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Macrophage Activation by Phosphoinositides

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Abstract

Macrophages are critical effectors and regulators of innate immunity and inflammation. Moreover, they serve resolution of inflammation, tissue repair and homeostasis. They can be diversely activated by the microenvironment to initiate specific functions. Activated macrophages can be broadly classified into two groups: M1 (or classically activated macrophage) and M2 (or alternatively activated macrophage). The M1 macrophage, which is activated by IFN-γ and Toll-like receptor ligands, exhibits potent microbicidal and tumoricidal properties and promotes IL-12-mediated Th1 responses. The M2 macrophage, which is activated by IL-4/IL-13, support Th2-associated effector functions and promote tissue remodeling and tumor progression. (1)

We found that phosphoinositides regulate macrophage activation. Phosphoinositides are lipids that are present in the cellular membranes and play important roles in a variety of cellular functions (2-4). There are seven phosphoinositides species in mammalian cells, and especially, phosphatidylinositol 3,4,5-trisphosphate (PtdInsP3) controls macrophage activation. SHIP1 (SH2 domain-containing inositol 5' phosphatase 1) is a PtdInsP3 phosphatase and is reported to repress the generation of M2 macrophage (5). However, we found that SHIP1$^{-/-}$ macrophage has different characteristics from typical M2 macrophage. In the poster, we present the recent data about macrophage activation regulated by PtdInsP3 metabolism.

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