A role for the *pir* gene family in establishing chronic *Plasmodium* infections

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Understanding how *Plasmodium* transmission is sustained in the face of increased control efforts is essential to eradicate malaria. In low malaria transmission settings, long-lasting infection increases the likelihood of the parasite completing its life cycle. It is widely accepted that establishment of chronic infection involves evasion of adaptive immunity by antigenic variation of *var* genes. However, these genes have been identified in only two human malarias: *P. falciparum* and *P. knowlesi*. So how long-term infection is established in *P. vivax, P. malariae* and *P. ovale* is unclear. Here we use the rodent malaria, *P. chabaudi* AS, to understand how chronic infections are established in the absence of *var* genes. Using global transcriptomic and phenotypic approaches, we demonstrate that, among a clonally variant population, only a minority of parasites expressing one of several clusters of virulence-associated *pir* genes establish a chronic infection. This clonal selection is independent of

adaptive immunity, showing that non-*var*-containing *Plasmodium* species use mechanisms distinct from classical antigenic variation. Furthermore, *pir* genes being common to most species of *Plasmodium* this process may be a more universal way of establishing chronic *Plasmodium* infections.