Immune cell type controls onset and course of severe malaria

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Scientists have determined that a subset of immune cells may cause malaria patients to contract the severe form of the disease, suffering worse symptoms. Led by Monash University immunologist Professor Magdalena Plebanski, the international team found that patients with the severe form of malaria have a specific type of cell in their body that people with uncomplicated disease do not. This type of cell, described in an article published April 24 in the open access journal *PLoS Pathogens*, turns off the immune system and can allow the parasite to grow uncontrollably.

The research team included scientists from Monash University's Department of Immunology; Menzies School of Health Research in Darwin; National Institute of Health Research and Development (NIHRD), Ministry of Health, Jakarta, Indonesia as well as researchers from NIHRD-MSHR Collaborative Research Program and District Health Authority, Timika, Papua, Indonesia; Centre for Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, Churchill Hospital, Oxford, UK and Queensland Institute of Medical Research, Brisbane, Australia.

Professor Plebanski and her team investigated the relationship between regulatory T (Treg) cells, parasite burden, and disease severity in adult malaria patients with either uncomplicated or severe malaria. When comparing Treg cell characteristics, the team was able to identify elevated levels of a new highly suppressive subset of Treg cells in those patients with severe malaria.

"The regulatory (Treg) cell subset associated with severe disease in humans expresses a unique combination of surface markers, including TNFRII . Regulatory T (Treg) cells are a small specialized subset of immune cells that suppress the activation and expansion of effector immune cells, which partake in parasite elimination," Professor Plebanski said.

"Our results indicate that severe malaria is accompanied by the induction of highly suppressive Treg cells that can promote parasite growth and caution against the induction of these Treg cells when developing effective malaria vaccines."

It is estimated that 500 million people live in areas where there is a risk of getting malaria. The severe form of the disease causes death in 1-3 million people each year. Professor Plebanski said until now it had been largely unknown what bodily factors enable some patients to fight and survive the disease, while other patients contract the severe form of the disease and sometimes die.

"Targeting this cell type may lead to new drugs and immunotherapeutics against malaria. Further studies are needed to determine if this new cell may also be promoting severe forms of other inflammatory diseases," Professor Plebanski said.

More information: Minigo G, Woodberry T, Piera KA, Salwati E, Tjitra E, et al. (2009) Parasite-Dependent Expansion of TNF Receptor II-Positive Regulatory T Cells with Enhanced Suppressive Activity in Adults with Severe Malaria. PLoS Pathog 5(4): e1000402. doi:10.1371/journal.ppat.1000402, dx.plos.org/10.1371/journal.ppat.1000402

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