

RIG-I-dependent production of type I interferons by human glial cells restricts bacterial burden during bacterial meningitis

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Abstract

Globally, bacterial meningitis causes 1.2 million cases of meningitis, contributing to 250,000 deaths annually. Meningitis is an infection of the meninges which provides protection to the brain and spinal cord; however, infection can progress to encephalitis, infection of the brain itself. During meningitis, potent inflammatory responses lead to life-threatening injuries and permanent neurological damage in 20% of survivors. Two main causative agents of bacterial meningitis include *Neisseria meningitidis* (Nm) and *Streptococcus pneumoniae* (Sp). Previous data indicates that in response to infection, resident glial cells in the CNS recognize bacterial ligands via host pattern recognition receptors, leading to the release of immune mediators and contributing to potent neuroinflammation. Recent data in peripheral cell types suggests a novel role for the nucleic acid sensor, retinoic acid-inducible gene I (RIG-I) in the identification of bacteria and stimulation of type I interferons (IFNs). While the antiviral effects of IFNs are well characterized, it is becoming increasingly evident that IFNs may function more broadly during bacterial infection. Currently, the role of RIG-I in initiating production of IFNs during bacterial infection of the CNS has not been explored. In this study, we demonstrate upregulation of RIG-I expression and subsequent type I IFN production by glial cells following infection. Additionally, we show a reduction in viable bacteria with increasing type I IFN production, promoting increased host cell survival. Collectively, these findings indicate a protective role for type I IFNs during bacterial meningitis and future studies will explore the role of RIG-I dependent responses in a murine model of meningitis.