RNA binding proteins as trans-regulators impacting surveillance and infectivity in *Leishmania.*

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Leishmania spp. protozoan Kinetoplastids present peculiar gene expression fundamentally dependent upon post-transcriptional control. This elevates the importance of RNA binding proteins for gene regulation in these parasites. Building upon the mRBPome we isolated previously (Pablos, Ferreira et al., MCP, 2019), 70 mRNA-bound RBPs were selected from the three main *L.mexicana* lifecycle stages. A trans-regulator knockout clone library was created through barcoded CRISPR and screened for essential roles in cellular differentiation and macrophage or mouse infections. Of the 70 RBPs screened, 40 are essential to cell viability and 18 contribute to lifecycle progression to human-infective stages and/or parasite infectivity. Examination of individual knockout lines for amastigote-specific mRBPs showed normal promastigote growth dynamics, whereas infection of peritoneal macrophages was inhibited or ablated, suggesting essential roles of RBPs for amastigote viability and virulence. Immunoprecipitation of multiple mRBPs will identify associated transcript targets that may represent novel virulence factors.

Key words: *Leishmania,* RBP, RNA, Knockout, infection.