Abstract of Presentation

Note: This paper should be typed in "Times New Roman" of 12pt.

Presentation Title(Should be no more than 20 words):

The power of mouse genetic referent populations for the identification of polygenic gene-phenotype networks.

Abstract :

Genetically-engineered mouse models (GEMMs) have been widely used over the past 20 years to decipher the role of a given gene in normal and/or challenged conditions and have been helpful at identifying new therapeutic targets for a given disease. However, human diseases are complex and often polygenic and their outcome is determined by interactions between gene variants and environment. In order to mimic the genetic complexity of human population, mouse genetic reference populations (GRPs) such as the collaborative cross resource have been generated. The power of these GPRs lies in the combination on reliable and comparable genotypic and phenotypic data. In that respect it is mandatory to phenotype all lines for a given trait in a systematic and standardized manner.

We will first present the way we envision to perform such standardized analysis at the EPFL. Indeed within the School of Life Sciences of the EPFL, a new center of PhenoGenomics (CPG) was created, which aimed at providing as a service phenotype characterization in the fields of behavior and physiology and metabolism as a start. The organization and the phenotyping activities of the CPG will be detailed. The power of the GRPs in that context will be exemplified by the results obtained with one GRP, the BxD strains. The BxD strains have been generated by intercrosses between C57BL/6J and DBA/2J and studied for a number of phenotyping traits in a systematic manner, with a primary focus on hypertension. Using a set of 27 recombinant BXD strains of mice a quantitative trait locus (QTL) for blood pressure (BP) was identified on chromosome 9. In subsequent human association studies the syntenic locus was shown to be associated with BP. In-depth analysis of the region identifies the UBP1 locus as a critical blood pressure determinant.

This study underscores the power of the GPR in the identification of new genes implicated in diseases and the marked complementarities of mouse and human genetic approaches. It also emphasizes the power of standardized phenotyping analysis.