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hAgo2-miRNAs complex and microparticles play resistant roles during blood stage of *P. falciparum* infection

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Red Blood Cells (RBCs) targeted by Haemosporina parasites especially the *Plasmodium* parasites, can shed vesicles to regulate host immune response. In this study, we demonstrated that under the conditions of *Plasmodium* invasion, normal RBCs (with normal hemoglobin A) could actively export a large number of microparticles (MPs) to infected RBCs. We found that in the infected RBCs, human argonaute 2 (hAgo2) protein complexes with hundreds of human miRNAs (hmiRNAs) inside the parasites, and these hAgo2-miRNA complexes were transferred from uninfected RBCs by MPs. The hAgo-binding miRNAs were immunoprecipitated with anti-hAgo2 antibody and sequenced by high throughput RNA-seq. Among the identified miRNAs, miR-451 and miR-140 are predicted to target the mRNAs of a critical parasite antigen - *Plasmodium falciparum* erythrocyte membrane protein 1 (PfEMP1). Our data indicate that miR-451 and miR-140 can down-regulate the expression of *var* genes of malaria by targeting the untranslated regions (UTR) of their mRNAs; depleting hAgo2 leads to accelerated parasite infection in culture; and MPs can protect RBCs from the infection. Our results demonstrate for the first time that normal RBCs are able to export Ago2-miRNA complexes via MPs to infected RBCs, providing evidence that mature RBCs have the innate ability of resisting malaria infection. This study may also help explain why RBC-related genetic mutations tend to exist in malaria endemic areas with a long history of heavy disease burden.

Biography

Heng Wang worked as Physician for 12 years and did her Postdoctoral studies from Naval Medical Research Institute, USA. She is the Director of the Laboratory of Molecular Parasitology at Institute of Basic Medical Sciences/Chinese Academy of Medical Sciences, School of Basic Medicine/Peking Union Medical College. She is Vice-President of Chinese Academy of Parasitology/Chinese Academy of Zoology and has published 25 papers in SCI journals and more in Chinese.

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