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High-resolution imaging of a trypanosome surface coat protein and its interaction with antibodies

The African trypanosome, T. brucei, is a unicellular pathogen responsible for sleeping sickness in humans and nagana in animals. Following transmission by the tsetse fly, the parasite replicates extracellularly in the bloodstream, where it faces constant exposure to the host's immune response. To evade this immune challenge, T. brucei employs an effective strategy of antigenic variation, achieved by switching to a new, antigenically distinct surface coat. This coat is primarily composed of Variant Surface Glycoprotein (VSG), and the trypanosome genome contains a repertoire of over 2,000 VSG genes to facilitate long-term survival.
While significant advancements have been made in elucidating the 3D structures of VSGs, structural information regarding VSG-antibody complexes has remained elusive. We have successfully resolved the cryo-electron microscopy (cryo-EM) structure of a VSG dimer bound to two Fab fragments at an overall resolution of 2.4 Å. This study marks the first detailed examination of a VSG epitope, allowing us to map the amino acids involved in the interaction.
In addition to investigating the interactions of purified VSG-antibody complexes, we aim to utilize cryo-EM tomography to explore antibody interactions on densely packed VSG vesicles and characterize the oligomeric state of VSGs on the trypanosome surface. By elucidating the protein packing, we hope to identify new interaction sites among individual VSG building blocks, which could serve as potential targets for destabilizing the trypanosome coat.

Research type

Basic research

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