

BLOOD STAGE SCHIZONTS OF *P. FALCIPARUM* ACTIVATE PLASMACYTOID DENDRITIC CELLS TO PRODUCE ALPHA INTERFERON

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A common feature of severe *P. falciparum* infection is the increase systemic release of pro-inflammatory cytokines that contributes to the pathogenesis of malaria. These mediators are partly produced from innate immune cells; monocytes and gamma delta T cells, in response to stimulation by parasite products. Here, we found that a heat labile molecule derived from schizonts selectively activated a unique subset of innate immune cells called plasmacytoid dendritic cells (PDCs) to up-regulate CD86 expression and produce alpha interferon. The schizont-stimulated PDCs elicited poor T cell response, but promoted gamma delta T cell proliferation and interferon-gamma production. The production of alpha interferon was also detected in malaria patients, but the levels of circulating PDCs was markedly reduced reflecting their accelerated migration to secondary lymphoid tissues. The schizont-stimulated PDCs demonstrated up-regulation of CC chemokine receptor 7 (CCR7), which is critical for migration. Because of anti-viral activity of alpha interferon, PDC response has been considered primarily as a host response against viral infection. However, our results provide a new direction of PDC response in malaria disease. The ability of these cells to produce alpha interferon and enhance gamma delta T cell activity in response to schizonts suggests that they may play key role in the immunoregulation and immunopathogenesis of human falciparum malaria.

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