INVESTIGATING FUNCTIONAL DISTINCTIONS FOR TWO *LEISHMANIA INFANTUM* HOMOLOGUES OF THE POLY-A TAIL BINDING PROTEIN, PABP2 AND PABP3, THROUGH A COMPARATIVE ANALYSIS INVESTIGATING PABP2 PARTNERS IN THE PRESENCE AND ABSENCE OF THE NON-ESSENTIAL PABP3

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Abstract

Leishmania and related protozoa are unique in having their gene expression mainly regulated by post-transcripitional mechanisms acting upon their mRNAs. These likely involve the poly(A) binding protein (PABP), found at the 3' ends of most eukaryotic mRNAs. Three PABP homologs are found in *Leishmania* species, with PABP1 found associated with unique target mRNAs and protein partners, including translation factors, while PABP2 and PABP3 coprecipitate together and bind to a similar set of mRNAs and protein partners, distinct from those found with PABP1. PABP3 is the only one not essential in *Leishmania* and it is not found in *Trypanosoma* species. In order to better define roles for the *Leishmania* PABPs, we sought here to identify proteins bound to PABP2 in the absence of PABP3. Promastigotes from *L. infantum* cell lines lacking PABP3 were transfected with a plasmid allowing the ectopic expression of PABP2 having a C-terminally tagged HA epitope. PABP2-HA was then immunoprecipitated followed by identification of co-precipitated protein partners through mass spectrometry. The results were compared with PABP2-HA data obtained in the presence of PABP3, and with data from similar experiments with PABP1 and PABP3. Overall, a large set of protein partners were found with greater association with PABP2 when PABP3 is missing. These include PABP1 and several of its known partners, including the EIF4E4 and EIF4G3 translation factors, the RNA binding protein RBP23 and a NTF2 domain-containing protein (LINF_180008000), some not previously detected with PABP2. Nevertheless, several known PABP2 partners remain associated with the tagged proteins including other RNA binding proteins, such as DRBD2 and ZC3H39, and another NTF2 domain protein (LINF_210009700). PABP2 does not then seem to require PABP3 in order to associate with its most abundant protein partners, but PABP3 is needed to prevent its association with PABP1 partners and might be involved in modulating the PABP2 interactions.

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