MICROBIOLOGIE, INFECTIOLOGIE ET IMMUNOLOGIE

Université de Montréal

CONFÉRENCE

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Redox-mediated antimicrobial tolerance in bacteria and fungi

Antimicrobial tolerance allows non-resistant bacteria and fungi to survive aggressive drug therapy. Since tolerance is a major cause of treatment failure in the clinic, inhibiting its development has become a major challenge of the post-antimicrobial era. Nonetheless, over 60 years after its discovery, tolerance remains poorly understood. This phenotype is characteristic of bacteria and fungi that face stressful conditions, and I am interested in how redox-stress responses and antioxidant defenses drive antimicrobial tolerance. This seminar will present our latest findings on the contribution of antioxidant defenses to antimicrobial tolerance in bacterial (*Pseudomonas aeruginosa*) and fungal (*Saccharomyces cerevisiae*) systems. We found that superoxide dismutase (SOD) activity drives survival against antimicrobial challenge in both organisms. However, only the mitochondrial enzyme defends *S. cerevisiae* against antifungal challenge, whereas antibiotic tolerance in *P. aeruginosa* is strongly correlated with its total SOD activity. Moreover, SODs are key elements of a complex tolerance mechanism that involves a cross-talk between nutrient-deprivation and redox-stress responses to modulate drug accumulation in *P. aeruginosa*. Specifically, SODs modulate cyclopropane fatty acid levels in the membrane of stationary phase *P. aeruginosa,* which results in lower permeability to hydrophilic dugs via decreased levels of outer membrane porins. Future work will map drug tolerance redoxomes, *i.e.,* what redox-mediated alterations at proteomic and metabolomic levels are associated with drug tolerance, and whether host-imposed oxidative stress triggers multidrug tolerance. Ultimately, this work seeks to target enzymes implicated in redox-driven tolerance using repurposed drugs and microbiome-derived products to potentiate antimicrobial lethality.

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Pavillon Claire-McNicoll, salle Z-255

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