

Insights: Publications

Cyclic GMP balance is critical for malaria parasite transmission from the mosquito to the mammalian host

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Transmission of malaria occurs during Anopheles mosquito vector blood meals, when Plasmodium sporozoites that have invaded the mosquito salivary glands are delivered to the mammalian host. Sporozoites display a unique form of motility that is essential for their movement across cellular host barriers and invasion of hepatocytes. While the molecular machinery powering motility and invasion is increasingly well defined, the signaling events that control these essential parasite activities have not been clearly delineated. Here, we identify a phosphodiesterase (PDEy) in Plasmodium, a regulator of signaling through cyclic nucleotide second messengers. Reverse transcriptase PCR (RT-PCR) analysis and epitope tagging of endogenous PDEy detected its expression in blood stages and sporozoites of Plasmodium yoelii. Deletion of PDEy (pdey(-)) rendered sporozoites nonmotile, and they failed to invade the mosquito salivary glands. Consequently, PDEy deletion completely blocked parasite transmission by mosquito bite. Strikingly, pdey(-) sporozoites showed dramatically elevated levels of cyclic GMP (cGMP), indicating that a perturbation in cyclic nucleotide balance is involved in the observed phenotypic defects. Transcriptome sequencing (RNA-Seq) analysis of pdey(-) sporozoites revealed reduced transcript abundance of genes that encode key components of the motility and invasion apparatus. Our data reveal a crucial role for PDEy in maintaining the cyclic nucleotide balance in the malaria parasite sporozoite stage, which in turn is essential for parasite transmission from mosquito to mammal.

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