

Signalling networks during *Toxoplasma* invasion: calcium provides both positive and negative control of organelle secretion.

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Abstract

Apicomplexans are intracellular parasites that use coordinated release of distinct secretory organelles to mediate the different stages of host cell invasion and parasitism. Micronemes are released first to enable extracellular motility and host recognition, rhoptries during invasion, and dense granules to establish parasitism once inside the host cell. cGMP and Ca²⁺ signalling are known to induce microneme secretion, but these signalling pathways are poorly understood, and controllers of rhoptry and dense granule release are unknown. We show that the apical complex controls the relay of cGMP-mediated responses to Ca²⁺ release that, in turn, is required for microneme secretion. We show that Ca²⁺ release also provides a negative signal for dense granules, presumably to limit their inappropriate secretion during extracellular parasite stages. These data therefore indicate that inverse responses to Ca²⁺ signalling provides a mechanism for coordinated secretory patterns that control the major events of host cell invasion and parasitism.