MS110.O06

Structure of viral spindles, in vivo crystals boosting insecticidal activity

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Entomopoxviruses (EV) produce two types of microcrystals in infected cells: virus-containing spheroids representing their main infectious form; and spindles, bipyramidal crystals of the viral fusolin protein, that contribute to the oral virulence of these viruses. In co-feeding experiments, spindles also enhance the insecticidal activity of unrelated insect pathogens, which suggested their use as bioinsecticide additives. To understand how fusolin contributes to virulence and assembles in vivo, we determined the structures of EV spindles by X-ray microcrystallography using crystals isolated from EV-infected common cockchafers. This structure reveals that fusolin is composed of a fibronectin III domain followed by an extended C-terminal molecular arm (CT). The globular domain is structurally homologous to CBP21, a protein that is secreted by Gram-negative bacteria to degrade chitin as a source of energy. Like CBP21, fusolin has all the hallmarks of a lytic polysaccharide monooxygenase enzyme (LPMOs) with two conserved histidine residues forming a copper binding site and a prominent di-tryptophan motif positioned to bind the planar surface of crystalline chitin. The LPMO domain assembles in vivo into ultra-stable crystals crosslinked by CT. This molecular arm mediates the formation of domain-swapped dimers and their assembly into a crystalline lattice stabilized by a 3-D network of inter-dimer disulfide bonds. Overall, the molecular organization of spindles indicates a mode of action where controlled released of the LPMO domain of fusolin by proteolytic removal of the CT extension leads to disruption of the chitin-rich peritrophic matrix of larvae to facilitate the initial steps of viral invasion of the host.

Keywords: Virus assembly, Virulence, In vivo crystallization