, we discovered presence of toxin producing *Bacteriodes fragilis* in malignant breast. *B. fragilis* is known for its potential to initiate and/or promote colon cancer. Its pathogenicity has been attributed to its unique toxin BFT. Mice infected with *B. fragilis* exhibited significant circulating BFT and distinct morphological alterations in mammary gland. While no changes were observed in cell growth and clonogenicity upon BFT treatment, significant increase in migration and invasion potential and decreased adhesion of MCF10A and MCF7 cells were observed. BFT-treated cells displayed acquisition of fibroblast-like appearance and increased formation of pseudopodia/microtentacles emanating from the cell membrane along with molecular markers of epithelial-to-mesenchymal transition. Decreased expression of epithelial marker, E-cadherin along with elevated levels of mesenchymal markers, N-cadherin and vimentin were observed. BFT also increased expression of EMT-related transcription factors, Snail, Slug and Twist. BFT-treated cells attained stem cell-like phenotype exhibiting an increased ability to form secondary and tertiary mammospheres and elevated expression of pluripotency-factors (Oct4, Nanog and Sox2). Mechanistic studies showed BFT induced expression and nuclear translocation of cleaved NOTCH1 and βcatenin resulting in activation of downstream targets. Inhibition of Notch1 and βcatenin using γ-secretase inhibitor and ICG001 successfully inhibited functional effects of BFT. Further, BFT-pretreated MCF7 cells exhibit increased tumor growth and form multifocal tumors in mice. MCF10A-KRas cells, pretreated with BFT, also showed increased tumor progression and multifocal tumors in mice. *In vivo* limiting dilution assay using breast tumors from BFT-pretreated MCF7 cells exhibited a striking increase in tumor-initiating cells. Follow-up analyses of these tumors demonstrated increased migratory, invasive, and mammospheres-forming behavior confirming that brief BFT exposure elicits long-term molecular changes.

Conclusion: Collectively, these findings present the first *in vitro* and *in vivo* evidence to show that *Bacteriodes fragilis* Toxin induces EMT, invasion/migration and stem cell-like phenotype and leads to concomitant activation of Notch and βcatenin axes.

YAP1 is a novel target to alleviate immune sensitivity in urothelial carcinoma of bladder

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Highly coordinated multifactorial intrinsic activity of immune system plays a critical role in the initiation and progression of almost all types of human malignancies. Conventional treatment with chemotherapeutic agents induces immunosuppression in the tumor tissue contributing tumor aggressiveness. Due to prolonged administration of chemotherapeutic drugs, immunosuppression is manifested by changing the infiltration of immune cells and their differentiation in the tumor microenvironment. Several reports have suggested that enrichment of myeloid-derived suppressor cells (MDSCs) in the tumor microenvironment is positively correlated with increasing stage of Urothelial Carcinoma of Bladder (UCB) and poor prognosis.

We recently reported that both the YAP1 and COX2/PGE2 signaling pathways accelerate urothelial Cancer stem cells (UCSCs) expansion via SOX2 in a mutually independent manner and the activation of these pathways hamper the efficacy of systemic chemotherapy. Here, we have found that expression of YAP1 may contribute to the immune suppressive cold environment in the UCB. Our data supports that *YAP1* expression may be directly associated with the infiltration and enrichment of the MDSCs in tumor microenvironment, spleen and blood of the tumor bearing animals. Furthermore, our in vitro and in vivo studies indicate that YAP1 regulates the activity of cytotoxic T cells and immune associated cytokines (TNF-α, IL-6, TGF-β) as well as chemokines (CXCL2, CXCL3, CXCL5). Inhibition of YAP1 results in increased cytotoxic efficiency of CD8+ T cells and improved immune sensitivity by the upregulation of PD-L1. TCGA database analysis of UCB revealed that YAP1 is one of the most enriched pathway in tumors with high level of MDSCs. Further studies are ongoing to understand YAP1 signaling in the UCB tumor microenvironment and to determine whether inhibition of YAP1 enhanced checkpoint inhibitors efficacy in UCB.

BaaS (Body as a System) digital model for Data-Driven Medicine

Shaheen N Shah, GenomicsCentral, India/ Qatar

Actionable patient data helps medicine to be (more) precise, more the data, the better the ML. Most current cancer models are biology- based like 3D tumor organoid models, which are quite effective in pre-metastatic stages. The unknowns (variables) of the human body system, particularly the haphazard cancer subsystem make the development of a “digital” human body system a far cry. Howeever, recent advances in whole body imaging (3D scans using vDISCO) in metastatic mice, and subsequently using Deep Learning (trained on images using CNN) to identify micrometastases (Erturk, Ali et al 2019), is a leap forward. The proposed human body system model – BaaS - is a continuous “learning” system with Human-in-the-Loop, improving with each actionable data iteration. This AI-based system, majorily based on UNets , at one point of time, would be able to predict the disease progression (from the learned previous related patient disease data), and in conjunction with existing enhanced algorithms, would be able to predicts the impact of drugs, both novel and others. To note, the BaaS needs to integrate with a larger Biological Big Data ecosystem, a connected Enterprise IT HIPPA-compliant ecosystem that collaborates between existing consortiums, biobanks and projects like the 100K Genome Project. Diversity in data is of paramount importance since the BaaS model would vary with the percentage variation seen in different population (the exact percentage calculations yet to be made). This would be an equivalent to the Human reference genome; however, being data-driven, updating the reference (as per updated inputs) catering to specific population in this digital human model would be easier, unlike the present GRCh38. Ultimately it’s a only a hybrid platform, having both biology and digital data components, contribute to attain comprehensive complete human cures; a digital human model like BaaS would mere be a stepping stone.

Use of SNK-01 (Autologous Non-Genetically Modified Natural Killer Cells with Increased Cytotoxicity) in Combination with Pembrolizumab in Solid Tumors to Improve Tumor Response and Decrease Checkpoint Inhibitor Related Toxicity.

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Background: Despite the increased promise of checkpoint inhibitors in the treatment of solid tumors, the overall response rate is no greater than 30% in PD-L1+ tumors with up to 30% moderate to severe side effects. Natural killer (NK) cells have recently been implicated in antitumor response to immune checkpoint inhibitors. SNK01 is a novel non-genetically modified autologous natural killer cell therapy with enhanced cytotoxicity which has been found to have tumoricidal effects against several solid tumor cell lines.

Methods: Patients with metastatic various solid tumors refractory to treatment (Non-Small Cell Lung, Bladder, Sarcoma, and Renal Cell) were treated with Pembrolizumab every three weeks and 5-6 weekly infusions of SNK01 at either 2 x 10^9 or 4 x 10^9 cells per infusion. Primary endpoint was safety and secondary endpoints are objective response rate (ORR) and quality of life (QoL).

Results: 9 patients have completed treatment. Median age is 69 (52-73). Six patients are PD-L1+ and three patients are negative for PD-L1 expression. Four patients have completed Pembrolizumab with 2 x 10 SNK01 and five patients have completed Pembrolizumab with 4 x 10 SNK01. Of patients receiving full combination therapy, there have been no adverse events or any reported toxicity while overall QoL has been improved. The overall response rate in the combination group is 77% using iRECIST (4/9 cPR, 3/9 PR).

Conclusions: These preliminary results demonstrate that combination therapy with Pembrolizumab and SNK01 is very safe and even appears to significantly reduce checkpoint associated toxicity while increasing overall tumor response compared to previously reported Pembrolizumab monotherapy alone results in patients with advanced solid tumors. We plan to investigate this further with a much umbrella larger study.

Characterizing CEBPD and its target genes expression In Inflammatory breast cancer.

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Inflammatory breast cancer (IBC) is a rare type of breast cancer accounting for 2-4% of all breast cancer patients, but accounts for 7-10% of breast cancer related mortality. IBC is characterized by extensive skin invasion and the formation of tumor cell emboli within the breast and dermal lymphatic system. Characteristics of emboli include cell to cell adhesions mediated by E-cadherin (CDH1). Studies from our laboratory suggest that CEBPD is expressed in IBC patient emboli and promotes emboli formation in vitro. Mechanistically we found that CEBPD promotes cell-cell adhesion within emboli at least in part by supporting the expression of E-cadherin adhesion complex proteins. To investigate novel genes and pathways that are regulated by CEBPD in support of emboli formation, we have conducted an mRNA-Seq analysis in SUM149 emboli ± C/EBPδ depletion (two independent siRNAs). The top significantly altered pathways identified by Ingenuity Pathway Analysis were "cholesterol biosynthesis" and "neutrophil degranulation". The data predict that C/EBPδ supports the expression of four enzymes, including DHCR7, in the cholesterol biosynthesis pathway, and 53 genes that mostly represent proteins that are secreted or involved in protein/vesicle trafficking. CD14 is another gene, which encodes for a surface antigen expressed on monocytes and macrophage that interacts with proteins to mediate an innate immune response. Together these data suggest that emboli may be secreting significant amounts of immune-modulators. We are now validating the expression of select number of genes by qPCR and Western blotting and are designing experiments to address the functional relevance of the pathways for IBC emboli biology. Understanding the molecular mechanisms of emboli formation may provide valuable insights into the uniquely aggressive nature of IBC.

Disclosure of Financial Relationships

In compliance with the standards set by the Accreditation Council for Continuing Medical Education (ACCME), it is the policy of the American Association for Cancer Research (AACR) that the information presented at CME activities will be unbiased and based on scientific evidence. To help participants make judgments about the presence of bias, the AACR has provided information that planning committee members, speakers, and abstract presenters have disclosed about financial relationships they have with commercial entities that produce or market products or services related to the content of this CME activity.

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Statement of Educational Need, Target Audience, and Learning Objectives

The incredible clinical success of immunotherapies, particularly immune checkpoint inhibitors, has resulted in widespread use across many cancers and exploration of use in autoimmune and rheumatic diseases. As utilization has increased, so too have observations and reports of toxicities, sometimes

severe, in nearly every organ system. These immune-related adverse events (irAEs) manifest differently depending on the pathway targeted by the therapy (i.e., CTLA-4 or PD-1/PD-L1), and the emerging use of combination therapies has only increased the frequency of events.

In order to better understand, predict, and treat immunotoxicities in cancer patients, clinicians need to first understand the mechanisms underlying irAEs. Recognizing the similarities to and associations with autoimmune diseases—which share many biologic underpinnings with irAEs—will also be beneficial, as will increased awareness of how irAEs present across multiple organ systems.

The NIH-AACR Cancer, Autoimmunity, and Immunology Conference will bring together world-renowned oncologists, immunologists, rheumatologists, and basic researchers to address these gaps. Attendees will hear about cutting-edge research on the role of the microbiome in determining response to immunotherapies, biomarkers for predicting irAEs, and irAEs resulting from combination therapies. They will learn how nontraditional nonclinical models are being used to interrogate response to treatment and the mechanistic bases for irAEs. There will be sessions dedicated to rheumatic toxicities and to multidisciplinary treatment models. Important considerations, such as biomarker validation and differentiation of adverse events from checkpoint inhibitors and traditional therapies when used in combination, will be discussed.

After participating in this CME activity, physicians should be able to:

1. Articulate influences and effects of the gut microbiome on patients' response to immunotherapy.
2. Integrate multidisciplinary treatment strategies into patient care.
3. Identify multiple biomarkers for predicting development of irAEs.
4. Extrapolate the relevance of research and clinical findings on irAEs to the study and treatment of rheumatic and autoimmune diseases, and vice versa.
5. Explain how more relevant nonclinical models are being developed and used to investigate mechanisms underlying irAEs following immunotherapy.

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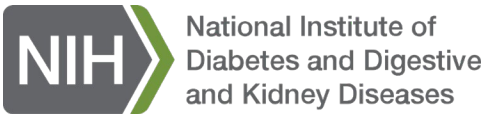

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