

## Stuck in the throat: Dissection of *Leishmania* parasite adhesion in the sand fly vector

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Within its sand fly vector, *Leishmania* parasites have two major morphological forms, a motile promastigote and a haptomonad, which is attached to the stomodeal valve through a shortened and modified flagellum. Dissecting haptomonad development and adhesion is critical to understanding parasite transmission. We have previously generated high-resolution 3D models of haptomonads attached to the stomodeal valve using volume electron microscopy. This showed that the adhesion complex consisted of filaments that run through the flagellum to an electron-dense plaque, with connections across to the surface of the valve. Using comparative proteomic approaches, we identified three Kinetoplastid-Insect Adhesion Proteins (KIAPs) that locate to different regions of the attachment complex. These proteins are present in other kinetoplastid parasites, suggesting a common mechanism of adhesion in the kinetoplastid parasites. Deletion analysis compromised *Leishmania* adhesion both *in vitro* and in the sand fly, confirming that we have identified the first critical components of the adhesion complex. Infection of sand flies with *Leishmania* parasites results in damage to the cuticle surface of the valve and distension of the midgut by secretion of the promastigote secretory gel, enhancing parasite transmission. Interestingly, we found that loss of parasite adhesion in the sand fly caused reduced distension of the midgut, with no observable damage to the cuticle surface of the valve. Overall, our study provides the first molecular insights into a kinetoplastid parasite vector adhesion interface and highlights the importance of *Leishmania* adhesion for the modification of the sand fly gut environment.