Mechanisms Regulating Innate Immune Signaling: New Insights into Inflammation and Disease

Abstract

The mammalian immune system relies on the coordinated actions of innate and adaptive immunity to defend against infections. Innate immune cells recognize pathogen-associated molecular patterns (PAMPs) through pattern recognition receptors such as Toll-like receptors (TLRs), triggering antimicrobial and inflammatory responses. While essential for host defense, excessive or dysregulated inflammation contributes to diseases including sepsis and chronic inflammatory disorders. Our research investigates how these immune responses are precisely regulated at multiple molecular levels. We previously identified the E3 ubiquitin ligase ZNRF1 as a positive regulator of TLR4 signaling via caveolin-1 (CAV1) degradation. Interestingly, we now reveal that ZNRF1 also suppresses endosomal TLR3 and TLR7 pathways in macrophages and plasmacytoid dendritic cells through distinct mechanisms. These findings highlight the complex, context-dependent regulation of TLR signaling and suggest potential therapeutic avenues for inflammation-related diseases.