MOLECULAR ASPECTS OF *LEISHMANIA*-SAND FLY INTERACTIONS

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The phlebotomine vectors of Leishmaniasis are in some cases only permissive to the complete development of the species or strain of *Leishmania* that they transmit in nature. The parasite-sand fly interactions that control this specificity are related to differences in the ability of the parasite to inhibit or to resist killing by proteolytic enzymes released into the midgut soon after blood feeding, and/or to maintain infection in the midgut during excretion of the digested bloodmeal. In each case surface expressed or released phosphoglycan-containing molecules appear to promote parasite survival. The evidence that the surface lipophosphoglycan (LPG) mediates promastigote attachment to the midgut epithelium so as to prevent their loss during bloodmeal excretion is especially strong based on the comparison of development in sand flies using LPG deficient mutants. LPG displays inter-species polymorphisms in their phosphoglycan domains that in most cases can fully account for species-specific vector competence. The ability of *P. papatasi* to transmit only *L. major* sp. has been attributed to the unique, highly substituted nature of *L. major* LPG that provides for multiple terminally exposed ß-linked galactose residues for binding, suggesting that *P. papatasi* midguts express lectin-like molecules with specificity for poly-galactose epitopes. *PpGalec*, a cDNA encoding a novel tandem repeat galectin, was identified by high throughput screening of a midgut library of *P. papatasi*. Recombinant PpGalec bound specifically to *L. major* promastigotes bearing poly-gal epitopes on their LPG, and native PpGalec was shown to be used by *L. major* as a receptor for mediating its specific binding to the *P. papatasi* midgut. This is the first description of the nature and specificity of a sand fly midgut LPG receptor; and the first indication that insect galectins, which have been mainly associated with embryonic development or innate immunity against pathogens, can be exploited by parasites to promote their survival and transmission.