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Targeting ether lipid metabolism for anti-leishmanial chemotherapy

Rachel Zufferey
St. John's University, USA

Statement of the Problem: Leishmaniasis is a parasitic disease transmitted by female sandflies. This disease is endemic in the tropical and subtropical areas of the world, and affects at least 12 million people worldwide. Every year, at least 2 million new cases are reported and 350 million humans are at risk of contracting this disease in more than 88 countries. The treatment of leishmaniasis relies primarily on expensive, poorly effective chemotherapeutic drugs that exhibit several undesirable side effects and can be sometimes difficult to administer. In addition, the rising occurrence of leishmaniasis and appearance of drug resistant parasites make the development of more effective drugs a necessity for the prevention and treatment of leishmaniasis. The purpose of this study is to characterize enzymes involved in the biosynthesis of the virulence factor lipophosphoglycan in order to identify suitable targets for chemotherapy.

Methodology: Genes or enzymes of the ether lipid biosynthetic pathway were assessed, especially their involvement in lipophosphoglycan biosynthesis and in virulence.

Findings: The dihydroxyacetonephosphate acyltransferase enzyme *Lm*DAT localizes in the peroxisomes and is specific for palmitoyl-CoA as substrate. Furthermore, *Lm*DAT is essential for lipophosphogycan biosynthesis, growth of the parasite, survival during the stationary phase of growth, ether lipid generation and for causing disease in mice. Lastly, a null mutant of *Lm*DAT was found to mediate some protection in mice against an ulterior challenge of wild-type parasites.

Conclusion & Significance: *Lm*DAT may be a good target for chemotherapeutic intervention and the null mutant lacking *Lm*DAT may serve as a potential live vaccine candidate.

Biography

Rachel Zufferey is a Parasitologist, studying lipid metabolism in *Leishmania* and *Trypanosoma brucei*. She is an Associate Professor in the Department of Biological Sciences at St. John's University, Queens, NY, USA.

zufferer@stjohns.edu

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