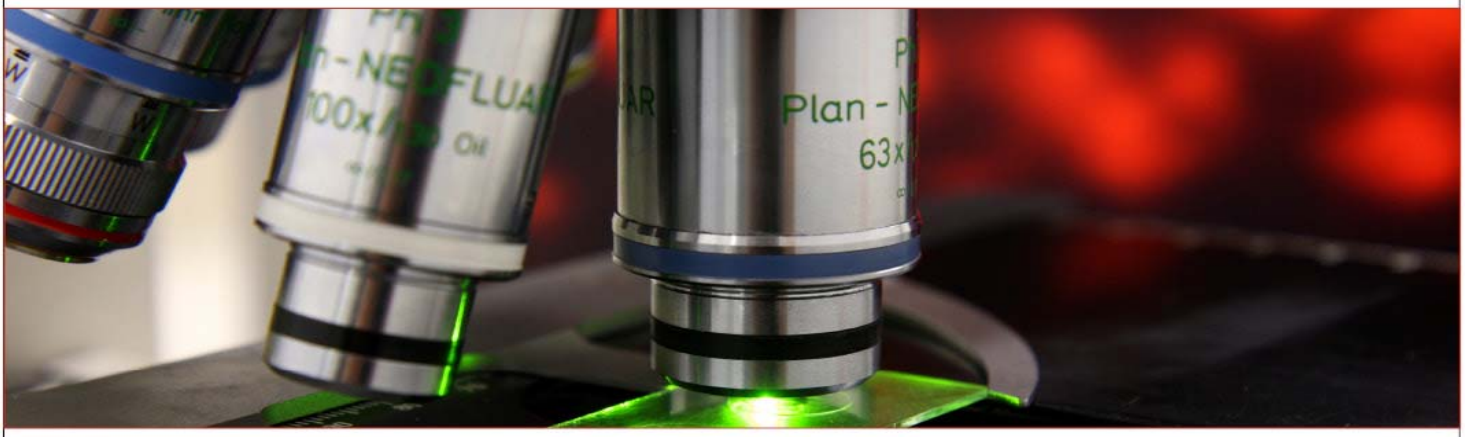
SÉMINAIRES ET CONFÉRENCES



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« Transient and functional protein-protein interactions perturb metabolon and cause gene dosage toxicity»

Gene dosage toxicity (GDT) is an important factor that determines optimal levels of protein abundances, yet its molecular underpinnings remain unknown. We demonstrate that overexpression of DHFR in *E. coli* causes a toxic metabolic imbalance triggered by interactions with several functionally related enzymes. Though deleterious in the overexpression regime, surprisingly, these interactions are beneficial at physiological concentrations, implying their functional significance *in vivo*. Moreover, we found that overexpression of orthologous DHFR proteins had minimal effect on all levels of cellular organization - molecular, systems, and phenotypic, in sharp contrast to *E. coli* DHFR. Dramatic difference of GDT between '*E. coli*'s self' and 'foreign' proteins suggests the crucial role of evolutionary selection in shaping protein-protein interaction (PPI) networks at the whole proteome level. We show how protein overexpression perturbs a dynamic metabolon of weak yet potentially functional PPI, with consequences for the metabolic state of cells and their fitness.

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Le mardi, le 1 août 2017, 12h00

Pavillon Roger-Gaudry
Salle : D-225

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