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Host Defense & Pathophysiology

Signal transducer and activator of transcription 3 (*Stat3*) regulates host defense and protects mice against herpes simplex virus - 1 (HSV - 1) infection

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Abstract

Signal transducer and activator of transcription 3 (STAT3) mediates cellular responses to multiple cytokines, governs gene expression, and regulates the development and activation of immune cells. STAT3 also modulates reactivation of latent herpes simplex virus - 1 (HSV - 1) in ganglia. However, it is unclear how STAT3 regulates the innate immune response during the early phase of HSV - 1 lytic infection. Many cell types critical for the innate immunity are derived from the myeloid lineage. Therefore, in this study, we used myeloid - specific *Stat3* knockout mice to investigate the role of STAT3 in the innate immune response against HSV - 1. Our results demonstrate that *Stat3* knockout bone marrow - derived macrophages (BMMs) expressed decreased levels of interferon - α (IFN - α) and interferon - stimulated genes (ISGs) upon HSV - 1 infection. In vivo, knockout mice were more susceptible to HSV - 1, as marked by higher viral loads and more significant weight loss. Splenic expression of IFN - α and ISGs was reduced in the absence of STAT3, indicating that STAT3 is required for optimal type I interferon response to HSV - 1. Expression of TNF - α and IL - 12, cytokines that have been shown to limit HSV - 1 replication and pathogenesis, was also significantly lower in knockout mice. Interestingly, *Stat3* knockout mice failed to expand the $CD8^+$ conventional DC (cDC) population upon HSV - 1 infection, and this was accompanied by impaired NK and CD8 T cell activation. Collectively, our data demonstrate that myeloid - specific *Stat3* deletion causes defects in multiple aspects of the immune system and that STAT3 has a protective role at the early stage of systemic HSV - 1 infection.

Citing Literature

Supporting Information