

## **Enhancing the usefulness of transcriptome data in the context of *Leishmania*-infected macrophages with pathways biocuration and mathematical modelling.**

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The interaction between a parasite and its host is a fight for dominance. Who wins? How does disease progress? A multitude of factors determine the course of infection. These depend upon both the status of the host and the parasite. Omics data shed light on the multitude of activated mechanisms within the host-parasite interactome, by providing long lists of differentially expressed molecules. However, such data is a means for generating knowledge, not an end. The ultimate goal is to interpret this data to build a mechanistic understanding of the interactions at hand. Our work encompasses the biocuration, in the Reactome database, and computational modelling of pathways determining *Leishmania*-host interaction outcomes, using existing RNA-seq data. First, we conducted a systematic curation of published studies documenting different aspects of the *Leishmania*-host interaction. The “*Leishmania* infection pathway” included four sub-pathways: phagocytosis, killing mechanisms, cell recruitment, and *Leishmania* parasite growth and survival. As proof-of-principle of the usefulness of the released pathway, we used it to analyze two previously released transcriptomic datasets of human and murine macrophages infected with *Leishmania*. Our results provide insights on the participation of ADORA2B signaling pathway in the modulation of IL10 and IL6 in infected macrophages. Second, we combined transcriptomic data curation/analysis paired with dynamic computational modelling as a tool to study the macrophage permissiveness to the *Leishmania* infection. The model shows large-scale, unexplained shifts in the immunometabolic profile of *Leishmania*-infected macrophages in the 24 hours following infection. We proposed a mechanistic hypothesis that accounts for these dynamics, and furthermore explains the permissiveness of macrophages to infection in a pro-inflammatory environment usually associated with parasite elimination.