UNIL | Université de Lausanne
Faculté de biologie et de médecine

Cardiovascular and Metabolism PhD Program

Mini-Symposium

"Adipose Tissue and Metabolism"

Organizer: Prof. Lluis Fajas Coll

When: 08 June 2017 from 8:30 – 12:30h
Where: UNIL-Sorge, Auditorium A at Genopode

PROGRAM

8:30 – 9:00	**Welcome coffee**
9:00-9:15	**Welcome: Prof. Lluis Fajas Coll** Center for Integrative Genomics, CIG, UNIL
9:15 -10:00	**Francesc Villarroya (**Department of Biochemistry and Molecular Biomedicine**,** University of Barcelona) *Brown adipose tissue and "batokines"*
10:00-10:45	Francisco Verdeguer (Department of Molecular Mechanisms of Disease, University of Zurich) *Transcriptional and epigenetic regulation of energetic metabolism*
10:45 – 11:00	**Coffee Break**
11.00-11:45	Charna Dibner (Endocrinology, Diabetes, Hypertension and Nutrition, Department of Internal Medicine Specialties; Department of Cell Physiology and Metabolism, Faculty of Medicine, University of Geneva; Diabetes Center, Faculty of Medicine, University of Geneva; Institute of Genetics and Genomics in Geneva (iGE3), Geneva, Switzerland) *Circadian timing of metabolism in mouse models and humans*
11.45-12.30	Aliki Perdikari (Institute of Food, Nutrition and Health, ETH Zurich) *Identifying kinases that power brown adipocyte development*
12.30 – 14.00	**Lunch**
14:00 – 16:00	**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.

The meeting is free of charge, but for organization purposes please register by filling the form here prior to May 20, 2017. The maximal number of participants is limited to 100.
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) or **Dr. Marta Bellone Toepel** (marta.bellone@unil.ch).

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

TALK ABSTRACTS

Francesc Villarroya (Department of Biochemistry and Molecular Biomedicine, University of Barcelona)

Brown adipose tissue and "batokines"

Brown adipose tissue (BAT) activity has a protective role against chronic metabolic disease such as obesity or diabetes which have been attributed to its capacity of using glucose and fat for thermogenesis. However, analogously to what was discovered for white adipose tissue years ago, BAT may also play a secretory role, which may contribute to the healthy systemic consequences of BAT activity. The secretory activity of BAT may have local actions, and several molecules released by brown adipocytes have been identified that act in a paracrine or autocrine manner to regulate BAT activity and recruitment in association with thermoregulatory requirements. Thus, most of these factors regulate BAT hypertrophy and hyperplasia, vascularization, blood flow or innervation. Moreover, BAT can release regulatory molecules that at a distance, on other tissues and organs. Growing awareness of the beneficial effects of experimental BAT and beige cells transplantation has been explained by this secretory capacity for BAT. Fibroblast growth factor 21, interleukin-6 and neuregulin 4 are among the first identified BAT-derived endocrine factors. Recent data indicate that BAT also releases miRNA-containing exosomes as well as regulatory lipidic molecules (lipokines), which influence metabolism in distant tissues. Identification of the so-called brown adipokines or batokines could help to identify novel tools to ameliorate obesity and associated metabolic diseases such as diabetes and hyperlipidemia. Moreover, brown adipokines may be used as biomarkers useful for estimating BAT activity, a current challenge considering the invasiveness of the existing methodologies for assessment of BAT activity in humans.

Francisco Verdeguer (Department of Molecular Mechanisms of Disease, University of Zurich)

Transcriptional and epigenetic regulation of energetic metabolism

The balance of energetic metabolism is a complex regulatory system that is largely orchestrated by transcriptional and chromatin factors that cross talk with cellular and endocrine regulatory mechanisms in order to ensure a balance between energy intake and energy expenditure. Perturbations of this delicate balance can lead to obesity, a current world wide epidemic affecting 11% of population that could reach 1 billion people by 2030 (World Health Organization). Recent advances indicate that activation of brown adipose tissue thermogenesis could be an attractive therapeutic approach to elevate of energy consumption rate. We have recently shown that the loss of the transcription factor Ying Yang 1 in brown adipose tissue protects against diet-induced obesity through elevation of energy expenditure.

How the excess of dietary nutrients or energy related environmental stimuli modulate the chromatin and epigenetic landscape is not completely understood. Our preliminary data show that YY1 is acetylated and dephosphorylated in response to increased adrenergic input. We hypothesize that YY1-specific post-translational modifications and the recruitment of specific chromatin factors could play a sensing role of environmental stimuli to coordinate a thermogenic response in brown adipose tissue. At present we are investigating the molecular function and physiological relevance of the YY1 post-translational modifications

which could lead to a better understanding of the molecular basis of the metabolic control in physiological and pathological conditions.

Charna Dibner (Endocrinology, Diabetes, Hypertension and Nutrition, Department of Internal Medicine Specialties; Department of Cell Physiology and Metabolism, Faculty of Medicine, University of Geneva; Diabetes Center, Faculty of Medicine, University of Geneva; Institute of Genetics and Genomics in Geneva (iGE3), Geneva, Switzerland)

Circadian timing of metabolism in mouse models and humans

A critical role of circadian oscillators in orchestrating insulin secretion and islet gene transcription has recently been demonstrated. However, these studies focused on whole islets and did not explore the interplay between α- and β-cell clocks. We performed a parallel analysis of the molecular properties of α- and β-cell oscillators, using a mouse model expressing three reporter genes: one labelling α-cells, one specific for β-cells, and a third monitoring circadian gene expression. Thus, phase entrainment properties, gene expression, and functional outputs of the α- and β-cell clockworks could be assessed in vivo, and in vitro at the population and single-cell level. Our experiments showed that α- and β-cellular clocks are oscillating with distinct phases in vivo and in vitro. Diurnal transcriptome analysis in separated α- and β-cells revealed that a high number of genes with key roles in islet physiology, including regulators of glucose sensing and hormone secretion, are differentially expressed in these cell types. Moreover, temporal insulin and glucagon secretion exhibited distinct oscillatory profiles, both *in vivo* and *in vitro*. Importantly, we show that circadian clock is indispensable for proper insulin and glucagon secretion by analyzing blood islet hormone content in clock proficient and deficient mice. Finally, we report that siClock-mediated circadian clock disruption in human islet cells resulted in decreased secretion levels of insulin and glucagon, highlighting importance of functional clock for the proper endocrine function of human islet. Disruption of the temporal programming of physiology, as occurs during shift work, jet lag, and ageing, has detrimental effects on human health. It is thus of major importance identifying the physiological basis of circadian rhythmicity. Our study highlights the importance of α- and β-cell circadian oscillator, their impact on islet transcriptome and function, and sheds light on the cross-talk between α- and β-cell clocks in mouse and human model systems. By dissecting the rodent and human pancreas oscillator function we hope to advance the understanding of clockwork connection to type 2 diabetes.

Aliki Perdikari (Institute of Food, Nutrition and Health, ETH Zurich)

Identifying kinases that power brown adipocyte development

Brown adipose tissue (BAT) is responsible for thermogenesis that is not associated with shivering by converting chemical energy into heat through uncoupling protein 1 (UCP1) in the mitochondria. Thus, expanding or activating BAT could be used as a potential tool against obesity. To analyze the effect of kinase signaling on brown adipocyte development, we performed lentiviral-mediated short hairpin knockdown or used pharmacological inhibitors in a high-content and high-throughput *in vitro* image-based screen. From our screening approach 190 kinases were identified to have a stimulatory or inhibitory effect on brown adipocyte proliferation, differentiation, or formation. Among these kinases, 5’ AMP–activated protein kinase (AMPK) was further analyzed and promoted the formation of brown adipocytes abundant in UCP1. Together, these results provide insight into the kinases, particularly AMPK, that regulate brown adipocyte formation.