With the approval of drugs like Nivolumab and Pembrolizumab patients are already feeling the impact of cancer immunotherapy. Still, with each step forward researchers are becoming increasingly aware of the complexity and unique challenges that come with each individual’s disease. Given that not all patients respond to existing treatments, there is an enormous need to start looking at the next generation of immunotherapy solutions. At Cambridge Healthtech Institute's Inaugural ImPACT: Immunotherapy Progress and Clinical Treatments, being held December 5-7, 2017 in San Diego, four cutting-edge conferences will showcase what’s coming next in immunotherapy.

PRE-PER CONFERENCE SHORT COURSES*

**Monday, December 4**

**Morning | 9:30 am - 12:30 pm**

**SC1: Omic Technology for Cancer Immuno-Oncology**
Instructors: Somdutta Saha, Ph.D., Post-Doctoral Fellow, Computational Biology, Microbiome, GSK
Lauren Ritterhouse, M.D., PH.D., Assistant Professor of Pathology, Genomic and Molecular Pathology Division The University of Chicago Medicine & Biological Sciences

This short course will be an introduction to cover strategies for integrating genomic, proteomic, metabolomic data and more for drug discovery and target validation for cancer immunotherapy. It will introduce current technologies and their limitations.
- Validating novel drug targets or pathways that emerge from human genetics
- Visualization for big data for proteomics
- Targeting the Microbiome in I/O

**Afternoon | 2:00 - 5:00 pm**

**SC2: Applications of a Quantitative Imaging Tool Box in Evaluating a CAR Immune Synapse and Contributing to Rational CAR Design**
Instructor: Malini Mukherjee, Instructor, Center for Human Immunobiology Cell & Gene Therapy, Baylor College of Medicine

There are many tools that can be utilized to quantitatively measure cell killing and this workshop will outline the following:
- What do we know about the CAR immune synapse?
- What are the tool box components and how do they evaluate a CAR cytotoxic function above and beyond traditional cytotoxicity assays?
- Examples of toolbox based mechanistic understanding of CARs
- Future applications of toolbox in the rational design of CARs

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**2016 IMMUNO-ONCOLOGY SUMMIT (BOSTON) DEMOGRAPHICS**

- **Location**
  - 77% United States
  - 15% Europe
  - 6% Asia
  - 2% Rest of World

- **US Breakdown**
  - 58% East Coast
  - 32% West Coast
  - 10% Midwest

- **Company Type**
  - 74% Biotech & Pharma
  - 10% Academic/Government
  - 10% Healthcare
  - 3% Financial
  - 3% Other
Cancer immunotherapies are an exciting treatment option, harnessing the body’s immune system to target cancer cells. However, not all patients respond to these treatments. There are myriad reasons for this, but it is becoming more apparent that the microbiome plays a bigger role than previously thought. At Cambridge Healthtech Institute’s Inaugural Microbiome in Cancer Immunotherapy conference, leading researchers from microbiology and immunology will come together to address the impact the microbiome can have on this emerging area of therapy. Multiple strategies will be addressed, including more traditional approaches, such as transplanting the gut microbiome to boost immunotherapy response, as well as newer strategies, such as supplementing the microbiome to increase response. Overall, this event will provide an in-depth look at an emerging, yet critical, area of study to continue moving immunotherapies to the clinic.

9:05 MycoBiome (Fungal Microbiome) in Cancer Immunotherapy
Pranab Mukherjee, MSc, Dr., Associate Professor, Dermatology, Case Western Reserve University
Fungi are integral components of the human microbiome, however this fungal microbiome (“MycoBiome”) has attracted far less attention than the bacterial microbiome. Recent studies have demonstrated that fungi induce specific interactions with bacteria and the host, thus affecting health and disease. Our group has conducted studies showing that fungal mycoBiome plays a critical role in skin diseases like atopic dermatitis and psoriasis, as well as in the setting of inflammatory bowel disease and HIV infection.

9:35 The Skin MicroBiome and its Role In Cutaneous Squamous Cell Carcinoma Progression
Anita Y Voigt, Ph.D., Post-Doctoral Researcher, The Jackson Laboratory for Genomic Medicine
The skin microBiome plays a critical role in homeostasis of the skin and the modulation of the immune system. Changes in the microBiome can play a role in skin disorders. We are investigating the connection with skin cancer development and progression in humans and mice and the beneficial or detrimental effects of certain microbes on the tumor development. Furthermore, we explore the diagnostic potential of the microBiome for skin cancer.

10:05 Coffee Break in the Exhibit Hall with Poster Viewing

UNDERSTANDING THE MICROBIOME IN IMMUNOTHERAPY

10:50 Targets and Pitfalls of the Microbiome during Immunotherapy
Julia Drewes, Ph.D., Post-Doctoral Fellow, Oncology, Johns Hopkins School of Medicine, Bloomberg Kimmel Institute for Immunotherapy
We now understand that the microBiome may be involved in all aspects of colorectal cancer, from protection and prevention, to initiation and progression, and more recently to the response to chemotherapy and immunotherapy. Drawing on studies in both patients and mice, this presentation will discuss recent advances in identifying potential microbial targets and potential pitfalls during immunotherapy.

11:20 Pharmacological Targeting of Gut Microbiota to Improve Anti-Cancer Drug Efficacy
Aadra Bhatt, Ph.D., Post-Doctoral Fellow, Chemistry, University of North Carolina at Chapel Hill
Irinotecan is an anti-cancer drug that causes gastrointestinal (GI) side effects in 88% of patients. Detoxified irinotecan metabolites are reactivated within the intestinal lumen by microbial β-glucuronidase (GUS) enzymes, resulting in epithelial cell death and acute diarrhea. Our pre-clinical studies using potent, selective and non-lethal GUS inhibitors reveal diminished GI side effects when administered in conjunction with compounds whose metabolites are reactivated by microbiota.

11:50 Late Breaking Presentation

12:20 pm Sponsored Presentation (Opportunity Available)
12:35 Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

1:05 Session Break
USING THE MICROBIOME TO PREDICT RESPONSE

2:05 Chairperson’s Opening Remarks
Wei Zhou, Ph.D., Post-Doctoral Research Associate, The Jackson Laboratory for Genomic Medicine

2:10 High Diversity and Differential Composition of the Gut Microbiome Are Linked to Slower Cancer Progression on Immune Checkpoint Blockade
Vancheswaran Gopalakrishnan, Ph.D., Post-Doctoral Fellow, Surgical Oncology, University of Texas MD Anderson Cancer Center
Recent evidence in murine models suggests that modulation of the gut microbiome may enhance responses to immune checkpoint blockade. We collected oral and gut microbiome samples from melanoma patients initiating treatment with PD-1 blockade (n=112). Responders had a significantly higher alpha diversity (p<0.05), and enrichment of the Ruminococcaceae family compared to non-responders, who had a significant enrichment of Bacteroidales. Immune profiling demonstrated a positive correlation between CD8 density and abundance of bacteria enriched in R.

2:40 Models of Microbial Adjuvants Biomarkers of Cancer Immunotherapy
Wei Zhou, Ph.D., Post-Doctoral Research Associate, The Jackson Laboratory for Genomic Medicine
Cancer immunotherapies harness the power and specificity of the immune system to attack tumors while sparing normal tissue. However, tumor responses to immunotherapy have been highly variable. Host genetics together with the mutational landscape of the tumor must account for some of this variability, but additional systemic factors are likely to further shape immunotherapeutic efficacy. A nascent body of evidence points to the host microbiome, via immune system interactions, as a modulator of treatment responses. Understanding and manipulating these interactions to improve treatment efficacy could transform outcomes for cancer patients. Thus, great potential lies in systematically identifying and validating these microbial factors, as they can be administered as a dietary probiotic during immunotherapy.

3:10 Investigating the Stool Bacteriome and Response to Immunotherapies in Metastatic Renal Cell Carcinoma (mRCC)
Manuel Maia, M.D., Fellow, Medical Oncology, City of Hope
Nivolumab has been approved in the 2nd-line for mRCC based on improvement in overall survival. However, no validated biomarkers exist to predict its activity at this point. Based on preclinical studies showing immunomodulatory effects of the gut microbiome in cancer by both inducing and augmenting the activity of immunotherapies, we are currently studying if any specific stool microbiome composition is predictive of clinical (or lack of) benefit in mRCC patients being treated with nivolumab.

3:40 Refreshment Break in the Exhibit Hall with Poster Viewing

4:15 Problem Solving Roundtable Discussions

5:15 Welcome Reception in the Exhibit Hall with Poster Viewing

WEDNESDAY, DECEMBER 6

8:00 am Morning Coffee

MICROBIOME THERAPEUTICS IN IO

8:40 Chairperson’s Opening Remarks
Shrish Budree, M.D., Senior Clinical Research Fellow, Clinical Research, Openbiome

8:45 Translational Aspects of Microbial Therapeutics in Immune-Oncology: Current Practices to Future Therapies
Shrish Budree, M.D., Senior Clinical Research Fellow, Clinical Research, Openbiome
Recent studies in animal models have demonstrated that restoring a healthy intestinal microbiome enhances T-cell infiltration into the tumor microenvironment and augments tumor regression. Mice with a dysbiotic microbial community exhibit a poorer response to checkpoint inhibitors in comparison to their genetically identical counterparts with a healthy microbiome. Co-housing these mice, which is effectively analogous to performing a fecal microbial transplant (FMT), ameliorated this difference in response and enhanced the anti-tumor response in the previously dysbiotic mice. These seminal studies have laid the ground work for future human FMT trials.

9:15 Microbiome Derived Immunotherapies in Cancer
Lorenzo Tibaldi, Ph.D., Project Leader, Drug Discovery, Enterome Bioscience
Based on its metagenomics platforms, Enterome discovers microbiome-derived molecules acting as specific and unspecific activator of adaptive immune response against tumors. Several candidates are in preclinical development for the treatment of various types of cancer such as glioblastoma, colon, pancreatic, lung and breast.

10:15 Coffee Break in the Exhibit Hall with Poster Viewing
FUTURE DIRECTIONS

10:45 Cancer Immunotherapy and the Gut Microbiome: A Biomarker or a Probiotic?
Sandip Patel, M.D., Assistant Professor, Cancer Immunotherapy Program, Experimental Therapeutics, Thoracic Oncology; Assistant Director, Clinical Trials Office, Medicine/Hematology & Oncology, University of California, San Diego Moores Cancer Center

A review of the state of microbiome science and cancer immunotherapy, with a focus on published data correlating gut microbiome to response to immune checkpoint blockade. Novel methods of microbiome assessment for discovery as well as host-immune interactions to develop microbiome signatures to correlate with immunotherapeutic response and toxicity. Overview of novel immunotherapy biomarkers and immunotherapeutic targets, and potential future directions in microbiome science as it pertains to novel cancer immunotherapeutics.

11:15 CLOSING PANEL DISCUSSION: Future Directions in Microbiome Research
Moderator: Arpita Maiti, PhD, Senior Director, External Science & Innovation, Inflammation & Immunology and Microbiome, Pfizer Inc.
- Microbiome as a biomarker for cancer
- Microbiome as a predictor of treatment response
- Beyond oncology, additional roles of the microbiome
- Commercialization of microbiome therapies
Panelists: Pranab Mukherjee, MSc, Ph.D., Associate Professor, Dermatology, Case Western Reserve University
Manuel Maia, M.D., Fellow, Medical Oncology, City of Hope

12:15 pm Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

12:45 Dessert Break in the Exhibit Hall with Poster Viewing

1:15 PLENARY KEYNOTE SESSION
See page 2 for more information

2:50 Close of The Microbiome in Cancer Immunotherapy
While a large portion of cancer immunotherapies focus on targeting T cells, there has been a surge of interest in harnessing the relatively underexplored innate immune system for therapeutic intervention, with particular focus on natural killer (NK) cells, macrophages and dendritic cells. A growing number of studies into pathways elucidating innate cell biology, and the development of therapeutic agents to activate or suppress cell function, have set the stage for a new generation of cancer immunotherapies. Cambridge Healthtech Institute’s Inaugural Targeting Innate Immune Cells conference will convene immunology researchers, cancer immunotherapy developers, and technology providers to discuss current challenges and opportunities, from discovery immuno-oncology to clinical studies, share latest technologies and development approaches, as well as to provide updates on preclinical, clinical, and combination studies.

**RECOMMENDED PRE-CONFERENCE SHORT COURSES**

SC1: Omic Technology for Cancer Immuno-Oncology
SC2: Applications of a Quantitative Imaging Tool Box in Evaluating a CAR Immune Synapse and Contributing to Rational CAR Design

*Separate registration required, please see page 2 for details

## TUESDAY, DECEMBER 5

### ADVANCES IN NK CELL-BASED THERAPIES

#### 8:30 Chairperson's Opening Remarks
Hans Klingemann, M.D., Ph.D., Vice President, Research & Development, NantKwest, Inc.

#### 8:35 Update: anNK and haNK for Cancer Treatment
Hans Klingemann, M.D., Ph.D., Vice President, Research & Development, NantKwest, Inc.

I will provide an update on clinical trial activities with anNK haNK cells expressing the high affinity Fc-Receptor for combination therapy with mAbs taNK cells engineered to express CARs for neo-epitopes. I will also discuss augmenting NK activity with IL-15 super-agonist Altor 803, as well as optimizing NK target activity through CRISPR-based gene manipulation.

#### 9:05 hnCD16-NK Cells: Cornerstone Approach for Off-the-Shelf Cancer Immunotherapy
Bahram (Bob) Valamehr, Ph.D., MBA, Vice President, Cancer Immunotherapy, Fate Therapeutics, Inc.

Through targeted transgene integration, we produced a clonal pluriptotent cell master cell line to continuously produce NK cells engineered to uniformly express a novel high affinity, non-cleavable version of CD16 Fc receptor (hnCD16-NK). Preclinical data highlight the therapeutic value of hnCD16-NK cells as an ideal ADCC-mediated “off-the-shelf” NK cell-based immunotherapeutic product with augmented persistence, anti-tumor capacity, manufacturing reliability and preclinical efficacy.

#### 9:35 Immune Responses in the Cancer Patients Who Receive the Random Donor-Derived Expanded NK Cell
Sungwoo Cho, Ph.D., CSO, Green Cross LabCell

Ex vivo-expanded and highly activated NK cells from random unrelated healthy donors were injected into patients with malignant lymphoma or advanced recurrent solid tumors with or without lymphodepletion. Different from CAR-T treatment, there is no SAE and cytokine storm in multiple high dose injection. NK cell treatment shows different from T cell therapy in GVHD/GvT aspect. NK cell persistency and efficacy can control by pre-treatment regimen, and the rejection and antibody induction from recipients can also be controlled.

#### 10:50 Coffee Break in the Exhibit Hall with Poster Viewing

#### 10:50 Autologous ex vivo Understanding of NK Cell Effector Functions: A Single-Cell Lab-on-a-Chip Perspective
Tania Konry, Ph.D., Assistant Professor, Department of Pharmaceutical Sciences, Northeastern University

Natural Killer (NK) cells are an essential component of innate immunity that actively inhibit tumor development. Here we present a novel single-cell method of analyzing the mechanisms underlying the cellular interactions of NK cells with multiple myeloma cells. The integrated droplet microfluidics device developed by our group permits compartmentalization of cell pairs and secreted products within sub-nanoliter volumes and thereby controls cell-to-cell communication by limiting it to interactions between the co-encapsulated cells. It allows monitoring of both contact-dependent (immune synapse formation, delivery of lytic hits) and contact-independent cellular interactions (release of cytokines, chemokines) simultaneously. This dynamic single-cell experimental model is expected to provide preclinical information particularly relevant to the scenario of NK cell-cancer cell interactions.

### KEYNOTE PRESENTATION: Engineering Human Pluripotent Stem Cells to Produce NK Cells with Improved Targeted Anti-Cancer Activity

#### 11:20 Dan Kaufman, M.D., Ph.D., Professor, Director of Cell Therapy Program, University of California, San Diego

NK cells can be routinely produced from human pluripotent stem cells – both human embryonic stem cells (hESCs) and induced pluripotent stem cells (iPSCs). hESC/iPSC-derived NK cells have phenotype and function similar to peripheral blood NK cells and can be expanded into clinical-stage doses. hESC/iPSC-derived NK cells serve as a platform to test novel NK cell-specific CARs with improved anti-tumor activity.

#### 12:20 pm Luncheon Presentation (Opportunity Available)

#### 12:35 Lunch on Your Own

#### 1:05 Session Break

### AT THE INTERFACE OF INNATE AND ADAPTIVE IMMUNITY

#### 2:05 Chairperson’s Opening Remarks
Holger Lode, Ph.D., Professor and Chair of Pediatrics, Pediatric Hematology and Oncology, University Medicine Greifswald

#### 2:10 Role & Exploitation of Invariant NKT Cells in Anti-Tumor Immune Responses
Mark Exley, Ph.D., Vice President, Agenus

We functionally defined two distinct human CD1d-reactive ‘NKT’ populations, invariant and ‘non-invariant’, from blood and tissues. NKT cells produce high levels of various cytokines/chemokines and potent CD1d-
specific cytotoxicity. NKT have physiological roles in anti-tumor and anti-viral responses. Reversible defects of NKT from cancer and other patients have led to promising translational observations. Our anti-NKT mAb is in clinical trials ex vivo, has been humanized and used in vivo, and is widely used in research. NKT can positively or negatively regulate anti-tumor immunity via NK and dendritic cells (DC). In mice, we found that interactions between NKT and CD1d+ DC augment Th1-type anti-viral and anti-tumor immunity – promising for therapy directly and with DC-based and other vaccines. NKT from tumor-bearing mice had reversible defects, similar to those we first identified in cancer patients. In humans, NKT cells appear to contribute to protective responses against cancers and viruses, and cancer patient survival is associated with Th1-biased NKT. We describe our INKT clinical trial in advanced melanoma. Further INKT augmentation is in progress.

2:55 Innate Immunotherapy of Cancer and a Crossroad to Checkpoint Blockade
Holger Lode, Ph.D., Professor and Chair of Pediatrics, Pediatric Hematology and Oncology, University Medicine Greifswald

We demonstrate by genotype and functional parameters that the mechanism of action is induction of antigen specific Ab-dependent cellular cytotoxicity (ADCC) in treated patients. Importantly, we describe for the first time during receptor drug combination levels upregulates the inhibitory checkpoint PD-1/PD-L1 on tumor and effector cells. Combination of dinutuximab beta Apeiron with PD-1/PD-L1 blockade (nivolumab) results in synergistic treatment effects in vitro and in vivo.

3:40 Refreshment Break in the Exhibit Hall with Poster Viewing
4:15 Problem Solving Roundtable Discussions
5:15 Welcome Reception in the Exhibit Hall with Poster Viewing

WEDNESDAY, DECEMBER 6

8:00 am Morning Coffee

TARGETING MYELOID CELLS IN THE TUMOR MICROENVIRONMENT

8:40 Chairperson’s Opening Remarks
Jeremy R. Graff, Ph.D., CSO and Senior Vice President, Research, Biothera Pharmaceuticals, Inc.

8:45 Imprime PGG - A Yeast-Derived Pathogen-Associated Molecular Pattern (PAMP) Triggers the Anti-Cancer Immunity Cycle to Potentiate the Efficacy of Immune Checkpoint Inhibitors
Jeremy R. Graff, Ph.D., CSO and Senior Vice President, Research, Biothera Pharmaceuticals, Inc.

Imprime has been safely administered to >400 human subjects. Imprime triggers a cascade of immune activating events that re-polarize the immunosuppressive tumor microenvironment and elicit maturation of antigen presenting cells. Unlike other PAMPs (TLR and STING agonists), Imprime is administered systemically. In preclinical tumor models, Imprime robustly enhances the anti-tumor efficacy of CPIs. Accordingly, Imprime is now being explored in multiple Phase II clinical trials in combination with pembrolizumab.

9:15 Potent Anti-Tumor Immunity Is Induced by STING Activation in the Tumor Microenvironment Using a Synthetic Human STING-Activating Cyclic Dinucleotide
Kelsey Gauthier, Ph.D., Scientist, Aduro BioTech

I will describe how a novel synthetic CDN derivative (ADU-S100) that has improved STING-activating and anti-tumor properties as compared to naturally derived CDNs was developed for clinical translation. I will show that activation of STING through IT administration of ADU-S100 results in effective anti-tumor efficacy and survival in several mouse syngeneic tumor models. I will discuss some of the mechanisms by which ADU-S100 induces tumor regression and plans for a Phase I clinical study with ADU-S100 to evaluate the safety and tolerability and possible anti-tumor effects in subjects with cutaneously accessible malignancies.

9:45 Targeting Metabolic Vulnerabilities of MDSCs to Enhance the Anti-Tumor Activity of PD-1 Blockade
Bin Zheng, Ph.D., Assistant Professor, Dermatology, Harvard Medical School, Massachusetts General Hospital

Our findings demonstrate a selective, inhibitory effect of phenformin, a mitochondrial complex 1 inhibitor, on G-MDSCs-driven immune suppression and support that phenformin improves the anti-tumor activity of PD-1 blockade immunotherapy in melanoma.

10:15 Coffee Break in the Exhibit Hall with Poster Viewing

DENDRITIC CELL-BASED IMMUNOTHERAPIES

10:45 Allogeneic DC-Based Immunotherapies
Alex Karlsson-Parra, M.D., Ph.D., CSO, Immunicum

Immunicum’s lead development candidate INTUVAX® uses dendritic cells harvested from healthy human donors that are specifically activated to produce significant amounts of vigorous immune stimulatory factors. By administration through intratumoral injection, these cells induce a local inflammatory reaction, leading to a local destruction of tumor cells and recruitment of the patient’s own dendritic cells into the tumor environment.

11:30 Development of Pluripotent Stem Cell-Based Therapies for Neurologic and Oncologic Disorders
Jane Lebkowski, Ph.D., President, R&D and CSO, Asterias

Our group has established protocols to produce oligodendrocyte progenitors that upon transplantation into animals with spinal cord injuries can remyelinate denuded axons, induce axonal sprouting, and improve locomotor activity. Extensive preclinical studies have been completed to examine the activity, biodistribution, dosing, delivery, and potential toxicity and tumorigenicity of the oligodendrocyte progenitors. In collaboration with Cancer Research UK, Asterias is preparing for a clinical trial using these hESC derived dendritic cells as a cancer immunotherapy in non-small cell lung carcinoma in the neoadjuvant setting.

12:15 pm A Novel Phenotypic Approach for Predicting Tumor Response
Mark Paris, Ph.D., Associate Director, Translational Applications, Mitra Biotech

12:45 Dessert Break in the Exhibit Hall with Poster Viewing

1:15 PLENARY KEYNOTE SESSION
See page 2 for more information

2:50 Close of Targeting Innate Immune Cells
Increasing the number of patients that respond successfully to cancer immunotherapies is the next big step in the fight against cancer. Recent studies have shown that the more tumor-specific mutations, or neoantigens, the cancer cells have, the greater the chance that the tumor will not be tolerated by the immune system. With increasing access to next generation sequencing (NGS) technologies, cancer researchers are scouring the tumor genome, including the mutanome, to find new therapies. Cambridge Healthtech’s Inaugural Neoantigen-Based Personalized Immunotherapies is proud to discuss the cutting-edge research that combines cancer, immunology and NGS to design the next generation of personalized cancer immunotherapies.

**RECOMMENDED PRE-CONFERENCE SHORT COURSES***

SC1: Omic Technology for Cancer Immuno-Oncology
SC2: Applications of a Quantitative Imaging Tool Box in Evaluating a CAR Immune Synapse and Contributing to Rational CAR Design

*Separate registration required, please see page 2 for details*

**WEDNESDAY, DECEMBER 6**

12:00 pm Conference Registration
12:15 Luncheon Presentation *(Sponsorship Opportunity Available) or Enjoy Lunch on Your Own
12:45 Dessert Break in the Exhibit Hall with Poster Viewing

1:15 PLENARY KEYNOTE SESSION
See page 2 for more information

2:50 Refreshment Break in the Exhibit Hall with Poster Viewing

**IDENTIFYING IMMUNOGENIC NEOANTIGENS – BIOINFORMATIC APPROACHES**

3:30 Chairperson’s Opening Remarks
Pamela Carroll, Ph.D., Senior Vice President, Immuno-oncology, Genocea Biosciences

3:35 KEYNOTE PRESENTATION: Neo-Antigens in Cancer Immunotherapy: Where Are We and Where Are We Going?
Laszlo Radvanyi, Ph.D., Senior Vice President, Senior Scientific Advisor, Immunology, Immuno-Oncology, EMD Serono

This talk will present the history and status of the emerging field of neo-antigen (mutanome) targeting in cancer immunotherapy. Current approaches used to identify cancer neo-antigen epitopes along with examples of how neo-antigens are being targeted in cancer immunotherapy clinical trials will be presented. How the mutanome is being used as a biomarker in immunotherapy will also be described. Finally, some of the current obstacles being faced in the field will be discussed along with a summary of the strategic position and future impact of neo-antigen targeting in the overall cancer immunotherapy landscape.

4:05 How to Find a Neoantigen in silico: Insights from the Tumor Epitope Selection Alliance
Danny Wells, Ph.D., Scientist, Informatics, Parker Institute for Cancer Immunotherapy

It is now accepted the mutation-derived neoantigens can elicit an anti-tumor immune response and may potentially drive a substantial part of it. Identifying neoantigens accurately from the exome sequence of a tumor could have immense therapeutic benefit but remains a steep challenge. Here I will discuss our efforts at the Parker Institute to understand i) what makes a neoantigen immunogenic and ii) what algorithmic approaches are best at identifying immunogenic neoantigens. In particular, I will describe new results from our consortium effort in this area, the Tumor Epitope Selection Alliance (TESLA).

4:35 Immunogenic Determinants of Tumor Neoantigens
Suchit Jhunjhunwala, Ph.D., Scientist, Bioinformatics & Computational Biology, Genentech

Neoantigens can drive anti-cancer immunity. This has generated high interest in using neoantigens for personalized cancer vaccination. Computational predictions can prioritize neoantigens that may be presented by MHC molecules. However, false positives remain, and understanding properties of immunogenic neoantigens may help further enrich for them. We vaccinated naive mice with mutated long peptides to identify immunogenic neoantigens, and investigated their properties that may help further prioritize immunogenic neoantigens.

5:05 Close of Day

**THURSDAY, DECEMBER 7**

8:00 am Breakfast Breakout Roundtable Discussions

**WORKING WITH MHC CLASS 1**

8:55 Chairperson’s Opening Remarks
Matthew M. Gubin, Ph.D., Instructor, Schreiber Lab, Pathology and Immunology, Washington University School of Medicine

9:00 Technologies for Personalized T Cell Receptor Engineered Cancer Immunotherapies
James R. Heath, Professor of Physics, Chemistry, California Institute of Technology

We are particularly concerned with Class I MHC (mutated) neoantigen-CD8+ T cell recognition. In principle, neoantigens that draw T cells into a tumor can comprise personalized vaccines, and the T cell receptors (TCRs) that recognize those neoantigens can be engineered as personalized cellular therapies. I will discuss our approach, called nanoparticle-barcode nucleic acid cell sorting (NP-barcoded NACS), designed for enumerating neoantigen-specific T cell populations from non-expanded tumor infiltrates or peripheral blood, and for pairing those neoantigen-specific CD8+ T cell populations with the cognate TCRα/β gene, using single cell sequencing methods.

9:30 Immunotherapeutic Responses to Cancer Neoantigens
Matthew M. Gubin, Ph.D., Instructor, Schreiber Lab, Pathology and Immunology, Washington University School of Medicine

Recognition of tumor-specific mutant neoantigens can drive the anti-tumor effects of immunotherapy. We previously developed a method to reliably predict MHC class I cancer neoantigens. This has allowed us
to delineate mechanisms of effective checkpoint blockade therapy and develop personalized immunotherapies targeting neoantigens. Preclinical models of which are now being tested in patients. The goal of our work is to better understand anti-tumor T cell responses and to develop safer, more specific and more effective immunotherapy as well as improved patient immunomonitoring.

10:00 An Integrated Machine-Learning Approach to Improve the Prediction of Clinically Relevant Neoantigens
Trevor Clancy, Ph.D., CSO, OncoImmunity
Current neoantigen discovery algorithms may not be optimal to predict presentation to the cell surface. Here, we outline a high-performing machine learning approach, trained on mass-spectrometry data, that predicts naturally processed and presented antigens. The predictor is integrated with several immune parameters, such as HLA binding, in a deep learning layer to predict bone fide neoantigens. We illustrate its application to significantly improve the identification of neoantigen targets for personalized cancer immunotherapy.

10:30 Networking Coffee Break

IDENTIFYING IMMUNOGENIC NEOANTIGENS - CONT

10:55 Identifying Immunogenic Neoantigens: Turning Tumor Mutations into Personalized Cancer Therapies
Karin Joos, Ph.D., CSO, Gritstone Oncology
DNA damage may cause mutations in tumors that can generate new antigens, known as tumor-specific neo-antigens (TSNAs), which were identified to be T-cell targets in clinical responders on immune checkpoint therapy. To increase responder frequency in clinic, Gritstone Oncology is applying a proprietary model that accurately identifies TSNAs and seeks to deliver them in the context of potent viral vector based vaccine platforms which have shown to induce hi-titer, polyfunctional and durable CD4+ and CD8+ T-cell responses in humans. The personalized vaccine is delivered in combination with immune checkpoint blockade, to keep TSNAs-induced T-cells active in the immunosuppressive tumor microenvironment.

11:25 Comprehensive Discovery of Tumor Antigens for Better Personalized Vaccines
Pamela Carroll, Ph.D., Senior Vice President, Immuno-oncology, Genocea Biosciences
By screening T cells in the natural context of patient disease with antigens presented by autologous dendritic cells, ATLAS detects bona fide antigens. ATLAS-discovered antigens have limited overlap with those identified by in silico methods and are classified as stimulatory or inhibitory modulators of T cell activity. ATLAS powered personalized neoantigen vaccines are planned to start in 2018.

11:55 Letting Biology Drive Neoantigen Discovery
Aaron M. Miller, M.D., Ph.D., Assistant Clinical Professor of Medicine, UC San Diego Health, Moores Cancer Center
Through a collaborative effort between UCSD and LJI we have developed a set of novel bioinformatic and cellular tools which allows for the functional validation of NeoAg recognized by both CD4+ and CD8+ T cells at a higher rate than previously reported. We have also applied a novel cellular reprogramming technology which allows for the routine generation of patient-specific xenograft cell lines that preserve expression of identified neoantigens and are recognized by a patient’s autologous T cells in vitro and in vivo as tumors growing in immunodeficient NSG mice. This has allowed effective identification and targeting NeoAg in solid tumors with low to moderate mutational burden through precision immunotherapy.

12:25 Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

12:55 Session Break

CLINICAL APPLICATIONS - ANTIBODIES AND CANCER VACCINES

1:55 Chairperson’s Opening Remarks
Philip M. Arlen, M.D., President & CEO, Precision Biologics, Inc.

2:00 The Discovery and Development of Novel Monoclonal Antibody, NEO-201 Targeting a Novel Neoantigen
Philip M. Arlen, M.D., President & CEO, Precision Biologics, Inc.
Immunogenic neoantigens were derived from a membrane preparation of pooled allogeneic colorectal cancer from patients undergoing surgery. Membrane fractions were isolated and tested for immunogenicity and utilized in a clinical trial in patients with chemotherapy refractory metastatic colorectal cancer. A positive correlation was observed in patients who were able to mount and sustain IgG responses to vaccine. Antibodies were screened using this vaccine and tested for sensitivity, specificity, and anti-tumor function. A novel monoclonal antibody, NEO-201, has demonstrated preclinical antitumor activity with sensitivity and specificity to several tumor types. First in man clinical studies are planned for 2017.

2:30 Combining a Potent Vaccine Technology with Patient-Specific Neoepitopes to Generate Commercially Viable Individualized Cancer Vaccines
Agnieszka Fredriksen, Ph.D., CSO, Vaccibody
Vaccibody has developed a unique platform technology able to substantially potentiate vaccines, able to attract, activate and deliver antigens to antigen presenting cells. By using the DNA vaccine format encoding for the Vaccibody protein, a rapid, cost-effective and robust manufacturing process has been generated which lends itself perfectly to develop commercially viable patient-specific vaccines on demand. Supportive preclinical data with neoantigen based DNA vaccines as well as clinical data with a similar Vaccibody DNA vaccine using viral antigens support a favourable safety, tolerability and efficacy profile. A clinical study using targeted Vaccibody neoepitope DNA vaccines in multiple advanced cancer indications is under preparation.

3:00 Networking Refreshment Break

3:15 An Immunogenic Personal Neoantigen Vaccine for Patients with Melanoma
Patrick Ott, M.D., Dana-Farber Cancer Institute
We designed a multi-epitope personalized neoantigen vaccine targeting tumor neoantigens consisting of up to 20 synthetic long peptides containing tumor neoepitopes together with the Toll Like Receptor 3 agonist poly-ICLC. We tested this vaccine approach in a Phase I study in patients with previously untreated high-risk melanoma and find that this approach is feasible, safe, and immunogenic, providing a strong rationale for further development of this personalized vaccine approach.

3:45 Stability Matters: Neoscreen
Sune Justesen, CSO, Immunitrack
Many different approaches are taken to identify good neo-antigens. Immunitrack is a spin-out from the academic group that developed netMHC and has an extensive recombinant MHC platform and accompanying affinity and stability assays as well as tetramers. We will try and give a view of how confirmed neo-epitopes look like from an in vitro assay point of view, and show how our platform can be used to identify them.

4:15 CLOSING PANEL DISCUSSION: Future Directions for Neoantigen Based Therapies
Moderator: Philip M. Arlen, M.D., President & CEO, Precision Biologics, Inc.
- How can we deal with scaling personalized therapies?
- How can we standardize neoantigen selection?
- What lies in the future for personalized therapies?

4:45 Close of Neoantigen-Based Personalized Immunotherapies
With record numbers of immunotherapies in active development, the importance of the tumor microenvironment (TME) in creating, tailoring, and monitoring therapies has become clear. Cambridge Healthtech Institute’s Inaugural Targeting the Tumor Microenvironment will address three critical components of the role of the tumor microenvironment in immunotherapy. First, the biology and composition of the TME will be examined to understand the function and presence of different immune cells. Then, the role of the TME in therapy prediction and monitoring will be addressed, with specific focus on immunoscoring. Finally, strategies for targeting cellular and molecular components of the TME will be discussed.

### RECOMMENDED PRE-CONFERENCE SHORT COURSES*

**SC1: Omic Technology for Cancer Immuno-Oncology**  
**SC2: Applications of a Quantitative Imaging Tool Box in Evaluating a CAR Immune Synapse and Contributing to Rational CAR Design**  
*Separate registration required, please see page 2 for details*

### WEDNESDAY, DECEMBER 6

12:00 pm  Conference Registration
12:15 pm  **A Novel Phenotypic Approach for Predicting Tumor Response**  
Mark Paris, Ph.D., Associate Director, Translational Applications, Mitra Biotech  
12:45 pm  **Dessert Break in the Exhibit Hall with Poster Viewing**
1:15 pm  **PLENARY KEYNOTE SESSION**  
See page 2 for more information
1:50 pm  **Refreshment Break in the Exhibit Hall with Poster Viewing**

### UNDERSTANDING THE FUNCTION OF IMMUNE CELLS IN THE TME

3:30 pm  **Chairperson’s Opening Remarks**  
Zhao Chen, Ph.D., Investigator III, Exploratory Immuno-Oncology, Novartis Institute of Biomedical Research

3:35 pm  **KEYNOTE PRESENTATION: Solving the ‘Last Mile Problem’: Delivering Oxygen Deep into Hypoxic Tumor Microenvironments**  
Stephen Cary, Ph.D., Co-Founder & CEO, Omniox  
The hypoxic tumor microenvironment promotes immune tolerance by altering the recruitment and function of innate and adaptive immune effector and suppressor cells. Reversing tumor hypoxia provides an attractive combinatorial approach to improve immunotherapy.

4:05 pm  **Genotype, Tissue Type and Tumor Microenvironment**  
Zhao Chen, Ph.D., Investigator III, Exploratory Immuno-Oncology, Novartis Institute of Biomedical Research  
Cancer cells play key roles in shaping the tumor microenvironment. Cancer genetic studies also tell us that much of the behavior of the tumor is dictated by genetic alterations and tissue origin. However, the link is missing between these tumor cell autonomous traits and their corresponding influence on tumor microenvironment. We are interested in characterizing genotype and tissue type dependency of tumor microenvironment, and its relevance to treatment responses.

4:35 pm  **Oncogenes: Regulators of Immune Privilege**  
Dean W. Felder, M.D., Ph.D., Director, Translational Research and Applied Medicine, Oncology Research, Stanford University School of Medicine  
We have shown that many oncogenes induce tumorigenesis that is completely reversible upon their inactivation, a phenomenon called oncogene addiction. Recently, we have found that oncogenes causally regulate the expression of key immune checkpoints including PD-L1 and CD47. Therapies that target specific oncogenic pathways can restore the immune response against cancers. Our observations have important implications for how therapies that target oncogenes can restore the immune system against cancers.

5:05 pm  **Tapping Into CAR T Cell Associated TME Gene Signature to Optimize Immunotherapy**  
Adrian Bot, M.D., Ph.D., Vice President, Translational Sciences, Kite Pharma  
Chimeric antigen receptor (CAR) engineered T cells have shown promising clinical efficacy and manageable toxicities in multicenter clinical trials, and are entering clinical practice. Clinical activity of CAR T cells has been previously associated with a range of blood biomarkers. Complementing this extensive analysis of blood markers, a detailed evaluation of CAR T cell treatment related TME changes is needed. Recently, utilizing nanostring applied to tumor biopsies pre-and 7-14 days post CAR T cell treatment, we identified a TME gene signature related to CAR T cell treatment. Emerging results from our study suggest that optimizing the CAR T cell proliferative capability by exploiting IL-15, in conjunction with modulation of interferon related pathways and TME checkpoints, could result in more efficacious T cell interventions.

5:35 pm  **Close of Day**
Targeting the Tumor Microenvironment | December 6-7, 2017 | San Diego, CA

THURSDAY, DECEMBER 7

8:00 am Breakfast Breakout Roundtable Discussions

UNDERSTANDING THE FUNCTION OF IMMUNE CELLS IN THE TME (CONT.)

8:55 Chairperson’s Opening Remarks
David Wustrow, Vice President, Drug Discovery, FLX Bio, Inc.

9:00 Small Molecule Approaches to Reversing Immunosuppression in the Tumor Microenvironment by Inhibiting Regulatory T Cells
David Wustrow, Vice President, Drug Discovery, FLX Bio, Inc.
Mechanistic studies have revealed that regulatory T cells (Treg) play a key role in suppressing immunity in the tumor microenvironment. Small molecule Treg targets that either reduce Treg numbers in the tumor or their suppressive function have been identified. The selectivity, titratability and access of small molecules to intracellular compartments provide differentiation with biologics and allow novel combinations with approved IO agents to increase response rates in established therapies as well as establishing efficacy across a broader variety of tumor types. This talk will discuss progress in identification and development of small molecules that can effectively enhance the immune response in the tumor microenvironment by inhibiting the suppressive effects of Treg on CD8+ effector T cells.

9:30 Next Generation Biomarkers for the Era of Combination Cancer Immunotherapies
Sarah Javid, Ph.D., Senior Scientist, Discovery Pharmacogenomics, Genentech, Pharmacogenomics, Merck
Immune checkpoint blockade therapies are revolutionizing the standard cancer treatment. Despite the current success of these therapies, not all patients respond to immunotherapy and even those that do often experience toxicities. Combination approaches are the keys to improving clinical response. Novel high throughput technologies enable us to understand the mechanisms underlying the complex interactions between the immune system and cancer and identify predictive biomarkers for patients.

10:00 Sponsored Presentation (Opportunity Available)

10:30 Networking Coffee Break

10:55 Targeting the Tumor Immunoenvironment
Michael R. Shunn, M.D., Ph.D., Professor, Pathology, Immunology, University of Pittsburgh Medical Center
Targeting immune regulatory cells in cancer has been proven as an effective monotherapy or a part of combinational cancer treatment. However, cancer chemoresistance is still the main reason for therapeutic failure. Our new data provide a new role of myeloid regulatory cells in chemoresistance and offer a novel nanodeelivery approach to cell specific targeting of these cells in the tumor microenvironment. In addition, our new data suggest that targeting the peripheral nervous system in cancer may alter the tumor immunoenvironment and potentially control tumor progression.

TARGET VALIDATION AND PRIORITIZATION

11:25 First-in-Class Anti-Semaphorin 4D Antibody Shifts the Immune Balance in the Tumor Microenvironment
Elizabeth Evans, Ph.D., Vice President, Preclinical Research, Vaccinex
Semaphorin 4D (SEMA4D) is highly expressed at invasive tumor margins, where it promotes immune suppression in the tumor microenvironment by restricting immune cell infiltration and activity. Preclinical mechanistic studies demonstrate that neutralizing anti-SEMA4D antibodies can restore the immune balance and inhibit tumor growth. Anti-SEMA4D antibody treatment synergizes with other immunomodulatory agents to enhance anti-tumor responses, supporting the initiation of Phase Ib/II studies of anti-SEMA4D in combination with immune checkpoint therapies.

11:55 USP7 Modulating Tumor Microenvironment with USP7 Inhibitors for Cancer Immunotherapy
Suresh Kumar, Ph.D., Senior Director, R&D, Progenra, Inc.
Immune suppressive Tregs in the tumor microenvironment correlate with poor prognosis. Depletion of Tregs or impairment of Treg function is an attractive cancer immunotherapy approach. USP7 controls Treg function by regulating Foxp3 and TIP60. Progenra has developed potent USP7 inhibitors that impair Treg functions and are efficacious in various syngeneic solid tumor models. USP7 inhibitors alone or in combination can improve the efficacy and expand the scope of cancer immunotherapy.

12:25 pm Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

12:55 Session Break

DRUG DELIVERY STRATEGIES

1:55 Chairperson’s Opening Remarks
Osama Rahma, M.D., Assistant Professor, Medicine, Center for Immunology, Gastrointestinal Cancer Center, Dana-Farber Cancer Institute, Harvard Medical School

2:00 Utilizing the Neoadjuvant Immunotherapy Setting for a Better Understanding of the Tumor Microenvironment
Osama Rahma, M.D., Assistant Professor, Medicine, Center for Immunology, Gastrointestinal Cancer Center, Dana-Farber Cancer Institute, Harvard Medical School
Despite the recent progress in cancer immunotherapy drugs development questions regarding their mechanism of action and resistance still exist. Many answers lay in the tumor microenvironment (TME) that may not be always accessible. Accordingly, neoadjuvant immunotherapy provides a perfect setting to test the effect of these agents. We will discuss the currently ongoing trials utilizing neoadjuvant immunotherapy to better understand the TME.

3:00 Networking Refreshment Break

IMMUNOSCORING AND OTHER PROGNOSTIC TESTS

3:15 Evaluation of Immune Cell Infiltrates in the Tumor Microenvironment Using Multiplex Immunohistochemistry
Shawn Jensen, Ph.D., Senior Scientist, Molecular and Tumor Immunology, Robert W Franz Cancer Research Center, Earle A Chiles Research Institute, Portland Providence Medical Center
The assessment of T cell infiltrates in the tumor microenvironment using immunohistochemistry has been shown to be a powerful prognostic biomarker in some cancers. Next generation “immunoscore” of the tumor microenvironment using multiplex immunohistochemistry imaging enables analysis of multiple cell phenotypes as well as their spatial relationships. Data from this analysis can improve prognosis of cancer patients as well as inform us on future targets for immunotherapy.

3:45 Integrated Immunotherapy Based upon Tumor/Host interaction
Alan L. Epstein, M.D., Ph.D., Professor, Pathology, Keck School of Medicine, University of Southern California
A better understanding of tumor/host interaction would enable clinicians to customize immunotherapy for optimal effects in cancer immunotherapy.
Using murine syngeneic tumors as models, we have identified these parameters to customize immunotherapeutic approaches and shown that addressing immune activation and suppression specifically for each tumor model will enable effective immunotherapy to be applied. Our data show that a small number of dominant features of immune activation and inhibition present in the tumor microenvironment need to be addressed to enable immunotherapy to become a potentially curative treatment for cancer regardless of its origin or tumor type.

**4:15 CLOSING PANEL DISCUSSION: Future Directions in Tumor Microenvironment Research**

*Moderator: Osama Rahma, M.D., Assistant Professor, Medicine, Center for Immuno-Oncology, Gastrointestinal Cancer Center, Dana-Farber Cancer Institute, Harvard Medical School*

- Challenges moving forward
  - Target validation and identification
  - Modulating the TME to make it less immunosuppressive
- Surface markers that define the TME
- Exploring TME mechanisms
- Getting to and designing clinical trials

*Panelists: Zhao Chen, Ph.D., Investigator III, Exploratory Immuno-Oncology, Novartis Institute of Biomedical Research
Elizabeth Evans, Ph.D., Vice President, Preclinical Research, Vaccinex
Michael R. Shurin, M.D., Ph.D., Professor, Pathology, Immunology, University of Pittsburgh Medical Center*

**4:45 Close of Targeting the Tumor Microenvironment**
**Pricing & Registration Information**

**December 5-7, 2017 | Hilton San Diego Resort & Spa | San Diego, CA**

**PREMIUM PACKAGE** *(Includes access to two conference tracks, excludes short courses.)*

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**BASIC PRICING** *(Includes access to one conference track, excludes short courses)*

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**CONFERENCE TRACKS**

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<tr>
<td>Track 1: The Microbiome in Cancer Immunotherapy</td>
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<td>Track 3: Neoantigen-Based Personalized Immunotherapies</td>
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<td>Track 2: Targeting Innate Immune Cells</td>
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<td>Track 4: Targeting the Tumor Microenvironment</td>
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**SHORT COURSE PRICING**

| | Monday | December 4 | 9:30 am - 12:30 pm | Monday | December 4 | 2:00 - 5:00 pm |
|---------------------|--------------|----------------|
| One Short Course | | $699 | $399 |
| Two Short Courses | | $999 | $699 |

**CONFERENCE DISCOUNTS**

**Poster Submission - Discount ($50 Off):** Poster abstracts are due by November 10, 2017. Once your registration has been fully processed, we will send an email containing a unique link allowing you to submit your poster abstract. If you do not receive your link within 5 business days, please contact jring@healthtech.com.

*CHI reserves the right to publish your poster title and abstract in various marketing materials and products.

**Register 3 – 4th is FREE:** Individuals must register for the same conference or conference combination and submit completed registration form together for discount to apply.

*Group, Protein Society or Antibody Society Membership, Twitter, LinkedIn, Facebook or any other promotional discounts cannot be combined. Discounts not applicable on Event Short Courses.

*If you are unable to attend but would like to purchase the IMPACT: Immunotherapy Progress and Clinical Treatments CD for $750 (plus shipping), please visit IMPACTImmunotherapy.com.

How to Register: **IMPACT IMMUNOTHERAPY.com**

reg@cambridgehealthtech.com | P: 781.972.5400 or Toll-free in the U.S. 888.999.6288

Please refer to the Registration Code below: