An Answer to Cancer?
Using the immune system to fight cancer

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6:00 – 7:30 p.m.

The Joseph B. Martin Conference Center
The New Research Building
Harvard Medical School
77 Avenue Louis Pasteur
Boston, MA 02115
An Answer to Cancer? Using the immune system to fight cancer

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Interim Co-Chair, Dept. of Microbiology and Immunobiology
Harvard Medical School
Leader, Cancer Immunology Program
Dana-Farber/Harvard Cancer Center

David McDermott, MD
Associate Professor of Medicine
Harvard Medical School
Director of Biologic Therapy and Cutaneous Oncology Programs
Beth Israel Deaconess
Leader, Dana-Farber/Harvard Cancer Center Kidney Cancer Program

Jerome Ritz, MD
Professor of Medicine
Harvard Medical School
Dana-Farber Cancer Institute
Brigham and Women’s Hospital

Catherine Wu, MD
Associate Professor of Medicine
Harvard Medical School
Medical Oncology, Dana-Farber Cancer Institute
Institute Member, Broad Institute
About the Speakers:

Arlene Sharpe, MD, PhD
Arlene Sharpe is the George Fabyan Professor of Comparative Pathology, head of the Division of Immunology, and interim co-chair of the Department of Microbiology and Immunobiology at Harvard Medical School. Dr. Sharpe is a member of the Department of Pathology at Brigham and Women’s Hospital, an associate member at the Broad Institute of MIT and Harvard, leader of the Cancer Immunology Program at the Dana-Farber/Harvard Cancer Center, and co-director of the Evergrande Center for Immunologic Diseases at Harvard Medical School and Brigham and Women’s Hospital. She earned her MD and PhD degrees from Harvard Medical School and completed her residency in pathology at Brigham and Women’s Hospital. Dr. Sharpe is a leader in the field of T cell costimulation. Her laboratory has discovered and elucidated the functions of T cell costimulatory pathways, including the immunoinhibitory functions of the CTLA-4 and PD-1 pathways, which have become exceptionally promising targets for cancer immunotherapy. Her laboratory currently focuses on the roles of T cell costimulatory pathways in regulating T cell tolerance and effective antimicrobial and antitumor immunity and translating fundamental understanding of T cell costimulation into new therapies for autoimmune diseases and cancer. Dr. Sharpe has published over 300 papers and was listed by Thomas Reuters as one of the most highly cited researchers (top 1 percent) in 2014 and 2015 and was named a Citation Laureate in 2016. She received the William B. Coley Award for Distinguished Research in Basic and Tumor Immunology in 2014 for her contributions to the discovery of PD-1 pathway.

David McDermott, MD
David McDermott is director of the Biologic Therapy and Cutaneous Oncology Programs at Beth Israel Deaconess Medical Center, leader of the Dana Farber/Harvard Cancer Center Kidney Cancer Program and a co-principal investigator of the National Cancer Institute Specialized Programs of Research Excellence grant for kidney cancer. He is director of the Cytokine Working Group, an innovator in the field of solid tumor immunotherapy and associate professor of medicine at Harvard Medical School. Dr. McDermott is a nationally and internationally recognized oncologist; clinical researcher; and expert in the research and clinical management of cancer immunotherapy, melanoma and kidney cancer. He has particular interest in therapies that enhance the immune response to cancer. His immunotherapy research has focused on approaches to improve the therapeutic index of interleukin-2 and the development of “targeted” immunotherapies for patients with solid tumors. Dr. McDermott has served on the program committee for the American Society of Clinical Oncology, the medical advisory board for the Kidney Cancer Association and the National Cancer Institute Genitourinary Steering Committee; he currently serves on the National Cancer Institute Kidney Cancer Task Force.
Jerome Ritz, MD

Dr. Ritz received his MD from Chicago Medical School in 1972, followed by a residency in internal medicine at the University of Wisconsin Hospital, Madison. He completed a clinical fellowship in hematology and oncology at Beth Israel Hospital and a research fellowship at Dana-Farber Cancer Institute, where he joined the staff in 1980. Dr. Ritz was a Scholar of the Leukemia Society of America and is a recipient of the prestigious Stohlman Scholar Award. He is an expert in hematologic malignancies, bone marrow transplantation and cancer immunology. He has published over 400 papers, review articles, book chapters and commentaries. His current research focuses on immune reconstitution after hematopoietic stem cell transplantation, cellular therapies and immunotherapy of cancer, and the development of novel approaches to treat and prevent graft versus host disease. Dr. Ritz is executive director of the Connell-O'Reilly Cell Manipulation Core Facility (CMCF) at Dana-Farber/Harvard Cancer Center and a professor of medicine at Harvard Medical School. The CMCF provides hematopoietic stem cells for patients who are undergoing hematopoietic stem cell transplantation and manufactured cellular products of various types for patients enrolled on clinical trials that evaluate novel cellular therapies. These include the manufacture of autologous tumor vaccines, genetically modified chimeric antigen receptor T cells and genetically modified hematopoietic stem cells for pediatric patients with congenital immune deficiencies. Dr. Ritz is a member of the executive committee of the Dana-Farber/Harvard Cancer Center and associate director for the center’s core facilities. He is a co-director of the Cancer Vaccine Center at the Dana-Farber Cancer Institute and a member of the executive committee of the Harvard Stem Cell Institute.

Catherine Wu, MD

Catherine Wu is an associate professor of medicine at Harvard Medical School. She received her MD from Stanford University School of Medicine and completed her clinical training in internal medicine and hematology-oncology at Brigham and Women's Hospital and Dana-Farber Cancer Institute. She joined the staff at Dana-Farber in 2000 where she has initiated an integrated program of research and clinical activities that focuses on dissecting the underlying mechanisms of pathobiology of chronic lymphocytic leukemia as a means to more rationally generate effective therapies, including immune-based treatments, for this common adult leukemia. Wu has been principal investigator of several clinical trials; a major priority of her studies is the identification of tumor-specific antigens that would allow effective tumor targeting without collateral toxicity. She has been using exome and transcriptome sequencing technologies to identify unique mutated leukemia antigens that arise from individual-specific genetic alterations within a tumor and that could be potentially targeted immunologically, thus paving the way for developing personalized tumor vaccines.
An Answer to Cancer? Using the immune system to fight cancer

Oncologists are turning to a novel form of therapy to combat cancer: retraining or reengineering the immune system to quash tumor growth. In this seminar, you will hear from Harvard Medical School scientists and clinicians on the latest approaches that use the body's own defenses to fight cancer.

Articles

Investing in Innovation
Kevin Jiang, Harvard Medical School News

Cancer Immunotherapy on the Cusp
Elizabeth Cooney, Harvard Medical School News

Vaccine works on hard-to-treat leukemia
Richard Saltus, Harvard Gazette

Cross-disciplinary team brings novel therapeutic cancer vaccine to clinical trials
Communications, Wyss Institute News

Increasing odds for survival
Bill Schaller, Harvard Gazette

New Immune Therapy Shows Promise In Kidney Cancer
Jerry Berger, Beth Israel Deaconess News

Videos

2016 WMIF | Immunotherapy I: Checkpoint Activation and Cancer Vaccines
World Medical Innovation Forum

Roles of the PD-1 pathway in controlling tolerance & tumor immunity
Prolimmune thinkpeptides

Discovering the PD-1 Checkpoint
Cancer Research Institute

Dana-Farber Cancer Institute, Chronic Lymphocytic Leukemia
Leukemia & Lymphoma Society
Mass cytometry gives better picture of blood cell diversity

Technology able to count and categorize dozens of cell types within a sample of blood has revealed new details of how a versatile cancer drug can alleviate a common side effect of stem cell transplants, Dana-Farber investigators report in a recent study.

The technology, known as mass cytometry, uses atomic-age science to parse the cell contents of blood. Conventional flow cytometry labels blood cells with tiny fluorescent tags. When the cells stream past a laser, the color they emit identifies them as a red blood cell, for example, or any of several kinds of white blood cells. The technique can combine about a dozen cell tags at a time but isn’t as precise as researchers would like. The wavelengths emitted by different tags often overlap, making it difficult to identify many cell types at the same time. The result: a less-than-exact picture of the enormous complexity among cell types within a given sample of blood.

Mass cytometry, by contrast, uses tags made of different metal isotopes, each with a unique mass. The technology is so precise it can distinguish between metals whose mass differs by a single proton. Because there is no overlap, mass cytometry can detect 35-40 tags at a time. These tags can be used to differentiate between cells based on what’s inside the cells, as well as what’s on their surface.

“It significantly increases the information we can glean from a single blood sample,” says Jerome Ritz, MD, director of the Connell and O’Reilly Families Core Facility, who, with Masahiro Hirakawa, MD, PhD, led the study, which appeared in the journal *JCI Insight*. “It’s more efficient and gives us a fuller picture of what’s happening within each cell type and subtype.”

The first mass cytometry instrument in the Longwood Medical Area, housed at Dana-Farber’s Flow Cytometry Core Facility, was acquired by a consortium of area research and clinical care institutions. A second instrument was purchased last year by the Belfer Center for Applied Cancer Science. The *JCI Insight* paper is one of the first published by Institute researchers to highlight the new technology in studying the immune system in cancer patients.

The study was undertaken to better understand how low doses of the drug interleukin 2 (IL-2) benefit patients undergoing a transplant of donor stem cells. Previous studies showed that low-dose IL-2 boosts the production and survival of immune system cells known as CD4+ T regulatory cells, or CD4Tregs. These cells play a key role in tamping down chronic graft-versus-host disease (GVHD), in which immune system cells from a transplant begin to attack a patient’s healthy tissue. Researchers wanted to discover which specific types of attack-dampening cells are stimulated by IL-2.

They exposed white blood cells to IL-2 for 15 minutes, then ran the blood through the mass cytometer, analyzing it for 35 different tags. They found the drug initiated a boon in two particular cell subsets – Helios+ CD4Tregs and CD56brightCD16- NK cells – which rein in an immune...
Mass cytometry continued

system attack. Mass cytometry analysis of blood samples from patients with chronic GVHD who were receiving IL-2 showed selective activation and expansion of precisely these two cell types. With continued IL-2 therapy, selective activation of these cells was maintained for at least one year.

The results demonstrate mass cytometry’s ability to pin down the effects of immune therapy on critical cell types not only in GVHD but a variety of other conditions as well, Ritz remarks. “The technology can be used to analyze and monitor the effect of a wide array of drugs on different types of blood cells.”

Other Dana-Farber contributors to the study include: Tiago Matos, MD; Hongye Liu, PhD; John Koreth, MBBS, DPhil; Haesook Kim, PhD; Nicole Paul, MS; Kazuyuki Murase, MD, PhD; Jennifer Whangbo, MD, PhD; Ana Alho, MD; Sarah Nikiforow, MD, PhD; Corey Cutler, MD; Vincent Ho, MD; Philippe Armand, MD; Edwin Alyea, MD; Joseph Antin, MD; and Robert Soiffer, MD.