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McGill researcher on a quest to cure disfiguring parasitic disease

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Eating a meal in a restaurant is one of those trivial, everyday activities we take for granted in the developed world. For Canadian aid worker Louisette Pouliot, however, the simple act of grabbing a quick bite at an outdoor eatery in Ouagadougou, the capital of the African nation of Burkina Faso, had profound implications for her life and health.

"I was in Ouagadougou in the fall of 2006 and ate outdoors at restaurants without having any insecticide with me," she recalled. "And I remember at least once sitting near a swimming pool, which was probably full of contaminated water."

When Pouliot returned home to Montreal, Quebec in 2007, she discovered she had contracted leishmaniasis, a devastating, disfiguring, and potentially fatal parasitic disease spread by insects. In her case, four three-centimetre-long scars formed on her legs which would not heal, even after an initial round of oral medication prescribed at McGill University's Centre for Tropical Diseases. Eventually, she needed regular injections of a powerful chemotherapy drug every day for 30 days to finally beat the infection.

"The side-effects of the drug were awful," Pouliot said. "My whole body became so stiff that I was walking like a very old woman.

Leishmania is rampant in Africa and other parts of the developing world, and like so many other neglected tropical diseases, it is difficult to treat. There are only a handful of effective drugs available, according to Dr.

Armando Jardim of McGill's Institute of Parasitology, and they are burdened with serious side-effects and concerns about their future effectiveness.

"The drugs themselves are extremely toxic," Jardim explained. "And in some parts of the world, drug resistance is developing. So there's a crying need for a new classes of molecules to treat Leishmania."

Jardim and a group of colleagues at McGill and the University of Victoria in British Columbia are hot on the trail of a totally new approach to treating Leishmania and related diseases like African Sleeping Sickness and Chagas' Disease, according to a study published in the Journal of Biological Chemistry. In particular, they are targeting a small microbody – or organelle – inside the parasite called a glycosome, which Jardim described as "a little bag that contains proteins and enzymes that are absolutely essential for the survival of the parasite.

"We believe there's some molecular machinery involved in recognizing the proteins that specifically must get into that organelle." he continued. "There must be a gateway that opens the membrane to allow the selective entry of protein into the glycosome. In the long term we predict that, if we can block the movement of proteins into this organelle, this will be lethal to the parasite. Right now we're trying to understand what the gateway looks like, how it opens and closes, and if there's a way we can block entry of proteins using small molecules or drug-like compounds."

Jardim cautions that this research is still in its infancy and candidate drugs for testing have not yet been selected. Nevertheless, he is optimistic that if and when new treatments are forthcoming, they will have far fewer side-effects than current drugs.

"Because the organelle we're targeting is not found in mammalian cells, we believe that development of drug that selectively target the assembly

of the glycosome, will have have low toxicity to the host."

For Pouliot, new treatments can't come soon enough. "I saw Leishmania scars on the legs of schoolchildren in Burkina Faso," she said. "It also affected a number of the adults I encountered. Our driver had the disease, for one, and another aid worker like me caught it. It's everywhere there."

Source: McGill University