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Toxoplasma gondii microneme proteins 1 and 4 recognize N-glycans of TLR2 and TLR4 triggers the initial immune response to the protozoan

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Toxoplasma gondii actively infect host cells through a dependent process of lectins release, called microneme proteins (MIC), from intracellular organelles. TgMIC1, TgMIC4 and TgMIC6 assembly a complex on *T. gondii* surface enabling the parasite to bind to host cells via carbohydrate recognition, since TgMIC1 binds to terminal sialic acid and TgMIC4 to terminal galactose. Our aim was to evaluate the carbohydrate-protein interaction between TgMIC1 and TgMIC4 with N-glycans of extracellular TLRs and the innate immune response triggered by this interaction. We observed that TgMIC1 and TgMIC4 (native complex and recombinant proteins) induced proinflammatory cytokines production, especially IL-12, by C57BL/6 mice dendritic cells (DCs) and macrophages similarly to TLR agonists, while TLR2-/-, TLR4-/-or DKO-TLR2-/-/TLR4-/- macrophages produced less IL-12 than wild type (WT) cells. Furthermore, we found that this activation was dependent on carbohydrate recognition since a punctual mutation in carbohydrate recognition domain (CRD) of TgMIC1 abrogated its capacity to induce IL-12 production by WT macrophages. Moreover, during the first hours of *T. gondii* infection, the absence of TLR2 and TLR4 resulted in lower IL-12 production by DCs. Finally, the infection of WT DCs and macrophages with parasites lacking TgMIC1 or both proteins (DKO-TgMIC1-/-/TgMIC4-/-) also resulted in impaired activation, indicated by lower IL-12 production, compared to infection with WT parasites. Since the decreased IL-12 production was observed in the first hours after infection, we found that TgMIC1 and TgMIC4 trigger the initial response to *T. gondii*, by recognizing N-glycans of TLRs. The established interactions and the resulting host cell activation may exert relevant biological role during *T. gondii* infection.

Biography

Camila Pinzan has completed her PhD at the age of 30 years from São Paulo University and her postdoctoral studies from São Paulo University School of Medicine. Currently she is doing her second post doc in University of Cambridge. She has published more than 8 papers in reputed journals.

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