TRAMP-CSS complex is essential for hepatocyte and erythrocyte infection by *Plasmodium berghei* zoites

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Abstract

Plasmodium sporozoites invade mosquito salivary glands, mammalian blood vessels in the skin and the hepatic parenchyma to ultimately enter inside hepatocytes and produce thousands of erythrocyte-invasive merozoites. Despite the importance of these steps in early malaria infection, little is known about their molecular basis. Here, using a rodent model and *in-vivo* conditional mutagenesis, we show the role of the TRAMP and CSS (TC) complex in *P. berghei* (Pb) sporozoite and merozoite infectivity. Conditional gene excision of these molecules did not significantly alter invasion of mosquito salivary gland by sporozoites, nor their motility or cell wounding activities. However, conditionally knocked out (cKO) sporozoites displayed impaired cell entry and development inside hepatoma cells. Similarly, cKO merozoites could not establish blood infection *in-vivo*, indicating that the Pb TC complex is essential for erythrocyte invasion. The multi-stage and essential role in hepatocyte and erythrocyte infection renders this complex a promising vaccine target and opens novel perspectives to unravel the mechanisms underlying *Plasmodium* entry into different cell types.