Finding Novel Malarial Proteases Using Systems Approaches

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Abstract

Malaria continues to be one of the most severe global infectious diseases, responsible for 1-2 million deaths yearly. The rapid evolution and spread of drug resistance in parasites has led to an urgent need for the development of novel antimalarial targets. Proteases are a group of enzymes that play essential roles in parasite growth and invasion. In this study, combining a comparative genomics approach and a machine learning approach, we identified the complement of proteases (degradome) in the malaria parasite *Plasmodium falciparum* and its sibling species, providing a catalog of targets for functional characterization and rational inhibitor design. Further network analyses revealed that these proteases appear to play diverse roles in metabolism, cell cycle regulation, heat shock response, signal peptide processing, transcriptional regulation, and signal transduction. Novel protease targets and previously unrecognized members of the protease-associated sub-systems provide new insights into the mechanisms underlying parasitism, pathogenesis and virulence.