Biology Seminar

Western
UNIVERSITY · CANADA

12:30 - 1:30 pm
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WSC 240

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Systematic humanization of yeast biological processes to understand human biology, disease and evolution

The remarkable extent to which protein-coding genes are still functionally equivalent between humans and yeast emphasizes the power of a distant organism for studying human gene function. Several human genome sequencing studies have discovered extensive genetic polymorphism in these genes, including many rare variants that cause or predispose to diseases. Exploring how this variation contributes to cellular function and overall human health remains a challenge and has not matched the rate at which variants are identified. Our laboratory has already created hundreds of humanized yeast strains (Science, 2015; eLife, 2017; BioRxiv, 2019). Humanized yeast act as physical reagents to characterize human genetic variation, opening previously inaccessible chemical and genetic screens with the potential to ultimately treat diseases.

I will discuss our progress towards making and applying humanized yeast. Particularly, the humanization paradigm allows us to test if complete yeast and human systems are interchangeable in yeast. I will show our extensions of this work to humanize yeast biological processes in their entirety, focusing on the proteasome core, heme, and sterol biosynthesis pathways. The resulting strains carrying multiple human genes are more suitable for screening human genetic alleles. These engineered strains allow the simultaneous introduction of human genetic variants at various loci in an easily manipulated system for the study of human polygenic disease, providing a pathway-level activity measure for combinations of human variant alleles. If successful, it will lead to new insights into human genetic traits and epistatic interactions among genes belonging to the same genetic processes, which is still unachievable at this scale in mammalian cells.

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