Experimental cerebral malaria develops independently of caspase recruitment domain-containing protein 9 signaling.

Abstract:
The outcome of infection depends on multiple layers of immune regulation, with innate immunity playing a decisive role in shaping protection or pathogenic sequelae of acquired immunity. The contribution of pattern recognition receptors and adaptor molecules in immunity to malaria remains poorly understood. Here, we interrogate the role of the caspase recruitment domain-containing protein 9 (CARD9) signaling pathway in the development of experimental cerebral malaria (ECM) using the murine Plasmodium berghei ANKA infection model. CARD9 expression was upregulated in the brains of infected wild-type (WT) mice, suggesting a potential role for this pathway in ECM pathogenesis. However, P. berghei ANKA-infected Card9(-/-) mice succumbed to neurological signs and presented with disrupted blood-brain barriers similar to WT mice. Furthermore, consistent with the immunological features associated with ECM in WT mice, Card9(-/-) mice revealed (i) elevated levels of proinflammatory responses, (ii) high frequencies of activated T cells, and (iii) CD8(+) T cell arrest in the cerebral microvasculature. We conclude that ECM develops independently of the CARD9 signaling pathway.