

# Phosphatases in Toll-Like receptor signaling: the unfairly forgotten

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## Video Byte

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# Abstract

Toll-like receptors (TLRs) are a highly conserved family of pattern recognition receptors that play a critical role in innate immunity. They evolved before the adaptive immune system, making them an indispensable first line of defense. TLRs are highly studied, and understanding their signaling is critical for developing treatments for autoimmune and chronic inflammatory disorders. But while kinases and E3 ubiquitin ligases are widely known TLR signaling effectors, another pathway is less well-characterized. Phosphatases are important regulators of TLR signaling through NF- $\kappa$ B, type I interferons, and mitogen-activated protein kinases. TLRs activate several pathways through phosphorylation, and thus an interplay must exist between kinases and phosphatases to tightly regulate TLR signaling. Many phosphatases have roles in TLR signaling, including classical protein tyrosine phosphatases and serine/threonine phosphatases. TLR regulation by phosphatases is implicated in many human diseases, including atherosclerosis, autoimmune rheumatoid arthritis, and neuroinflammatory disorders. Finally, a role may exist for TLR signaling and phosphatases – in particular those associated with TLR4 and TLR7 - in patient responses to coronaviruses such as COVID-19. While many aspects of the TLR-associated kinase-phosphatase network remain to be uncovered phosphatases could represent novel therapeutic targets to control pathogenic TLR signaling.