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Artemisinin resistance in P. falciparum: Probing the interacting partners of Kelch13 protein in parasite

Abstract:

Objectives: Artemisinin (ART) resistance in Plasmodium is threatening the artemisinin combination therapies—the first line of defence against malaria. ART resistance has been established to be mediated by the Plasmodium Kelch13 (PfK13) protein. For the crucial role of PfK13 in multiple pathways of the Plasmodium life cycle and ART resistance, it is imperative that we investigate its interacting partners.

Methods: We recombinantly expressed PfK13-p (Bric a brac/Poxvirus and zinc finger and propeller domains), generating anti-PfK13-p antibodies to perform co-immunoprecipitation assays and probed PfK13 interacting partners. Surface plasmon resonance and pull-down assays were performed to establish physical interactions of representative proteins with PfK13-p.

Results: The co-immunoprecipitation assays identified 17 proteins with distinct functions in the parasite life cycle– protein folding, cellular metabolism, and protein binding and invasion. In addition to the overlap with previously identified proteins, our study identified 10 unique proteins. Fructose-biphosphate aldolase and heat shock protein 70 demonstrated strong biophysical interaction with PfK13-p, with KD values of 6.6 µM and 7.6 µM, respectively. Additionally, Plasmodium merozoite surface protein 1 formed a complex with PfK13-p, which is evident from the pull-down assay.

Conclusion: This study adds to our knowledge of the PfK13 protein in mediating ART resistance by identifying new PfK13 interacting partners. Three representative proteins—fructose-biphosphate aldolase, heat shock protein 70, and merozoite surface protein 1—demonstrated clear evidence of biophysical interactions with PfK13-p. However, elucidation of the functional relevance of these physical interactions are crucial in context of PfK13 role in ART resistance.

Biography

Preeti Chaudhary completed my PhD from IGNOU University, New Delhi and Host-Parasite Interaction Biology Group, ICMR-National Institute of Malaria Research, New Delhi, India under the supervision of professor Neera Kapoor and Dr. Kailash C. Pandey (Scientist-F) and I have published more than 7 papers in reputed journals.