Regulation of mitochondria by proteolysis

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Proteolysis is increasingly documented as a method of regulation of mitochondrial function. Our studies of rhomboid-family proteins' roles in organelles show that this is also the case in the social amoeba *Dictyostelium discoideum*, in which four of these membrane-bound, evolutionarily ubiquitous, serine proteases are found. Rhomboid proteases act on disparate substrates in different organisms so far studied, but their mode of action is conserved: their location in the membrane means that their membrane-tethered substrates can act in signalling upon release, or be activated, by rhomboid-mediated cleavage. Among eukaryotic rhomboids is the mitochondrial protease 'PARL', which ensures the maintenance of the structural and functional integrity of mitochondria and plastids, but we have found that other *Dictyostelium* rhomboids also affect the organelle. Studying the development and behaviour of *Dictyostelium*, a microbial model organism with a complex life cycle that includes uni- and multicellular stages, allowed investigation of the role of rhomboids in unicellular vegetative growth, multicellular development and sporulation, phagocytosis, and response to the environment. We found that two rhomboid-null mutants gave rise to changes in development, *rhmA* altering the response to chemoattractants and demonstrating decreased motility in general, whereas *rhmB* null cells had slower growth rates with decreased response to folic acid. RhmA, although located in the contractile vacuole, affects the ultrastructure of mitochondria, and RhmB-GFP fusions protein was localised to the mitochondrion. qPCR analysis revealed RhmA and RhmB transcript levels peaking during the multicellular growth phase and transcriptional networks suggest the *Dictyostelium rhmA* is regulated along with the orthologues of *Saccharomyces cerevisiae* mitochondrial rhomboid substrates.