Type of presentation: Invited

LS-7-IN-6080 A structural understanding of how to build, divide and change a trypanosome parasite cell

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The precise shape and form of single celled parasites enabled their early classification as etiological disease agents based solely on microscopy. The changes in shape and form of the kinetoplastid parasites (amastigote, promastigote, epimastigote, slender/stumpy trypomastigotes) have evolved for particular pathogenicity niches and coordinate with cell functions at different lifecycle stages.

The cytoskeleton defines their shape and form, providing a clear rationale for the importance of understanding how it functions to define each form. Leishmania, Trypanosoma brucei, T. cruzi still represent major threats to world health and agricultural development. Trypanosomes in sub-Saharan Africa cause Human African Trypanosomiasis and the livestock disease nagana.

We have studied the structural organization of these parasites using light and electron microscopy techniques ranging form immunofluorescence, ImmunoEM, EM tomography, SEM, serial block face SEM etc. The T. brucei trypomastigote cell form possesses a single flagellum that is attached to the side of the cell body. The Basal Body duplicates in the cell cycle, performs a 3D traverse around the old flagellum axis, facilitating kinetoplast (mitochondrial genome) segregation and new Flagellar Pocket formation. Concomitantly, the new flagellum extends outside of the cell with its tip attached to the side of the old flagellum via the mobile, transmembrane Flagella Connector junction. Internally, a Flagellum Attachment Zone (FAZ) filament and associated microtubule quartet extend forming a seam in the sub-pellicular microtubule array. Double transmembrane complexes then assemble to cross-link the flagellum to the cell body. I will describe this process and then show how it is modified bloodstream form parasites and in Leishmania parasites that can reduce the motile flagellum to a short, immotile sensory 9+0 and 9v sensory flagellum in the amastigote form. In addition I will describe, using freeze fracture approaches, how these cytoskeletal structures define membrane domains that characterize the cell body, flagellum and flagellar pocket.

These structural features will be discussed in relation to the pathogenicity features of these parasites.