2017 IGBMC Summer Internship

Mixed model analysis of unbiased high-throughput mouse knockout data to identify genes and protein-protein interaction networks involved in brain malformation disorders

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Field of research:
Neurogenetics, Statistical Genetics, Bioinformatics, Mouse Knockout Studies

Description of project:
Among the most prevalent and severe brain disorders are brain malformation disorders. They also remain one of the least understood of all health problems. Genetic mutations account for about half of the currently undiagnosed cases, and despite recent successes in identifying some of the mutations responsible, it has been suggested that up to 2,500 further genes remain to be identified. We are collaborating with the Sanger Mouse Genetics Project (MGP), allied to the International Mouse Phenotyping Consortium (IMPC), to systematically study the neuroanatomy of the MGP/IMPC knockout mouse strains. We designed the experiment so that we can detect a variety of mechanisms that underlie brain malformation disorders, resulting in an array of 78 standard measurements across 22 brain regions. So far we have collected data on 9000 mouse brains representing 1500 knockout genes (n=3 samples per knockout gene). The high-throughput phenotyping involved in this experiment means that experimental variation is complex and structured. Consequently a rigorous statistical analysis of this data set, with the aim of detecting which genes and protein-protein interaction (PPI) networks are associated with malformations, will be based on a multivariate mixed model framework.

The specific aims of the project are the following:
1) Determine the normal range of neuroanatomical features in control mice
2) Identify genes associated with brain malformations using mixed model analysis
3) Integrate genetics, brain morphology data, and other whole-body phenotypic traits such as obesity, cancer susceptibility and immunology to investigate causal pathways.

Location: IGBMC, Department of Translational Medicine and Neurogenetics

Expected Results:
This project is ideal for a student who has some programming experience and is keen to discover neuroscience. Training in mixed model analysis and multivariate statistics will be provided if necessary. The primary expected outcome is a set of genes associated with neuroanatomical defects in mice. A secondary outcome is a correlation analysis between different brain regions and other phenotypic traits.