

Tpl2 promotes neutrophil trafficking, oxidative burst, and bacterial killing

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First published: 29 March 2017

<https://doi.org/10.1189/jlb.3A0316-146R>

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Abstract

Tumor progression locus 2 (Tpl2) is a serine/threonine kinase that promotes inflammatory cytokine production by activating the MEK/ERK pathway. Tpl2 has been shown to be important for eliciting the inflammatory properties of macrophages; however, there is relatively little known about the contribution of Tpl2 to neutrophil effector functions. This is an important consideration, as neutrophils provide the first line of defense against infection in the innate immune system. We found that Tpl2 is expressed in both human and murine neutrophils, suggesting a potential function for Tpl2 in this lineage. Despite significantly higher proportions of bone marrow (BM) neutrophils in Tpl2 - deficient (*Tpl2*^{-/-}) mice compared with wild - type (WT) mice, *Tpl2*^{-/-} mice have significantly reduced proportions of circulating neutrophils. *Tpl2*^{-/-} neutrophils show impaired recruitment to thioglycollate, which was primarily a result of neutrophil - extrinsic factors in the host. In response to infection, neutrophils secrete inflammatory cytokines and produce reactive oxygen species (ROS), which promote bacterial killing. Tpl2 ablation impaired neutrophil TNF secretion in response to LPS stimulation, superoxide generation in response to the chemotactic peptide fMLP, and killing of the extracellular bacterium, *Citrobacter rodentium*, despite normal bacterial phagocytosis. These results implicate Tpl2 in the regulation of multiple neutrophil antimicrobial pathways, including inflammatory cytokine secretion and oxidative burst. Furthermore, they indicate that Tpl2 functions early during infection to bolster neutrophil - mediated innate immunity against extracellular bacteria.

Citing Literature

Number of times cited: 1

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