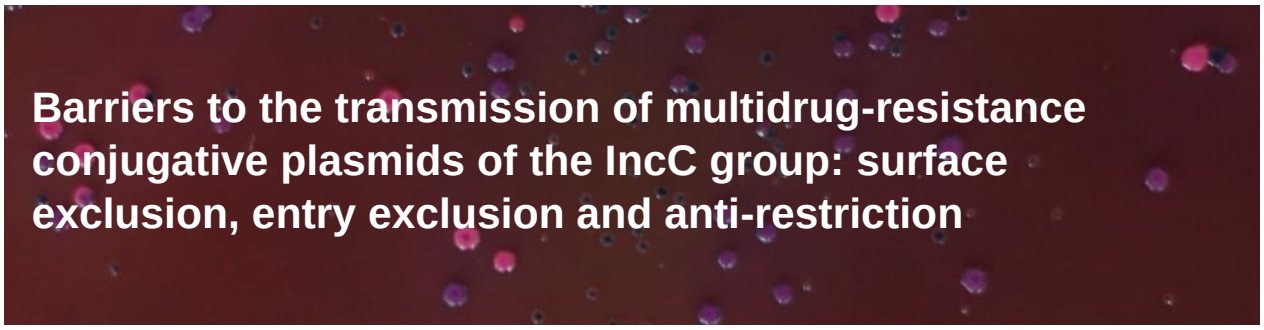
Université de Sherbrooke



Barriers to the transmission of multidrug-resistance conjugative plasmids of the IncC group: surface exclusion, entry exclusion and anti-restriction

MSc and PhD positions available at the Université de Sherbrooke

Research projects

Multidrug resistance to antibiotics has increased considerably over the past 40 years worldwide. Resistance genes are often passed on between bacteria by conjugative plasmids. Incompatibility group C (IncC) plasmids circulate in multidrug-resistant *Enterobacteriaceae* and *Vibrionaceae* commonly isolated in the environment, farm animals, food products derived from these animals, and humans. These plasmids pose a considerable threat to animal and human health because they frequently carry carbapenemase-like resistance genes, giving rise to the infamous CRE (carbapenem-resistant Enterobacteriaceae), against which treatment options are limited. IncC plasmids also facilitate the dissemination of various resistance genomic islands integrated into the chromosome of their bacterial host. The SGI1 (*Salmonella* Genomic Island 1) genomic island is a widespread example of islands transmissible by IncC plasmids. SGI1 confers a multidrug resistance phenotype in *Salmonella* isolated from human and chicken infections. We are seeking MSc and Ph.D. candidates for three CIHR-funded projects that aim to understand the barriers to the propagation of IncC plasmids and their interplay with SGI1. By understanding these mechanisms, we hope to leverage and exploit these barriers to identify new targets and molecules that could help curb the emergence of multidrug-resistant pathogens.

- **Project 1. Surface exclusion in IncC plasmids.** Surface exclusion prevents the redundant and futile exchange of a conjugative plasmid between donor cells. Our recent results indicate the existence of such a mechanism in IncC plasmids. The project aims to investigate the mechanism of surface exclusion and its extent to closely and distantly related plasmids. The proteins mediating surface exclusion and the host membrane receptors involved in the phenomenon will be researched and characterized. The student will also investigate whether and how SGI1 can escape surface exclusion mediated by IncC plasmids.
- **Project 2. Entry exclusion in IncC plasmids.** IncC plasmids also limit the redundant transfer of the same plasmid between donor cells via entry exclusion. This mechanism acts after the contact between partner cells has been established. Entry exclusion blocks DNA transfer by a poorly understood mechanism. This project aims to determine how DNA transfer is inhibited by investigating the interactions between the inner-membrane proteins TraG and EexC that mediate entry exclusion by acting in the donor and recipient cells, respectively.
- **Project 3. How do IncC plasmids resist or evade defence mechanisms encoded by their bacterial host?** IncC plasmids easily circumvent the barriers put in place by their bacterial hosts (CRISPR-Cas, restriction-modification systems) to prevent invasion by exogenous genetic material or bacteriophage attacks. These resistance mechanisms allow IncC plasmids to broaden their host spectrum and establish themselves in a wide variety of bacterial species pathogenic for humans. The study will study these resistance mechanisms, determine their prevalence in related plasmids, and characterize the molecular mechanisms allowing resistance.

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Hosting group

The Bacterial Molecular Genetics group is part of the Département de biologie of the Faculté des sciences of the Université de Sherbrooke (https://www.usherbrooke.ca). Our group aims to better our understanding of the molecular mechanisms that facilitate the exchange of genetic material between bacteria to find new molecular targets that can be used to fight against the emergence and spread of multidrug-resistant bacteria.

Our research group is funded by the Canadian Institutes of Health Research (CIHR), the Natural Sciences and Engineering Research Council of Canada (NSERC), as well as by provincial funds from the Fonds de Recherche du Québec (FRQ). The laboratory is equipped for carrying out biosafety level 2 microbiology, molecular biology and biochemistry experiments. For more information, please visit https://laboburrus.wordpress.com/

Profile of the candidates

We are seeking candidates who are curious, motivated and determined to understand complex molecular mechanisms. Ideal candidates will be fluent in French or English and have a strong background in microbiology, molecular biology, biochemistry or bacterial genetics. Research laboratory experience is required. The work will be performed in a biosafety level 2 laboratory.

Candidates for the doctorate must have completed their master's degree less than one year ago. Fast-track enrollment in the doctoral program is available only to applicants with exceptional transcripts and reference letters.

The Université de Sherbrooke values diversity, equality, equity and inclusion in employment within its community and invites all qualified people to apply. We are an inclusive group and encourage individuals of all sexual orientations and gender identities to join us.

How to apply

Candidates must provide the following documents in one single file in PDF format by e-mail to vincent.burrus@usherbrooke.ca:

- *An up-to-date curriculum vitae (French or English) with research articles and oral or poster communications, if applicable*
- *A cover letter (French or English)*
- *Three (3) reference letters*
- *A copy of the last diploma*
- *A copy of official transcripts of the last diploma*

Incomplete applications will not be considered. Candidates are encouraged to consult the Université de Sherbrooke website for information regarding the costs of graduate studies (tuition fees and living expenses) in Quebec before submitting their application.

See https://www.usherbrooke.ca/admission/couts-et-aide-financiere/