*In red : Compulsory/in black : optional*

**Please indicate if it’s a First Step or Master project :**

Master Project

**Director :**

Sven Bergmann

**Direct Supervisor :**

Roger Mallol Parera

**Project titile :**

Integration of genomics and metabolomics data to investigate metabolic syndrome

**Introduction (max 2987 caractères) :**

The prevalence of metabolic syndrome is increasing dramatically, taking the leading place as a risk factor for type 2 diabetes and cardiovascular disease. Metabolic syndrome is defined as a cluster of at least three of the following risk factors [1]: low HDL cholesterol, high triglycerides, high fasting glucose, high waist circumference, and/or high blood pressure. Genome-wide association studies (GWAS) have permitted to elucidate partially the genetic determinants of the various metabolic syndrome components, discovering genes related to beta 3-adrenergic receptor, hormone-sensitive lipase, lipoprotein lipase, IRS-1, PC-1, skeletal muscle glycogen synthase [2]. However, GWAS have shown two main limitations: 1) the biological mechanisms underlying the variant to phenotype links are rarely understood, and 2) most of these variants fail to substantially improve the explanatory power for disease risk [3]. Because organism functions and development are affected by a large amount of different small molecules, known as metabolites, GWAS on metabolite concentrations (mGWAS) can inform on these mechanisms, by uncovering the intermediate phenotypes involved in the links. Large-scale profiling of metabolite species is known as metabolomics, and it is paving the way for advancing our knowledge on the underlying processes regulating a specific biological activity and its subsequent metabolic impairment, which in turn can contribute to the aetiology and onset of a disease.

**Aim of the project (max 981 caractères) :**

The aim of this project is to improve the genetic and molecular characterization of metabolic syndrome by investigating the relationship between genetic variants and components of the metabolic syndrome using metabolite concentrations as intermediate phenotypes. Because we will make use of existing data from the Cohorte Lausannoise (*CoLaus*), whose individuals were phenotyped both at baseline and at 5 years of follow-up, we will also explore the possibility of predicting longitudinal changes in the components of the metabolic syndrome, as well as its incidence. For the purpose of this project, we will develop a complete computational pipeline to deal with large-scale data management and visualization.

**Experimental approach (max 1978 caractères) :**

During this master project we will make use of existing genotype, metabotype, and phenotype data from the CoLaus study, a longitudinal and population-based study to investigate the epidemiology and genetic determinants of cardiovascular diseases and risk factors. Because metabolomics data are only available at baseline, we will study the relationships between genetic variants, metabolome features, and components of the metabolic syndrome (i.e. waist circumference, systolic blood pressure, glucose, HDL-C, and triglycerides) at baseline. We will then investigate the relationship between the baseline concentrations of the genetically-influenced metabolites found in the previous stage and longitudinal changes in the levels of metabolic syndrome components during the follow-up (using linear regression analysis), as well as the incidence of metabolic syndrome at 5 year follow-up (using logistic regression analysis). Information such as age, gender, and smoking status will be integrated in our analysis to take into account potential confounders. Regarding the metabolomics data, currently most of the previous studies investigating metabolite influences on metabolic syndrome have used a targeted approach. During this project we aim to compare the targeted and untargeted approaches using NMR-based metabolomics data available in CoLaus.

**Significance (max 487 caractères) :**

This project aims to link genetics and metabolomics data to the different components of the metabolic syndrome to improve its current diagnostic performance and therapeutic approaches. From the students point of view, the development of this project will allow the student to gain competences in bioinformatic tools development, apply different statistical methods to test and answer scientific questions, and improve the scientific thoughtful by, among others, participating at group meetings and departmental seminars.

**References (max 989 caractères) :**

[1] Definition of Metabolic Syndrome. Report of the National Heart, Lung, and Blood Institute/American Heart Association Conference on Scientific Issues Related to Definition. Scott M. Grundy, H. Bryan Brewer, James I. Cleeman, Sidney C. Smith and Claude Lenfant

[2]. Adamski J. Genome-wide association studies with metabolomics. Genome Med. 2012;4: 34.

[3] Groop, L. (2000) ‘Genetics of the metabolic syndrome’, British Journal of Nutrition, 83(S1), pp. S39–S48. doi: 10.1017/S0007114500000945.

**Link :**

**Department/Service :**

Departement of Computational Biology

**Master Category :**

Please choose from bellow possibilities

*(BEC, MB immunology and cancer, MB metabolism, MB neuroscience, MB pharmacology, MLS bioinformatics, MLS integrative biology, MLS microbiology)*

MLS bioinformatics

Subject Area : (please put in bold the subject areas which are linked to your project)

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| Subject Area | |  |  |  |  |  | | --- | --- | --- | --- | --- | | behaviour | biochemistry | biodiversity | **bioinformatics** | biological interactions | | biology and society | biotechnology | **cardiovascular** | cellular biology | chemistry | | circadian clocks | conservation | design | development | ecology | | energy | environmental factors | ethics | evolution | **gene expression** | | genetics | genomics | growth | heredity | immunology | | infectious diseases | mathematics | **metabolism** | microbiology | molecular biology | | mutation | neurosciences | organismic biology | physiology | pharmacology | | physics | plant biology | regulation | reproduction | selection | | signalling | **statistics** | systematics |  |  | |