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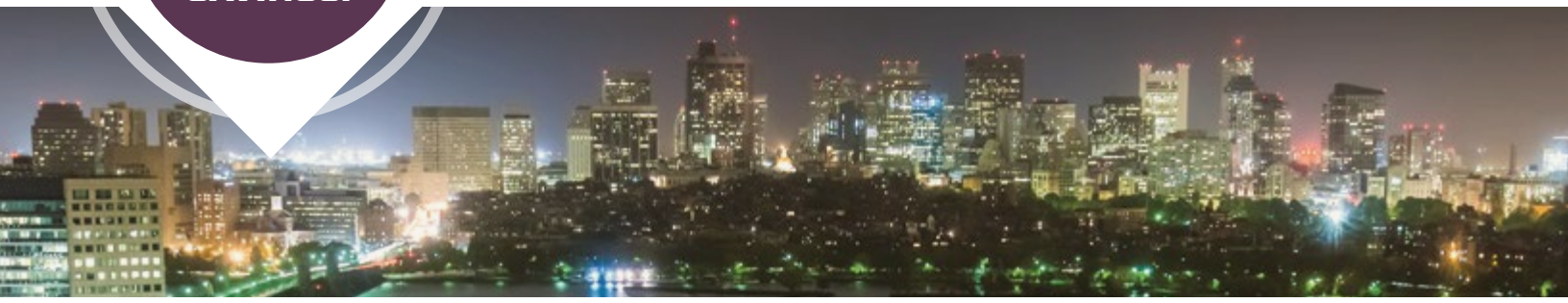

SEPTEMBER 23-25, 2019 | HYATT REGENCY CAMBRIDGE | CAMBRIDGE, MA

KEYNOTE SPEAKER

MIHAI G. NETEA, PhD

Professor, Internal Medicine, Radboud University Medical Center, The Netherlands

KEYNOTE SPEAKER

SHILADITYA SENGUPTA, PHD

Principle Investigator, Engineering in Medicine, Brigham and Women's Hospital, Harvard Medical School and Massachusetts Institute of Technology

FEATURED SPEAKER

MICHAEL KLICHINSKY, PharmD, PhD

Co-Founder, Vice President, Discovery, Carisma Therapeutics

SHORT COURSES

SC1: Gene Edited Cell-Based Therapies: Opportunities and Challenges

SC2: Understanding and Modulating Tumor Microenvironment for Immunotherapy

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Cambridge Healthtech Institute's Inaugural

September 23-25, 2019
Hyatt Regency Cambridge
Cambridge, MA

TARGETING **INNATE** IMMUNITY

Differentiating Friends from Foes

As our knowledge of the complex innate immune system increases, new opportunities to develop novel treatments by utilizing the innate immune cells are significantly enhanced. Cambridge Healthtech Institute's Inaugural Targeting Innate Immunity Congress will convene all the thought leaders including industry experts, academic researchers and clinicians to deepen our understanding of the innate immunity and how to harness their power for effective immunotherapies. This congress focuses on the current landscape and novel advances in the field of innate immunotherapy such as natural killer cells, macrophages and dendritic cells. Be part of the conversation on mechanisms of action of innate cells, effective modulating strategies, the impact of tumor microenvironment and much more.

SHORT COURSES* MONDAY, SEPTEMBER 23

12:30 – 3:00 PM

SC1: Gene Edited Cell-Based Therapies: Opportunities and Challenges

Instructors:

Khalid Shah, MS, PhD, Director, Center for Stem Cell Therapies and Imaging, Harvard Medical School; Vice Chair of Research, Brigham and Women's Hospital

H. Trent Spencer, PhD, Associate Professor of Pediatrics; Director, Gene and Cell Therapy Program in the Aflac Cancer and Blood Disorders Center, Emory University School of Medicine; President and Co-Founder, Expression Therapeutics LLC

Additional Instructors to be Announced

Engineered cell-based therapies are yielding promising clinical benefits for treating many diseases, especially cancer. This course will cover some of the important topics such as sources of therapeutic cells (stem cells, T cells, NK cells and cancer cells), novel engineered viral vectors and their engineering capabilities, the role of CRISPR gene editing and clinical translation and safety aspects of engineered cell therapies. The instructors will give short talks followed by open discussion with attendees, where they can elaborate on their experiences and expertise.

3:30 – 6:00 PM

SC2: Understanding and Modulating Tumor Microenvironment for Immunotherapy

Instructors:

RJ Tesi, MD, CEO, CMO, INmune Bio

Mark Lowdell, PhD, Director, Centre for Cell, Gene & Tissue Therapeutics, RFH; Professor, Cell & Tissue Therapy, University College London

This interactive short course tackles our emerging understanding of the role of the tumor microenvironment (TME) in tumor immunotherapy. The TME can have a marked immunosuppressive effect leading to suboptimal responses of tumors to immunotherapies. Strategies to change the immunosuppressive nature of the TME to one that supports immune responses and enhances the impact of tumor immunotherapy will be discussed.

**See registration page for pricing details.*

PRESENT A RESEARCH POSTER

Share Your Advancements and Discover the Latest Opportunities in Cancer Research in the Exhibit Hall

Cambridge Healthtech Institute encourages attendees to gain further exposure by presenting their work at the Targeting Innate Immunity Congress. To secure a poster board and inclusion in the conference materials, please submit abstracts and coordinate registration by August 16, 2019.

POSTER CONTRIBUTORS RECEIVE A $50 REGISTRATION DISCOUNT!

TUESDAY, SEPTEMBER 24

8:00 am Welcome Remarks from Conference Director
Ngoc 'Emily' Le, PhD, Conference Producer, Cambridge Healthtech Institute

8:10 Chairperson's Opening Remarks
Hans Klingemann, MD, PhD, Vice President, Research & Development, NantKwest, Inc.

8:15 KEYNOTE PRESENTATION:

Beyond T Cell Immunotherapy
Shiladitya Sengupta, PhD, Principle Investigator, Engineering in Medicine, Brigham and Women's Hospital, Harvard Medical School and Massachusetts Institute of Technology
The talk shall address novel findings in the role of immune cells other than T cells in exerting an anticancer effect, especially novel immune checkpoints and engineering novel therapeutic approaches to activate these cells. We anticipate that a robust immune response that encompasses the different pillars of the immune system, together with T cells, is critical for improving the outcomes with immunotherapy.

ENGINEERING STRATEGIES FOR NK, NKT AND GAMMA DELTA T CELLS

8:45 Her2-CAR Engineered Natural Killer Cell Line as Off-the-Shelf Adoptive Immunotherapy in Solid Cancer
Torsten Tonn, MD, PhD, Group Leader, Research Laboratory Experimental Transfusion Medicine; Professor, Transfusion Medicine, Medical Faculty Carl-Gustav-Carus, Technische Universität Dresden, Germany
This presentation will summarize preclinical data with CAR-NK cells in murine glioblastoma (GBM) models, and describe the ongoing clinical development of ErbB2/HER2-specific NK-92/5.28.z cells, a CAR-engineered derivative of the human NK cell line NK-92 currently applied in the CAR2BRAIN Phase I clinical trial (NCT03383978, clinicaltrials.gov) as an off-the-shelf cellular therapeutic for the treatment of relapsed glioblastoma.

9:15 Translation of Pluripotent Cell-Derived Engineered NK Cells as a Cornerstone Approach for Off-the-Shelf Cancer Immunotherapy
Bob Valamehr, PhD, MBA, Chief Development Officer, Fate Therapeutics, Inc.
In this review, we outline a roadmap for development of off-the-shelf cell therapy based on natural killer (NK) cells derived from induced pluripotent stem cells (iPSCs). We discuss strategies to engineer iPSC-derived NK (iPSC-NK) cells for enhanced functional potential, persistence, and homing.

9:45 Networking Coffee Break

10:05 Advances in Tri-Specific Killer Engager (TriKE) Molecules for NK Cell Antigen-Specific Recognition of Tumor Cells in High Risk MDS and Refractory AML Settings
Martin Felices, PhD, Assistant Professor of Medicine, Co-Director, Translational Therapy Laboratory, Hematology, Oncology, and Transplantation, University of Minnesota
Tri-specific killer engager (TriKE) molecules drive NK cell antigen-specific recognition of tumor cells coupled with an expansion signal. These molecules, which essentially form a cytolytic bridge between NK cells and tumor cells, have been validated preclinically in a number of cancer settings and received FDA IND approval for a clinical trial in the high risk MDS and refractory AML setting.

10:35 Bispecific Gamma Delta T Cell Engagers for Cancer Immunotherapy
Hans J. van der Vliet, Medical Oncology, VU University Medical Center, Cancer Center Amsterdam, The Netherlands
We show that a novel bispecific nanobody-based construct targeting both Vg9Vd2-T cells and EGFR induced potent Vg9Vd2-T cell activation and subsequent tumor cell lysis both ***in vitro*** and in an ***in vivo*** mouse xenograft model. In combination with the conserved monomorphic nature of the Vg9Vd2-TCR and the facile replacement of the tumor-specific nanobody, this immunotherapeutic approach can be applied to a large group of cancer patients.

11:05 Novel Innate Killer Cell Platform for Empowering Cell Therapies for Cancers
Mark A. Exley, PhD, Vice President, Cellular Immunology, AgenTus Therapeutics, Inc.
Translating the success of immune cell therapies in early solid tumor trials to wider use and broader durable responses requires dealing with several major hurdles, including practical logistics, prevention of relapse and control of serious side-effects. Allogeneic innate killer cell platforms offer potential to improve all these areas, alone and in combination with CARs and rTCRs. We will describe the status of our approaches exploiting innate killer cells in the context of the field, including clinical plans.

11:35 Accessing Innate Immunity Cells by Electroporation
Sponsored by Celetrix Electroporation
Jian Chen, PhD, CEO, Celectrix Electroporation
Our ability to modify the innate immunity cells would enable designed and targeted therapies. Electroporation of NK cells, macrophages, dendritic cells has unique challenges due to their special biological and physical properties. A new electroporation technology is introduced to address the cell size transformation issue and has achieved significant improvements.

12:05 pm Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

12:35 Session Break

THE ROLE OF ONCOLYTIC VIROTHERAPY IN IMMUNOTHERAPY

1:30 Chairperson's Remarks
Dai Fukumura, MD, PhD, Deputy Director of Edwin L. Steele Laboratory and Investigator, Massachusetts General Hospital; Associate Professor, Harvard Medical School

1:35 The Role of Natural Killer Cells in Cancer Immunotherapy and Oncolytic Virotherapy
Jianhua Yu, PhD, Professor, Hematology & Hematopoietic Cell Transplantation, City of Hope
We discovered that innate immune cells can limit the efficacy of virotherapy at the early treatment stage due to their eradication of virally-infected GBM cells, limiting oHSV propagation. On the other hand, the oncolytic virus treatment combines the effects of both virotherapy and immunotherapy. Our recent work shows promising to modulate innate immune cells and increase oHSV viral spread in the solid tumor and thereby enhances the efficacy of oncolytic virotherapy.

2:05 ONCR-177, an Oncolytic HSV-1 Designed to Potentiate Systemic Anti-Tumor Immunity
Sonia Feau, PhD, Associate Director, Immunology, Oncorus
ONCR-177 is a highly modified recombinant oncolytic herpes simplex virus (oHSV) designed for the treatment of solid tumor indications. ONCR-177 is proposed to have a dual mechanism of action whereby the microRNA attenuation strategy allows for selective oncolysis of tumors cells and the transgenes mediate potent stimulation of systemic anti-tumor immunity. This talk will explain how this modality combined with immunologic payloads can enhance innate and adaptive immune responses in the tumor microenvironment.

2:35 Sponsored Presentation *(Opportunity Available)*

3:05 Refreshment Break with Exhibit and Poster Viewing

REPROGRAMMING TUMOR MICROENVIRONMENT: TARGETING MYELOID CELLS, DENDRITIC CELLS AND INNATE LYMPHOID CELLS

3:45 Chairperson's Remarks
Kipp Weiskopf, MD, PhD, Resident Physician, Internal Medicine, Brigham and Women's Hospital

3:45 Reprogramming Immune Cells in the Tumor Microenvironment to Treat Pancreatic Cancer
Scott A. Gerber, PhD, Assistant Professor, Co-Director, Center for Tumor Immunology Research, Surgery, Microbiology, Immunology, Radiation Oncology, University of Rochester Medical Center
We have devised a therapy that targets both adaptive and innate intratumoral cells, and when combined with stereotactic body radiotherapy, results in complete cures in an orthotopic model of pancreatic cancer. Furthermore, our therapy, although given locally, stimulates a systemic anti-tumor immune response capable of eliminating distal metastases. This two-pronged approach is critical for optimal therapeutic response.

4:15 Receptor Mediated Antigen Delivery and Simultaneous Metabolic Modulation of Dendritic Cells for Inducing Tumor Immunity
Subramanya Hegde, PhD, Senior Scientist III, Foundational Immunology, Abbvie
Dendritic cells (DCs) play a major role in both inflammatory diseases and cancer. DCs within the tumor are inefficient in taking up, processing and presenting the tumor antigens effectively. Reprogramming DC metabolism and targeting the tumor antigens via surface receptors could improve anti-tumor immune response.

4:45 Innate Lymphoid Cell (ILC) Functional Manipulation for Innovative Cancer Immunotherapy
Sara Trabanelli, PhD, Research Associate, Oncology, Ludwig Institute for Cancer Research, University of Lausanne, Switzerland
We have recently reported the identification of novel, dominant ILC2-dependent circuits of immunosuppression in cancer patients. ILC2 may therefore represent attractive cell targets to reprogram the immunosuppressive tumor microenvironment. By decoding the transcriptional programs of human ILC2 we have identified candidate targets for ILC2 functional reprogramming. By therapeutically interfering with these circuits we are exploring the impact of these discoveries in preclinical mouse models, in view of Phase I clinical trials.

5:15 Welcome Reception with Exhibit and Poster Viewing

6:15 End of Day

WEDNESDAY, SEPTEMBER 25

8:00 am Breakfast Breakout Roundtable Discussions

MODULATING MACROPHAGES IN THE TUMOR MICROENVIRONMENT

8:55 Chairperson's Remarks

Mark A. Exley, PhD, Vice President, Cellular Immunology, AgenTus Therapeutics, Inc.

9:00 KEYNOTE PRESENTATION:

Therapeutic Targeting of Trained Immunity

Mihai G. Netea, PhD, Professor, Internal Medicine, Radboud University Medical Center, The Netherlands

I will share my thoughts and vision of how to target innate immune cells and regulate trained immunity to achieve long-term therapeutic benefits in a range of immune-related diseases. These include conditions characterized by excessive trained immunity, such as inflammatory and autoimmune disorders, allergies and cardiovascular disease and conditions driven by defective trained immunity, such as cancer and certain infections.

9:30 FEATURED PRESENTATION: CAR Macrophage Immunotherapy: A New Frontier for Innate Immunity

Michael Klichinsky, PharmD, PhD, Co-Founder, Vice President, Discovery, Carisma Therapeutics

Our approach can overcome the hurdles of cell therapy in the treatment of solid tumors by modulating the tumor microenvironment (TME) through macrophages with key characteristics: recruitment and access to the solid tumor TME, ability to survive in the hostile solid tumor milieu, maintenance of an anti-tumor phenotype in the presence of immunosuppressive factors, capacity to selectively destroy cancer cells, and activation of an adaptive immune response by presenting engulfed tumor material.

10:00 Sponsored Presentation *(Opportunity Available)*

10:30 Coffee Break with Exhibit and Poster Viewing

11:10 Modulating Macrophage Activities for Disease Intervention

Jianzhu Chen, PhD, Professor of Biology, Biology & Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology

We have screened macrophage responses to over 4,000 compounds, including FDA-approved drugs, bioactive compounds and natural products, and identified compounds that can polarize macrophages from M1 to M2 or vice versa. We have validated selected compounds to drive tumor-associated macrophages to inflammatory phenotype ***in vivo*** to achieve anti-tumor effect alone or in combination with antibody therapeutics. These studies elucidate molecular basis underlying macrophage heterogeneity and provide a basis for modulating macrophage activities for disease intervention.

11:40 Myeloid Derived Suppressor Cell (MDSC): The Queen Bee of the Tumor Microenvironment (TME)

RJ Tesi, MD, CEO, CMO, INmune Bio

The most efficient way to reverse TME immunobiology is to target myeloid derived suppressor cells (MDSC). This talk will address the complexity of the TME and how it contributes to failure of therapy, understanding of how targeting soluble TNF offers a solution to the resistance to therapy when part of combination therapy; and results of the Phase I trial of INB03 in patients with advanced cancer.

12:10 pm Sponsored Presentation *(Opportunity Available)*

12:40 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:10 Session Break

ADVANCING INNATE CELL THERAPIES TO THE CLINIC

2:10 Chairperson's Remarks

Rizwan Romee, MD, Associate Professor of Medicine, Haploidentical Donor Transplant Program, Oncology/BMT and Leukemia Program, Dana Farber Cancer Institute, Harvard Medical School

2:15 Targeting TIM-3 and IL-1b in Cancer Immunotherapy: Deciphering Key Roles in the TME

Pushpa Jayaraman, PhD, Senior Investigator I, Exploratory Immuno Oncology, Novartis Institutes for Biomedical Research

The success of PD-1 pathway inhibitors has led to the rapid expansion of clinical trials in immuno-oncology, including multiple trials exploring partner pathways to enhance responses and durability and to tackle nodes of resistance. Next-generation inhibitors including TIM-3 and IL-1b modulate innate immune biology, and preclinical research reveals novel and critical mechanisms of action for these pathways. Translational data from clinical trials also informs understanding of novel mechanisms. Our work highlights the pathophysiological role of TIM-3 and IL-1b in tumor immunomodulation and inhibitory consequences on T cell function and checkpoint blockade in cancer.

2:45 Off-the-Shelf NK Cells for Malignancies and Infections

Sumithira Vasu, MBBS, Assistant Professor, The Ohio State University Medical Center

Natural killer cells have shown efficacy in hematologic malignancies and some solid tumors. Administering NK cell therapy without cytokines requires an ***ex vivo*** expanded, readily available off-the-shelf NK product. We discuss a framework of evaluating these third-party NK cells in clinical trials.

3:15 Refreshment Break with Exhibit and Poster Viewing

3:45 Tumor Cell-Autonomous Mechanisms Regulating Activity of NK Cells

Constantine Mitsiades, MD, PhD, Assistant Professor, Medicine, Harvard Medical School; Principal Investigator, Medical Oncology, Dana-Farber Cancer Institute

Despite extensive efforts towards developing diverse NK cell-based therapeutic approaches against human neoplasias, the mechanisms which operate in tumor cells to regulate the degree of their responsiveness vs. resistance to NK cells remain incompletely understood. This presentation will provide an overview of recent developments in the characterization of cell-autonomous mechanisms which enhance or suppress the response of malignant cells to NK cells and discuss the implications of these developments on current and future efforts to develop NK cell-based immunotherapies.

4:15 Off-the-Shelf, Engineered NK Cell Lines for Patient-Specific Cancer Treatment

Hans Klingemann, MD, PhD, Vice President, Research & Development, NantKwest, Inc.

We have developed the NK cell line NK-92 into an "off-the-shelf" activated NK (aNK) cell therapeutics. The safety of aNK as well as their activity against a broad range of cancers have been confirmed in Phase I trials in the U.S., Canada and Europe. aNK cells can be administered in the outpatient setting and serve as a universal cell-based therapy without need for individualized patient matching. aNK cells have been bioengineered to incorporate a high-antibody binding Fc-receptor (haNK). Both aNK and haNK cells can be equipped with chimeric antigen receptors (CARs) (taNK and t-haNK) to further optimize targeting and potency in the therapeutic setting.

4:45 The Role of Off-the-Shelf Expanded Hematopoietic Progenitors as Adoptive Therapy to Improve Treatment Outcomes in AML Patients

Colleen Delaney, MD, MSc, Founder and CSO, Executive Vice President, Research and Development, Nohla Therapeutics

This talk will focus on the use of cellular therapies in the setting of AML treatment, and potential mechanisms of action in inducing an autologous anti-tumor immune response.

5:15 End of Congress

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