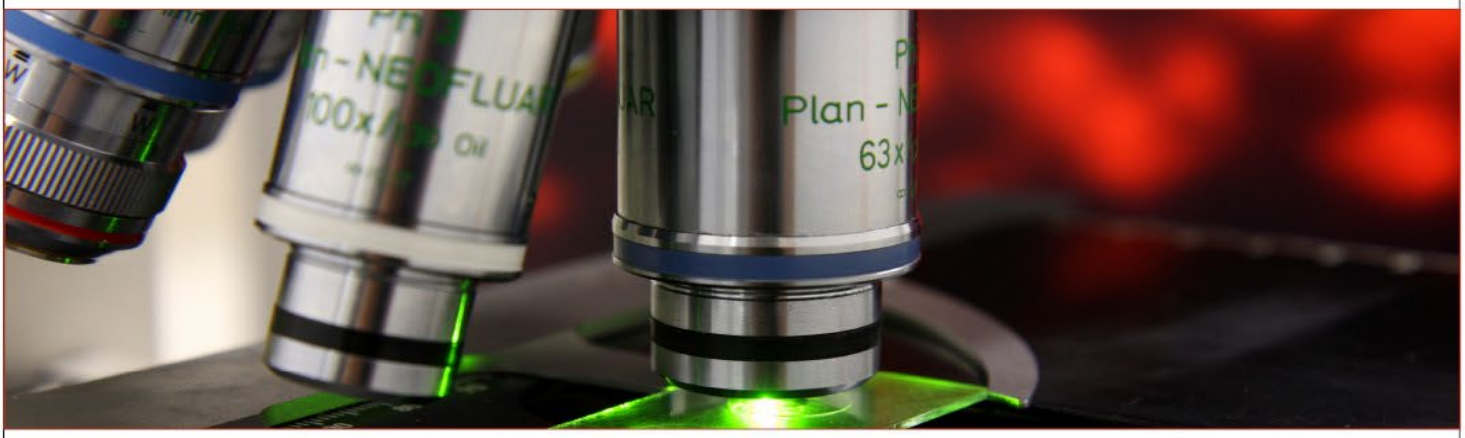
SÉMINAIRES ET CONFÉRENCES



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"Genetic landscape of an *in vivo* protein interactome"

The dynamics of protein-protein interaction (PPI) networks accurately map environmental perturbations to their molecular consequences in cells, but how and to what extent PPIs are modulated by genome-wide genetic variation is unknown. If a PPI network integrates both genetic and environmental effects to phenotype, then probing it could help define biochemical mechanisms underlying complex polygenic traits. In this seminar, I will describe a new approach to quantify the genotype-phenotype-environment relationship via piQTL (protein-interaction QTL) mapping analysis. Using inbred strains of the yeast *Saccharomyces cerevisiae* with ~12,000 single-nucleotide polymorphisms (SNPs) spread across the genome at a density of ~1 SNP/kb, we identified genomic loci that significantly modulate 61 *in vivo* PPIs. In contrast to QTL mapping via mRNA expression and protein abundance that are primarily affected by SNPs local to the gene (in "cis"), PPIs are dominantly affected by SNPs far (in "trans") from the gene locus of the interacting protein pair. Consistent with the small-world characteristic of PPI networks, these trans-acting SNPs, although distant in the genome, are enriched in genes that are neighboring nodes in the PPI network. We likewise discovered several SNPs in cryptic non-coding RNAs and post-transcriptional regulators (3' UTRs) with, counterintuitively, larger PPI-modulating effects than SNPs within protein-coding regions. Finally, we inferred known and novel mechanisms of action for four yeast and human drugs. This approach provides a roadmap to determine the mechanisms of polygenic and complex traits across the kingdom of life

Lundi 18 novembre 2024, 11h30

Pavillon Joseph-Armand-Bombardier, Salle : 1035

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