

# Native Structure of Mosquito Salivary Protein Uncovers Domains Relevant to Pathogen Transmission

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Female mosquitoes inject saliva into vertebrate hosts during blood feeding. This process transmits mosquito-borne human pathogens that collectively cause ~1,000,000 deaths/year. Among the most abundant and conserved proteins secreted by female salivary glands is a high-molecular weight protein called salivary gland surface protein 1 (SGS1) that facilitates pathogen transmission, but its mechanism remains elusive. Here, we determine the native structure of SGS1 by the cryoID approach, showing that the 3364 amino-acid protein has a Tc toxin-like Rhs/YD shell, four receptor domains, and a set of C-terminal daisy-chained helices. These helices are partially shielded inside the Rhs/YD shell and poised to transform into predicted transmembrane helices. This transformation, and the numerous receptor domains on the surface of SGS1, are likely key in facilitating sporozoite/arbovirus invasion into the salivary glands and manipulating the host's immune response.