

## **The role of neutrophil elastase in severe *Plasmodium knowlesi* malaria**

The most common malaria in Malaysia is caused by animal-to-human transmission of monkey malaria parasites from its natural monkey hosts to humans via mosquito bites. As the immune system responds, white blood cells such as neutrophils are recruited, activated and release products with cell-killing activity. The products released kill indiscriminately, hence their overproduction due to increasing parasite numbers results in severe disease. The project aims to shed light on the potential role of neutrophils in severe malaria. These findings have implications for development of new strategies to prevent host organ damage and help clinicians provide better treatment for this monkey malaria.

### **Abstract**

Neutrophils are crucial in human innate immune response against external pathogens, including *Plasmodia* parasites responsible for malaria. Previous studies have shown that neutrophil activation products inhibit the growth of *P. falciparum* parasites, but also positively correlate with parasite biomass, mediating host organ damage, and potentially contributing to severe disease. This study investigated the role of neutrophil elastase (NE), a marker of neutrophil activation, in *P. knowlesi* malaria pathogenesis. Plasma samples were collected from 200 consenting knowlesi malaria patients from Sabah, Malaysia. Quantitative enzyme-linked immunosorbent assay (ELISA) revealed a correlation between plasma NE concentrations with parasite counts and other indicators of disease severity. Immunofluorescent microscopy was carried out to enumerate neutrophil extracellular traps as a secondary marker of neutrophil activation. The results showed that plasma NE concentrations were higher in severe malaria than in uncomplicated cases ( $p < 0.001$ ). Additionally, among the severe malaria cohort, patients who met WHO severity criteria for jaundice were observed to have higher plasma NE concentrations ( $p < 0.001$ ), suggesting a role in hepatocellular damage. These preliminary findings suggest that enhanced neutrophil activation plays a role in the pathogenesis of knowlesi malaria and may contribute to severe disease if left unregulated during routine treatment.

### **Keywords**

Severe malaria, *Plasmodium knowlesi*, neutrophils, Malaysia.