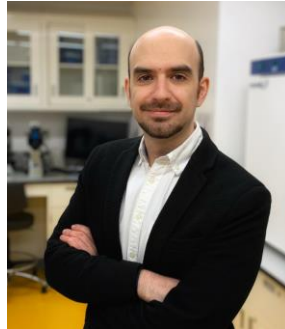


CONFÉRENCE

Conférence prononcée par **Dr Christopher Fernandez Prada**.



Jeudi 6 avril 2023 à 11h30

Université de Montréal, Pavillon Roger-Gaudry (B)
2900 boul. Édouard Montpetit (Chemin de la tour) Montréal, QC H3T 1J4
Salle : N-425-4

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I Extracellular vesicles and drug resistance: the ‘Matryoshka Trojan Horse’

We recently explored the composition of leishmanial EVs in the context of drug resistance. In this way, we were able to identify *L. infantum* EVs' core proteome, as well as the proteins specifically enriched in EVs released by drug-resistant (DR) parasites. We demonstrated for the first time that DR mechanisms can induce changes in the morphology, size, and distribution of EVs in *Leishmania*, with DR parasites releasing larger vesicles in comparison to their WT counterparts. Several virulence factors, transcription factors, and proteins encoded by DR genes were identified. Based on these exciting findings, we then explored the potential transfer of different traits of drug resistance from DR to naïve parasites. To date, horizontal gene transfer (HGT) events had never been demonstrated in eukaryotic parasites. Herein, we explore the DNA content of EVs derived from drug-resistant parasites, as well as their role in both intra- and interspecies HGT. NGS and PCR assays confirmed the enrichment of circular amplicons carrying drug-resistance genes associated with EVs. Transfer assays showed a marked shift in the drug-sensitivity profile of recipient parasites; this phenomenon was confirmed to be induced by the expression of genes transferred. Recipient parasites displayed enhanced growth and better control of ROS. Overall, our work provides the first evidence that EVs constitute an efficient platform for HGT, facilitating the rapid transmission of drug-resistance genes while increasing the global fitness of recipient parasites.

INVITÉ PAR

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