

## CARDIOMET MINISYMPOSIUM

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### Computational Biology in Metabolism and Cardiovascular Research

#### Friday September 19 - CHUV, Lausanne

**Focus** - A number of recent studies have led to a new appreciation of genetic diversity. As soon as genomes are looked at individually, important differences appear: different single-nucleotide polymorphisms are scattered throughout, and singular combinations of particular genes forming haplotypes emerge. Genome-wide scans of these variations in humans have pointed at an increasing number of new genes involved in common diseases and complex traits such as obesity, diabetes and hypertension. This mini-symposium will address DNA sequence variation and its role in population genetics and complex traits, comparative genomics, and large-scale studies of gene and protein expression. Internationally-recognized scientists will emphasize technologies and applications in human and animal models, with a particular focus on metabolic and cardiovascular traits.

This meeting is free of charge, but for organization purposes we ask the participants to register by e-mail to [Marina.Leuba@chuv.ch](mailto:Marina.Leuba@chuv.ch)

**Deadline for registration: September 12**

The afternoon sessions are primarily designed for PhD students but will be open to anyone with an interest in the chosen topics

**Organizers:** Peter Vollenweider and Fabienne Maurer  
**Enquiries:** Marina Leuba ([Marina.Leuba@chuv.ch](mailto:Marina.Leuba@chuv.ch))  
**Forms :** [http://www.cardiomet.ch/cmet\\_affiche\\_news?newsid=31148](http://www.cardiomet.ch/cmet_affiche_news?newsid=31148)

## PROGRAM

### MORNING: AUDITOIRE DE LA MATERNITÉ - AVENUE PIERRE DECKER 2 - CHUV

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- 8.30 - 9.00 *Welcome (and coffee)*
- 9.00 - 9.45 **Prof. Bernard Thorens** (CIG, UNIL, Lausanne)  
**Genomic and lipidomic analysis of resistance to diet-induced obesity**
- 9-45 - 10.30 **Ruth Loos, PhD** (Program Leader, MRC Epidemiology Unit, Cambridge, UK)  
**Searching for genes for obesity - Is genome-wide association the solution ?**
- 10.30 - 10.45 *Coffee break*
- 10.45 - 11.30 **Toby Johnson, PhD** (Department of Medical Genetics, CHUV-UNIL, Lausanne)  
**Life after a whole genome association scan: What next ?**
- 11.30 - 12.30 **Prof. Eleazar Eskin** (Departments of Computer Science and Human Genetics, UCLA, Los Angeles, USA)  
**Integrated genomics approaches to discovering the genetic basis of complex traits in inbred mouse strains**
- 12.30 - 13.30 *Lunch*

## AFTERNOON: SEMINAR ROOMS BH-2 AND BH-4 - BUGNON 46 - CHUV (BH08)

### PAPER DISCUSSION WITH STUDENTS

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#### 13.30 - 14.30 Ruth Loos

##### Papers for discussion

1. Weedon et al. Combining information from common type 2 diabetes risk polymorphisms improves disease prediction. *PLoS Med* 3(10): e374, 2006
2. Cauchi et al. Post Genome-Wide Association Studies of Novel Genes Associated with Type 2 Diabetes Show Gene-Gene Interaction and High Predictive Value. *PLoS ONE* 3(5): e2031, 2008

#### 14.30 - 15.30 Eleazar Eskin

##### Papers for discussion

1. Frazer et al. A sequence-based variation map of 8.27 million SNPs in inbred mouse strains. *Nature* 448:1050-53, 2007
2. Kang et al. Efficient control of population structure in model organism association mapping. *Genetics* 178:1709-23, 2008

15.30 - 16.00 *Break*

#### 16.00 - 17.00 Toby Johnson

##### Paper for discussion

1. Hoggart et al. Simultaneous analysis of all SNPs in genome-wide and re-sequencing association studies. *PLoS Genet* 4(7): e1000130, 2008
2. Balding DJ. A tutorial on statistical methods for population association studies. *Nature Reviews Genetics* 7:781-791, 2006

*Useful background/introductory reading may be found in:*

17.00 - *Wine and cheese*

## NOTES ON SPEAKERS

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### Bernard Thorens

#### Genomic and lipidomic analysis of resistance to diet-induced obesity

**B. Thorens is Professor of Physiology at the Department of Physiology and Center for Integrative Genomics of the University of Lausanne.** He is leading a group studying the physiopathology of obesity and diabetes using integrative physiology and genomics analysis of various animal models. The aim is to understand how defects in gene expression in liver, pancreatic beta-cells, and brain regions controlling glucose and energy homeostasis interact with each other to maintain health and how they are deregulated in pathological conditions.

##### Selected publications:

1. De Fourmestreaux et al. Transcript profiling suggests that differential metabolic adaptation of mice to high fat diet is associated with changes in liver to muscle lipid fluxes. *J. Biol. Chem.* 279:50743-53., 2004
2. Marty et al. Regulation of glucagon secretion by GLUT2 and astrocyte-dependent glucose sensors. *J. Clin. Invest.* 115:3545-53, 2005
3. Marty et al. Brain glucose sensing, counterregulation, and energy homeostasis. *Physiology*, 22:241-51, 2007
4. Klinger et al. Increasing GLP-1-induced beta-cell proliferation by silencing the negative regulators of signaling CREMa and DUSP14. *Diabetes*, 57 :584-593, 2008

### Ruth Loos

#### Searching for genes for obesity - Is genome-wide association the solution ?

**R. Loos belongs to the MRC Epidemiology Unit of the Institute of Metabolic Science in Cambridge, UK.** She is programme leader of the research programme that explores the genetic epidemiology of obesity. The aim of her research work is to identify genes that contribute to risk of obesity and obesity-related traits, to examine

how the environmental exposures, such as diet and physical activity, modify these genetic effects, and to estimate the role of this gene-environment interaction at the population level to better understand the etiology and underlying physiology of obesity.

**Selected publications:**

1. Kurokawa et al. The ADRB3 Trp64Arg variant and BMI: a meta-analysis of 44 833 individuals. *Int. J. Obes.*, 2008 in press
2. Loos et al. Common variants near MC4R are associated with fat mass, weight and risk of obesity. *Nat. Genet.* 40:768-75, 2008

## **Toby Johnson**

### **Life after a whole genome association scan: What next ?**

**T. Johnson is a postdoc in the Computational Biology Group of the Department of Medical Genetics at the University of Lausanne.** He will present a brief reminder about association studies and (some of) their problems. For instance, false positives can be generated by population stratification, whereas false negatives also occur, mostly as a consequence of small effect sizes and limited power of single scans. He will show how combining scan results from multiple studies can help solve both these problems. He will outline an ongoing effort to identify the genetic basis of blood pressure, combining data from at least thirteen different human studies. He will further discuss computational issues regarding the combination of evidence from multiple studies that use different phenotype measurements and sets of SNPs. He will also describe preliminary results from an attempt to combine results from whole genome scans in humans and mice.

**Selected publications:**

1. Loos et al. Common variants near MC4R are associated with fat mass, weight and risk of obesity. *Nat. Genet.* 40:768-75, 2008
2. Weedon et al. Genome-wide association analysis identifies 20 loci that influence adult height. *Nat. Genet.* 40:575-83, 2008
3. Sandhu et al. LDL-cholesterol concentrations: a genome-wide association study. *Lancet* 371:483-91, 2008

## **Eleazar Eskin**

### **Integrated Genomics Approaches to Discovering the Genetic Basis of Complex Traits in Inbred Mouse Strains**

**E. Eskin is Assistant Professor in the Computer Science and Human Genetics departments at the University of California Los Angeles, USA.** His research focuses on developing techniques for solving the challenging computational problems that arise in attempting to understand the genetic basis of human disease. Inbred mouse strains in particular are a very powerful and well studied human disease and complex trait model. A tremendous amount of information is available for various inbred strains including phenotypic information stored in the Mouse Phenome Database (MPD) and high-throughput genomic data such as expression microarray data. Recently, several high density SNP maps have also been developed for inbred mouse strains. These resources combined with what is already known about mouse genetics in terms of quantitative trait loci (QTLs) and known pathways, make inbred mouse strains an ideal model system. Prof. Eskin will present results of his analyses which combines multiple types of data in order to understand the genetic basis of complex traits. He has performed whole genome association analyses of the mouse SNP maps over the phenotypes in the MPD. He will describe how he augments association analysis results with information from expression data, known pathways and QTLs. He will further demonstrate how his approach is able to discover many regions in the mouse genome associated with phenotypes and how many of these predictions are consistent with genes known to influence specific traits.

**Selected publications:**

1. Frazer et al. A sequence-based variation map of 8.27 million SNPs in inbred mouse strains. *Nature* 448:1050-53, 2007
2. Kang et al. Efficient control of population structure in model organism association mapping. *Genetics* 178:1709-23, 2008