

Abstract:

Malaria disease severity is correlated with the levels of infected red blood cells (iRBCs) adhering within blood vessels. Our research has revealed that an RNA Polymerase III (RNA Pol III)-dependent process regulates pathogen growth and the expression of a key virulence factor in response to external factors. This discovery links the sequestration of *P. falciparum* iRBCs to a specific group of non-coding RNAs transcribed by Pol III. Moreover, we identified the *P. falciparum* Maf1 protein as a crucial regulator of transcription by Pol III, essential for both maintaining cellular balance and by responding to environmental stimuli. Previous studies have linked changes in iRBC adhesion capacity to seasonal asymptomatic malaria infections, although the reasons behind this remain unclear. Our findings show that in *P. falciparum*, RNA Pol III transcription is reduced in samples taken from asymptomatic individuals during the dry season from the Gambia. Additionally, we have discovered seasonal variations in plasma metabolites among individuals, with evidence suggesting these differences can influence Pol III activity. Our results introduce a novel perspective that contributes to our understanding of *P. falciparum* virulence. Furthermore, it establishes a connection between this regulatory process and the occurrence of seasonal asymptomatic malaria infections.