Protein phosphatases in TLR signaling

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Video Byte

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Abstract

The activation of toll-like receptors (TLRs) is critical to detecting potentially harmful microbes, but overactivation can be life-threatening, leading to autoimmune and inflammatory diseases. While much research has been dedicated to positive regulators of TLR signaling, such as protein serine/threonine kinases, much less has focused on phosphatases, which counterbalance and limit TLR signaling. Fortunately, a growing number of studies are exploring the roles of these enzymes and how they might be harnessed to prevent excessive immune activation. Two important families of protein phosphatases are phospho-protein phosphatases (PPPs) and metal-dependent protein phosphatases (PPMs). PPPs contain a highly conserved catalytic core domain, which can combine with regulatory subunits to home in on specific enzymatic targets. PPMs, on the other hand, rely on magnesium or manganese ions and do not form multi-subunit complexes. Together, these phosphatases regulate TLR signaling by reversing phosphorylation events, a mechanism often hijacked by certain microbes to promote effective infection. While much work remains to understand how these enzymes deactivate the immune system, they represent a powerful new approach to combating autoimmune and inflammatory diseases.