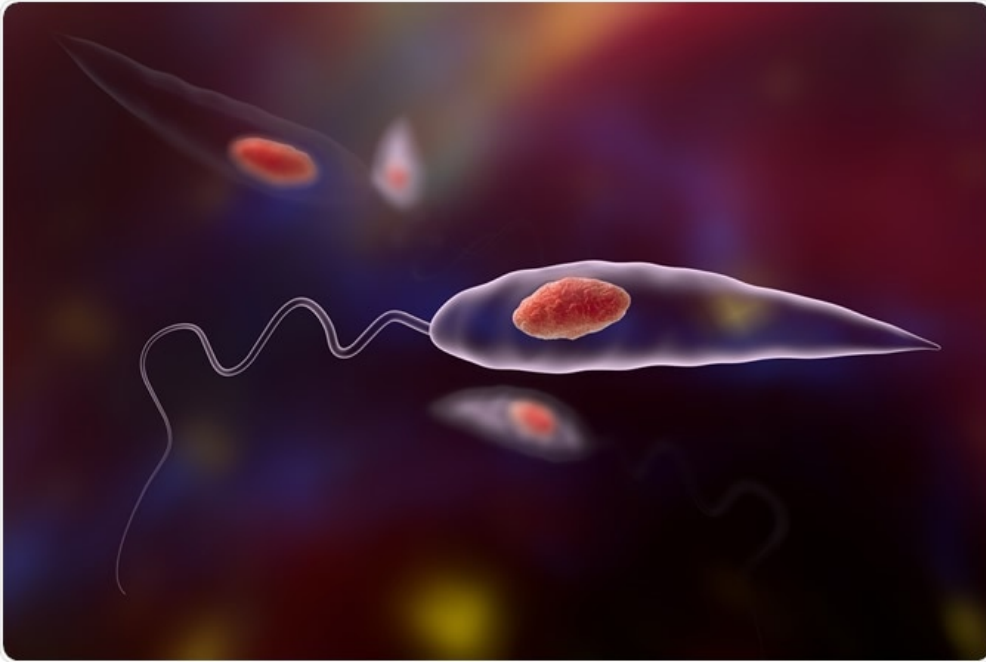


Discovery of the molecular mechanism behind the spread of a leishmania infection

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Researchers at the National Research Institute (INRS) have made a breakthrough to understand the reason for the virulence of the Leishmania parasite. Leishmania parasite is responsible for the development of leishmaniasis, which affects over 12 million people worldwide and is a chronic parasitic disease.

Leishmania Parasites That Cause Leishmaniasis, 3D Illustration – Credit:

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According to experts, Leishmania can harm the immune system, especially the macrophage defense system of the host's body. This resulted in skin or skin or systemic whole-body leishmaniasis. The researchers said that the underlying mechanism by which this parasite affects macrophages was previously unknown. The study, entitled "The secretory pathway of the host cell mediates the export of *Leishmania* virulence factors from the parasitophore vacuole" was published in the latest issue of the journal *PLOS Pathogens* .

Albert Descoteaux and Guillermo Arango Duque of the National Research Institute (INRS) in Quebec, Canada, have achieved a scientific breakthrough in the virulence strategy of the Leishmania parasite to infect cells of the immune system. Image Source: Communications, National Research Institute (INRS)

The team led by INRS Professor Albert Descoteaux collaborated with researchers from McGill University, Université de Montréal and Tohoku University to discover the molecular mechanism underlying the parasite In attacking the virus immune system helps the hosts. They explain that the macrophages or the defense cells of the first line of the body contain certain intracellular transport systems that help them transport various nutrients and other material in and out. These transport systems are used by the Leishmania parasite to transmit their virulence factors, the researchers found. Descoteaux explained in a statement: "It is as if a train is traveling through the various intracellular compartments where the parasite releases its virulence factors into the infected cell. Our study sheds new light on the pathogenesis of infections.

The team explains that Leishmania parasite infects the phlebotomine sandfly. When this infected fly bites mammalian hosts or humans, the infection is transmitted. Each parasite has two major molecules on its surface that cause it to infect the host cells. These virulence factors are called "GP63 metalloprotease and lipophosphoglycan (LPG)," the researchers wrote. Once the parasite infects the macrophages of the host cell, leishmania enters a vacuole called parasitophor. A vacuole is a pouch like an organelle in the cell. The parasite captures the vacuole with the help of virulence factors for its transport and the vacuole protects the parasite like a bubble around it. Through this vacuole, the parasite can also escape the body's defense system. In the host cell, the parasite thus finds a place where it can reproduce and multiply safely.

The question that this study answers is the mechanism by which the virulence factors of the parasite invade the macrophages and reach their goals. Guillermo Arango Duque, a doctoral student led by Professor Descoteaux, is the first author of this study. He explained, "Most research teams are studying the effects of virulence factors, but so far no one has understood how Leishmania can transfer virulence factors from the vacuole to the cytoplasm of the infected cell. We have just shown this with our work. He added, "We discovered that leishmania interacts with the membrane fusion machinery of the macrophage to export virulence factors from the vacuole.

Authors write: " *Leishmania* Promastigotes are internalized by phagocytes into a highly modified phagosome that promotes parasite growth and differentiation into the amastigote form. *Leishmania* uses surface-bound glycoconjugates such as GP63 metalloprotease and lipophosphoglycan to undermine the microbicidal

potential of the phagosome. "

The team found that the parasite can transmit its virulence factors – the GP63 and LPG molecules – to the other side of the vacuole membrane into which they have hacked. From there it was shown that the virulence factors also affect the other compartments of the cell. For example, these factors then reached the endoplasmic reticulum (ER) of the cell, which forms a large part of the cell's intracellular organ system. The ER is also linked to other parts of the intracellular structure, so that the virulence factors can easily spread across the ER.

The team studied the movements of these virulence factors in the cell using effective genetic tracking methods and found a unique method for stopping the movement of these virulence factors within the macrophages. They stopped the formation of two host proteins, sec22b and syntaxin-5. Once these proteins were blocked, the movement of virulence factors across the ER also stopped effectively, the team explained. These two proteins – sec22b and syntaxin-5 – are the key molecules that support the movement of molecules through the ER, they added.

The authors concluded that the ER / ERGIC-resident membrane fusion regulators Sec22b and syntaxin-5 revealed this. These host molecules were essential for the phagosomal escape of *Leishmania* virulence factors. These findings provide new insights into how *leishmania* sabotages the endomembrane system of the host cell to their own advantage. "

Professor Descoteaux stated, " To fully understand what enables the compartment in which Leishmania replicates to bind to other compartments of The infected host cell is a major advance. This pathway could also be used by other intracellular microorganisms, such as Mycobacterium tuberculosis, the causative agent of tuberculosis, or Legionella pneumophila, which causes Legionnaires' disease. "The researchers have therefore used the therapeutic potential to block this important way to stop the spread of this parasitic infection in the body and its replication.

The study was funded by the Canadian Institutes of Health Research (CIHR).

Reference:

The secretory pathway of the host cell mediates the export of Leishmania virulence factors from the parasitophorous vacuole, Guillermo Arango Duque, Armando Jardim, Étienne Gagnon, Mitsunori Fukuda, Albert Descoteaux, Published: July 29, 2019, <https://doi.org/10.1371/journal.ppat.1007982>, <https://journals.plos.org/plospathogens/article?id=10.1371/journal.ppat.1007982>[19659018<//