Team unveils new Leishmania virulence strategies

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Professor Albert Descoteaux of INRS-Institut Armand-Frappier Research Centre and his team have discovered novel virulence strategies employed by the *Leishmania* parasite. These scientific breakthroughs recently published in the prestigious *PLOS Pathogens* journal represent two important clues to understanding the cellular and molecular mechanisms governing the parasitic infections that cause leishmaniasis, a neglected tropical disease endemic in one hundred countries.

Leishmania uses macrophages, a type of white blood cell that neutralizes pathogenic micro-organisms, as host cells to circumvent the immune system. Upon infecting the macrophage, *Leishmania* enters a vacuole that it hijacks by manipulating the host cell membrane fusion machinery. Research results revealed that GP63, a zinc-dependent metalloprotease found on the surface of *Leishmania*, plays a central role in this process.

By promoting the cleavage of the VAMP8 membrane fusion regulator, GP63 allows *Leishmania major* to evade LC3-associated phagocytosis, a process whose purpose is to boost the antimicrobial properties of macrophages. Researchers have also found that cysteine peptidase CPB, which the parasite needs to survive in the macrophage, controls the virulence of *Leishmania mexicana* by regulating GP63 expression through an as yet unknown mechanism.

These two proteases occupy a central role in the biology of *Leishmania* and contribute to the formation and growth of parasitophorous vacuoles where the parasite develops and replicates. Researchers have thus

uncovered a new *Leishmania* virulence mechanism heavily influenced by GP63 and CPB proteases.

"Our results give us a better understanding of *Leishmania* pathogenesis and identify a new strategy used by intracellular pathogens to disrupt the host cell's antimicrobial," stated Professor Descoteaux. This discovery will be useful in developing preventive or therapeutic measures against leishmaniasis.

More information: Christine Matte et al, Leishmania major Promastigotes Evade LC3-Associated Phagocytosis through the Action of GP63, *PLOS Pathogens* (2016). DOI: 10.1371/journal.ppat.1005690

Pierre-André Casgrain et al. Cysteine Peptidase B Regulates Leishmania mexicana Virulence through the Modulation of GP63 Expression, *PLOS Pathogens* (2016). DOI: 10.1371/journal.ppat.1005658

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