

Six Genes Are Preferentially Transcribed by the Circulating and Sequestered Forms of *Plasmodium falciparum* Parasites That Infect Pregnant Women.

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In areas of stable malaria transmission, susceptibility to *Plasmodium falciparum* malaria increases during first pregnancy. Women become resistant to pregnancy malaria over successive pregnancies as they acquire antibodies against the parasite forms that sequester in the placenta, suggesting that a vaccine is feasible. Placental parasites are antigenically distinct and bind receptors, like chondroitin sulfate A (CSA), that are not commonly bound by other parasites. We used whole-genome-expression analysis to find transcripts that distinguish parasites of pregnant women from other parasites and employed a novel approach to define and adjust for cell cycle timing of parasites. Transcription of six genes was substantially higher in both placental parasites and peripheral parasites from pregnant women, and each gene encodes a protein with a putative export sequence and/or transmembrane domain. This cohort of genes includes *var2csa*, a member of the variant PfEMP1 gene family previously implicated in pregnancy malaria, as well as five conserved genes of unknown functions. Women in East Africa acquire antibodies over successive pregnancies against a protein encoded by one of these genes, *PFD1140w*, and this protein shows seroreactivity similar to that of VAR2CSA domains. These findings suggest that a suite of genes may be important for the genesis of the placental binding phenotype of *P. falciparum* and may provide novel targets for therapeutic intervention.