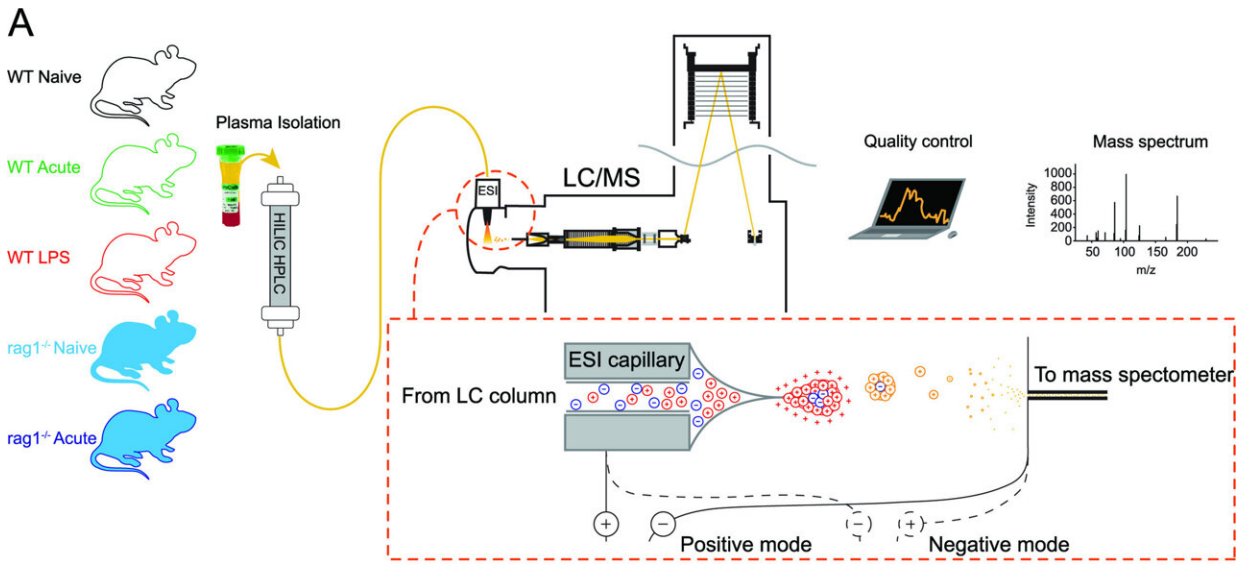
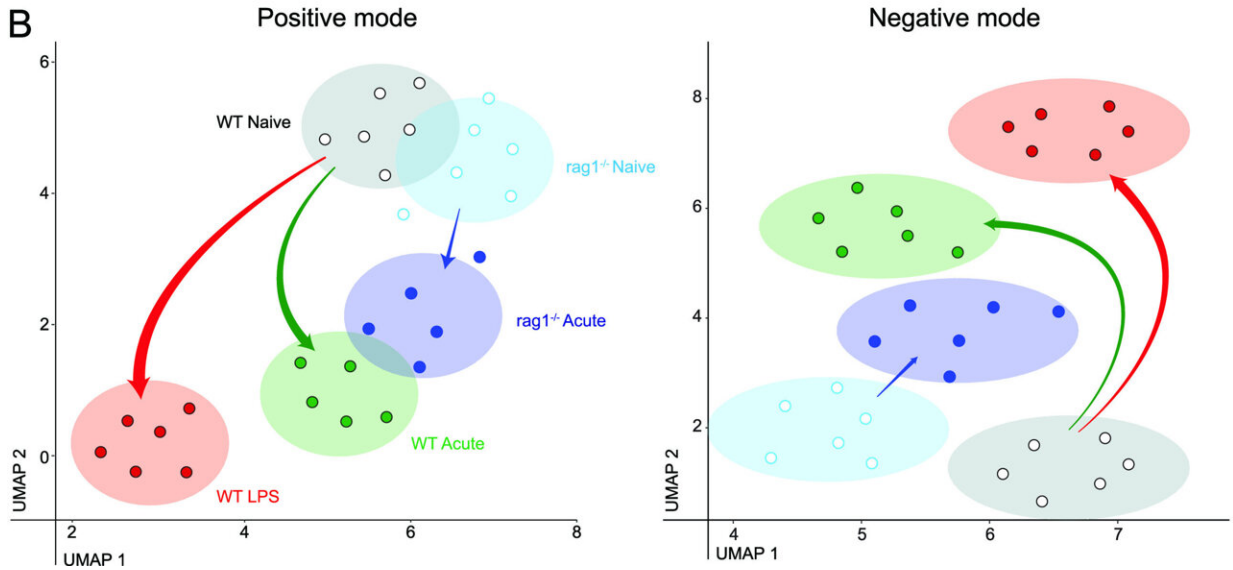
Inflammation slows malaria parasite growth and reproduction in the body, research finds

August 9 2023





Systemic inflammation alters the metabolomic profiles of circulating plasma in vivo. Credit: *mBio* (2023). DOI: 10.1128/mbio.01129-23

Research led by the Peter Doherty Institute for Infection and Immunity (Doherty Institute) and the Kirby Institute found that inflammation in the body can slow down the development of malaria parasites in the bloodstream—a discovery that may constitute a potential new strategy for preventing or limiting severe disease.

A mosquito-borne disease, malaria is caused by Plasmodium parasites, which invade and multiply within red blood cells. Previous research has shown that the parasites can rapidly sense and respond to conditions within the host by intimately syncing with their internal body clocks. While it is known that the body's nutrient levels and daily circadian rhythms affect the parasites' development, little was known about the impact of host inflammation on the parasites—until now.

This animal-model study, published in the journal *mBio*, reveals that when the body's immune system responds to inflammation it alters the chemical make-up of the plasma, which directly hinders the maturation of the Plasmodium parasites as they circulate in the bloodstream.

University of Melbourne's Associate Professor Ashraful Haque, Laboratory Head and co-lead of the Bacterial and Parasitic Infections theme at the Doherty Institute, and one of the senior authors of the paper, said this work highlights the captivating dynamic of the host-parasite relationship.

"First, we discovered that inflammation in the body prevented the early stage of the parasites from maturing. We also noticed that inflammation triggered significant changes in the composition of the plasma—we were

actually quite surprised by the magnitude of these changes," said Associate Professor Haque.

"As we dug deeper, we found substances in the altered plasma that, we believe, are what may inhibit parasite growth in the body. This work reveals a new mechanism that slows down the malaria parasite's development in the bloodstream. Our research was done using animal models, so it would be really interesting to study if such inhibitory mechanisms occur in humans too."

Dr. David Khoury, Lead of the Malaria Analytics Group at the Kirby Institute and co-senior author of the paper, said the scientists found a remarkable response by the parasites to the changes in their environment.

"Parasites residing in red blood cells rapidly sense and respond to their new environment, showing fascinating adaptability. Using cutting-edge genome sequencing technology, we observed that even after just four hours in this changed plasma, the parasites adjusted their genetic and protein activity, resulting in slower maturation within red blood cells. It's almost like the parasites actively sense an inhospitable host environment, and as a result trigger a coping mechanism," said Dr. Khoury.

"We believe this is the first study to show that inflammation can change how individual parasites behave genetically in the body."

Professor Miles Davenport, Program Head of the Infection Analytics Program at the Kirby Institute and co-senior author of the paper, said this work on the interaction between systemic host inflammation and malaria parasite maturation offers several potential benefits.

"This study, while based on animal models, broadens our understanding of malaria. It provides a foundation for further investigations into the

specific mechanisms involved in the modulation of parasite maturation by inflammation, and opens avenues for future studies to explore the identified inhibitory factors, genetic changes and their implications for malaria development," said Professor Davenport.

"Ultimately, our work aims to, one day, inform the development of potential new strategies to control, prevent and reduce the burden of malaria which affects over 240 million people globally."

This research was conducted in collaboration with researchers from the Doherty Institute, The Kirby Institute, QIMR Berghofer Medical Research Institute, Wellcome Sanger Institute (UK) and Monash Institute of Pharmaceutical Sciences.

More information: Lianne I. M. Lansink et al, Systemic host inflammation induces stage-specific transcriptomic modification and slower maturation in malaria parasites, *mBio* (2023). DOI: 10.1128/mbio.01129-23

Provided by The Peter Doherty Institute for Infection and Immunity