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Immunometabolism: Fundamentals to Prospective New Therapies

Virtual Conference | June 8, 2021

Organizers:

- **Evanna Mills** (Harvard Medical School / Dana-Farber Cancer Institute, US)
- **Luke O'Neill** (Trinity College Dublin, Ireland)
- **Mike Murphy** (University of Cambridge, UK)
- **Abcam**

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Ana Domingos

Associate Professor of Neuroscience (University of Oxford, UK)

Talk title

Sympathetic *Neuroimmunometabolism*

Talk summary

- Discovery of the sympathetic neuro-adipose junction and its myeloid regulation
- How these discoveries inspired the development of a new class of anti-obesity drugs that we named as *Sympathofacilitators*.

Biography

Ana Domingos is an Associate Professor at the University of Oxford. After studying undergraduate Mathematics in Lisbon and in Paris, she went to The Rockefeller University in New York City for her doctoral neurobiology studies with Leslie Vosshall, and postdoc with Jeffrey Friedman, investigating how the hormone leptin affects neurocircuitry underlying food choices in mouse models of obesity. Her current research interests on neuroimmunometabolism started in her first lab, nearly four years before coming to Oxford. Her laboratory discovered the sympathetic neuro-adipose junction, a functional synapse-like connection between white adipocytes and the sympathetic nervous system (Cell, 2015). They found that this neuro-adipose junction is necessary and sufficient for fat mass reduction via norepinephrine (NE) signalling (Cell, 2015 and Nature Communications, 2017). They then discovered Sympathetic neuron-Associated Macrophages (SAMs) that contribute to obesity by importing and metabolizing NE (Nature Medicine, 2017). These findings inspired the development of a new class of anti-obesity compounds that they named as *sympathofacilitators*, which do not enter the brain, nor have the typical cardiovascular nor behavioural side effects of centrally acting sympathomimetic drugs (Cell Metabolism, 2020).

Ana Domingos is a member of the advisory board of *Cell Metabolism*, a member of the board of reviewing editors of eLife, and she has received awards from HHMI, Wellcome Trust, ERC, HFSP, and EMBO, among others.

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Vamsi Mootha

Investigator (Howard Hughes Medical Institute)
Professor of Systems Biology and Medicine (Harvard Medical School)

Talk title

Mitochondria, oxygen, and human disease

Talk summary

- Dual genetic control of mitochondria
- Oxygen as an environmental modifier of disease

Biography

Vamsi Mootha is an Investigator of the Howard Hughes Medical Institute and a Professor of Systems Biology and Medicine at Harvard Medical School. He also directs a research laboratory dual localized at Massachusetts General Hospital and the Broad Institute, where he is an Institute Member and Founding Co-Director of the Metabolism Program.

His team focuses on mitochondria, combining classical techniques in bioenergetics with modern genomics and systems biology. His group has characterized the mitochondrial proteome, discovered all of the molecular components of the mitochondrial calcium uniporter, identified 20 disease genes, and discovered that hypoxia can buffer diverse forms of mitochondrial dysfunction.

Vamsi received his undergraduate degree in Mathematical and Computational Science at Stanford University and his M.D. from Harvard Medical School in the Harvard-MIT Division of Health Sciences and Technology. After completing his internship and residency in internal medicine at Brigham and Women's Hospital, he pursued postdoctoral training both at the Whitehead Institute. He has received a number of awards, including a MacArthur Prize, election to the National Academy of Sciences, the Keilin Medal, and a Padma Shri from the Government of India.

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Erika Pearce

Bloomberg Distinguished Professor (Johns Hopkins University)
Scientific Director (Bloomberg~Kimmel Institute for Cancer Immunotherapy)

Talk title

The role of mitochondria in regulating T cell differentiation and function

Talk summary

- Mitochondrial dynamics
- Fission and fusion
- CD4+ T cell differentiation

Biography

Dr. Pearce obtained her Ph.D. in Cell and Molecular Biology in 2005 at the University of Pennsylvania in Philadelphia, where she studied the regulation of T cell responses during infection. During her postdoctoral studies, also at the University of Pennsylvania, she began her research into how cellular metabolic processes govern immune responses to infection and cancer. She launched her independent career in 2009, holding faculty positions at the Trudeau Institute in NY and then Washington University School of Medicine in St. Louis. She moved her research group to Europe in 2015 to become a Director at the Max Planck Institute for Immunobiology and Epigenetics in Freiburg, Germany. In 2018 she was awarded the Gottfreid Wilhelm Leibniz Prize from the DFG for her work on immunometabolism. In 2021 she became a Bloomberg Distinguished Professor at the Johns Hopkins University and Scientific Director of the Bloomberg~Kimmel Institute for Cancer Immunotherapy in Baltimore. Her work continues to investigate the connection between metabolism and cell function.

Johns Hopkins Medicine

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Jonathan Powell

Professor of Oncology (Johns Hopkins University)
Associate Director (Bloomberg~Kimmel Institute for Cancer Immunotherapy)

Talk title

Some T effector cells just GOT1 it (and some don't)

Talk summary

- Differential expression of GOT1 vs GLUD1 by effector vs memory CD8 T cells (high GOT1 in effector cells while high GLUD1 in memory cells) regulates CD8 differentiation.

- GOT1 might inhibit T_H17 differentiation by increasing AMPK activity and inhibiting glycolysis linked fatty acid and cholesterol synthesis.

Biography

Jonathan Powell is an Associate Director of the Bloomberg~Kimmel Institute of Cancer Immunotherapy at the Johns Hopkins University School of Medicine in Baltimore MD USA.

After receiving his M.D. and Ph.D. from Emory University, Dr. Powell completed an Internal Medicine residency at the Johns Hopkins Hospital followed by a Fellowship in Hematology Oncology at the Brigham and Women's Hospital in Boston and the National Institutes of Health in Bethesda. While at the NIH Dr. Powell studied T cell activation and anergy under the mentorship of Dr. Ronald Schwartz. He subsequently joined the Oncology Department at Johns Hopkins where he has led a research lab since 2001.

Dr. Powell's group has provided fundamental insight into the role of mTOR in regulating T cell activation, differentiation and function. These studies have further led to further elucidating the role of metabolic programming in regulating immune responses. Throughout, his group has applied the insight gained from these studies to develop strategies to enhance immunotherapy for cancer. His Work regarding the role of glutamine in the immune system and cancer has led to the development of a novel prodrug glutamine antagonist which is currently in Phase 1 Clinical trials.

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