IL35 modulation altered survival, cytokine environment and histopathological consequences during malaria infection in mice

ABSTRACT

Background: The immune modulating potential of IL-35 in multiple human disorders has been reported. Consequent upon the recognition of inflammatory cytokine activation and its preponderance for mediating pathology during malaria infection, the study aimed to characterize the expression and functional contribution(s) of IL-35 in Plasmodium berghei (strain ANKA) infected mice. Methods: Plasmodium berghei infection in male ICR mice was used as the rodent model of choice. The time course of IL-35 expression in the systemic circulation and tissues of P. berghei infected mice as well as their healthy control counterparts was assessed by enzyme linked immunosorbent assay and immunohistochemistry respectively. The effect of modulating IL-35 by recombinant IL-35 protein or neutralizing anti-Epstein-Barr virus-induced gene 3 antibody on the cytokine environment during P. berghei infection was assessed by flow cytometry. Furthermore, the influence of modulating IL-35 on histopathological hallmarks of malaria and disease progression was evaluated.Results: Interleukin-35 was significantly up regulated in serum and tissues of P. berghei infected mice and correlated with parasitaemia. Neutralization of IL-35 significantly enhanced the release of IFN-γ, decreased the expression of IL-6 and decreased parasitaemia patency. Neutralization of IL-35 was also associated with a tendency towards increased survival as well as the absence of pathological features associated with malaria infection unlike recombinant IL-35 protein administration which sustained a normal course of infection and unfavourable malaria associated histological outcomes in P. berghei infected mice. Conclusion: These results indicate the involvement of IL-35 in P. berghei induced malaria infection. IL-35 neutralization strategies may represent viable therapeutic modalities beneficial for the resolution of malaria infection.

Keyword: Plasmodium berghei; Interleukin-35; Immunohistochemistry; Cytokines