



Biological DNA Sensor: Chapter 4. Regulation of Intracellular dsDNA-Induced Innate Immune Responses by Autophagy-Related Proteins

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Microbial double-stranded (ds)DNA potently stimulates innate immunity. Stimulator of interferon genes (STING) plays a major role in dsDNA-induced expression of type I interferons (IFNs) and elimination of invading pathogens. After stimulation, STING translocates from the endoplasmic reticulum to cytoplasmic punctate structures where it associates with TANK-binding kinase 1 (TBK1). TBK1 phosphorylates interferon regulatory factor 3 to induce type I IFNs and optineurin to induce autophagy, an intracellular clearance system. Autophagy-related protein, Atg9a, regulates membrane trafficking involved in STING movement and suppresses type I IFN expression. Absent in melanoma 2 (AIM2) plays a major role in dsDNA-induced inflammatory responses. After stimulation, AIM2 forms an inflammasome with an adaptor protein, ASC, and caspase-1, a protease, to induce the production of IL-1 β , an inflammatory cytokine. Autophagy mediates degradation of activated AIM2-inflammasome to terminate the response. Thus, autophagy-related proteins, essential components of autophagy machinery, regulate innate immune responses induced by dsDNA.

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