UNIL | Université de Lausanne
Faculté de biologie et de médecine

Cardiovascular and Metabolism PhD Program

Mini-Symposium

"Microbes and metabolites: implications for cardiovascular and metabolic health and disease"

Centre Hospitalier Universitaire Vaudois (CHUV) Lausanne, December 3, 2015
Auditorium Yersin, CHUV main building, floor 8

Organizer: Prof. Benjamin Marsland

PROGRAM

9:00 – 9:30	Welcome coffee
9:30-9:40	**Welcome: Prof. Benjamin Marsland, Service of Pneumonology, CHUV Lausanne, Switzerland**
9:40 -10:25	**Erika Pearce (Max Planck Institute of Immunobiology and Epigenetics, Freiburg, Germany)** *"Metabolic Interactions In The Tumor Microenvironment"*
10:25-11:10	**Stefan Freigang (University of Bern, Switzerland)** *"Fatty acids as pro- and anti-inflammatory mediators in metabolic disease"*
11:10 – 11:30	Coffee Break
11.30-12.15	**Eran Elinav (Weizmann Institute of Science, Rehovot, Israel)** *"Host microbiome interactions in health and disease"*
12.15-13.00	**Kathryn J Moore (New York University School of Medicine, NY, USA)** *"MiR-33 regulation of macrophage metabolism directs immune cell polarization in atherosclerosis"*
13.00 – 14.30	Lunch
14:30 – 16:30	**Afternoon workshops for PhD students with symposium speakers**

This mini-symposium will be accredited by the Association of Cantonal Veterinarians (SCAV), section Lausanne, as a half day of continuing education.

This meeting is free of charge but for organization purposes we would like participants (limited to a maximum number of 120) to register by filling the form here prior to November 15, 2015.
The UNIL doctoral school attributes 1.0 ECTS for PhD students who present a signed participation form for the mini-symposium (0.25 ECTS morning session, 0.75 ECTS afternoon session).
For additional information, please contact Dr. Ulrike Toepel (ulrike.toepel@unil.ch).

Co-organized by UNIL | Université de Lausanne Faculté de biologie et de médecine CHUV

Talk abstracts

Metabolic Interactions In The Tumor Microenvironment

Erika Pearce, Jing Qiu and Chih-Hao Chang
Department of Immunometabolism, Max Planck Institute of Immunobiology and Epigenetics, Freiburg, Germany

Metabolism is the set of biochemical reactions that occur within cells to sustain life. As such, metabolism, by definition, remains the single most fundamental force driving cell fate. Given the critical nature of T cells in clearing and controlling infections and cancer, as well as mediating protective immunity over the long-term, it is logical that a considerable effort is made to target these cells for therapeutic purposes. However, while metabolism regulates the fate and function of T cells, or of any immune cell for that matter, metabolic interventions for manipulating immunity are rare and can be considered a largely untapped opportunity. Our research is focused on establishing fundamental mechanisms of metabolic regulation in T cells, with a view toward identifying new ways to regulate immune cell function through the manipulation of metabolic pathways. Underlying mechanisms of how T cell metabolism and function is altered in the tumor microenvironment will be discussed.

Fatty acids as pro- and anti-inflammatory mediators in metabolic disease

Stefan Freigang
Institute of Pathology, University of Bern, Switzerland

Lipids represent critical structural components of biological membranes as well as a significant energy source for cellular metabolism, and thus are of fundamental importance for the survival of our organism. In addition, endogenous and environmental lipids may become targets of innate and adaptive immune responses. The immune recognition of microbial and self-lipids is essential for successful anti-infectious immunity, but also promotes chronic inflammation in metabolic disorders, such as diabetes and cardiovascular disease. Using murine models of atherosclerosis in combination with in vitro studies, our group investigates molecular pathways of lipid-induced inflammation in metabolic diseases. Here, we will discuss two distinct mechanisms by which fatty acids and their metabolites regulate vascular inflammation.

Host microbiome interactions in health and disease

Eran Elinav
Weizmann Institute of Science, Rehovot, Israel

The mammalian intestine contains trillions of microbes, a community that is dominated by members of the domain Bacteria but also includes members of Archaea, Eukarya, and viruses. The vast repertoire of this microbiome functions in ways that benefit the host. The mucosal immune system co-evolves with the microbiota beginning at birth, acquiring the capacity to tolerate components of the community while maintaining the capacity to respond to invading pathogens. The gut microbiota is shaped and regulated by multiple factors including our genomic composition, the local intestinal niche and multiple environmental factors including our nutritional repertoire and bio-geographical location. Moreover, it has been recently highlighted that dysregulation of these genetic or environmental factors leads to aberrant host-microbiome interactions, ultimately predisposing to pathologies ranging from chronic inflammation, obesity, the metabolic syndrome and even cancer. We have identified various possible mechanisms participating in the reciprocal regulation between the host and the intestinal microbial ecosystem, and demonstrate that disruption of these factors, in mice and humans, lead to dysbiosis and susceptibility to common multi-factorial disease. Understanding the molecular basis of host-microbiome interactions may lead to development of new microbiome-targeting treatments.

MiR-33 regulation of macrophage metabolism directs immune cell polarization in atherosclerosis

Kathryn J Moore
New York University School of Medicine, New York, USA

Cellular metabolism is increasingly recognized to control immune cell fate and functions. “Inflammatory” M1 and “pro-resolving” M2 macrophages use different metabolic programs to fuel their effector functions, and recent findings indicate that disrupting cellular energy metabolism can directly alter macrophage M1/M2 fate and inflammatory functions. We report that miR-33, a central regulator of lipid metabolism, instructs macrophage polarization and shapes innate and adaptive immune responses by altering the balance of aerobic glycolysis and mitochondrial oxidative phosphorylation. By reducing fatty acid oxidation (FAO) and related spare respiratory capacity in macrophages, miR-33 promotes an inflammatory M1-like macrophage phenotype that is associated with metabolic diseases such as atherosclerosis. Notably, inhibition of miR-33 metabolically reprograms macrophages to the M2 phenotype by upregulating the master FAO switch AMP Kinase as well as multiple enzymes that execute FAO, which fuels alternatively activated macrophage responses involved in resolving inflammation and tissue repair. In atherosclerosis, where macrophages are key integrators of inflammatory and metabolic signals that drive plaque progression, metabolic reprogramming by anti-miR-33 promotes the accumulation of M2 macrophages and Foxp3+ regulatory T cells in plaques, decreases markers of systemic inflammation, and reduces plaque size. Importantly, we show that miR-33 exerts its effects on macrophage polarization and inflammation independently of its previously described roles in cholesterol efflux and plasma HDL levels. Together, these data define a novel role for miR-33 in regulating the cellular pathways that underpin macrophage polarization and suggest that metabolic reprogramming of plaque macrophages to alternatively activated M2 cells by miR-33 inhibition promotes the resolution of atherosclerosis.