A comparative study of malaria parasite cell death following exposure to titratable lethal doses of antimalarial drugs

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Human malarial parasites undergo regulated cell death (RCD) in response to heat-stress. This appears to be a survival strategy employed by the parasite to control the level of parasitaemia, such that is doesn't overwhelm and then kill the host. Induction of RCD following exposure to lethal doses of known antimalarial drugs highlights the potential of targeted induction of RCD in the search for new molecular targets for antimalarial drug development. To date, however, side-by-side comparisons of these studies have proven conflicting, essentially as the actual extent of kill induced by the various treatments used is not defined. Using a novel bioluminescent assay of cell viability, a defined and titratable loss of viability using different drugs can be affected. Here we report our initial comparative studies of ultrastructural markers of cell death using 4-amino quinolines, amino alcohols and artemisinin analogues. Moreover we report that mitochondrial membrane collapse ($\Delta\psi_m$) provides an early biochemical marker for cell death on drug perturbation. This study aims to continue to compare and contrast morphological, molecular and biochemical markers induced on cell death to dissect the RCD cascade, initiating an evaluation of potential targets for future RCD-inducing therapies.