The Invasion and Depredation of the Human Reticulocyte by *Plasmodium vivax*

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**Abstract**

Vivax malaria affects 100s of millions each year, causing a particularly heavy economic and social burden to Indonesia, India, Burma and Cambodia. The parasite responsible for this relapsing disease; *Plasmodium vivax*, specifically targets reticulocytes (immature red blood cells) for invasion. Despite the importance of this disease, little is known about its pathobiology, especially its invasion process.

In an attempt to unravel these mysteries we first needed to revisit the neglected study of reticulocyte maturation (Heilmeyer reticulocyte classes I-IV). We show for the first time that significant biomechanical and immunophenotypical changes associated with reticulocyte maturation play an important part in the invasion of *P. vivax*. We also show that *P. vivax* completely remodels the reticulocyte dramatically altering its shear modulus (becoming highly deformable), cytoadhesive and nanoterrain characteristics within <3 hours of invasion.

Aside from the important pathophysiological consequences of the above information, our data brings us very close to the discovery of the allusive primary receptor-ligand of *P. vivax*; which promises to be a vital target for future vivax malaria vaccine strategies.

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