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Inorganic Polyphosphate: A Key Modulator of Inflammation

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Inorganic polyphosphate (Polyp) is a molecule with prothrombotic and proinflammatory properties in blood. Polyp activates the NF-κB signaling pathway, increases expression of cell surface adhesion molecules and disrupts the vascular barrier integrity of endothelial cells. Polyp-induced NF-κB activation and vascular hyper permeability are regulated by the mTORC1 and mTORC2 pathways, respectively. RAGE and P2Y1 receptors, Polyp dramatically amplifies the proinflammatory responses of nuclear proteins. Moreover, Polyp-mediated activation of the contact pathway results in activation of the kallikrein-kinin system, which either directly or in cross-talk with the complement system induces inflammation in both cellular and animal systems. Thus, polyp is a novel therapeutic target for the treatment of metabolic and acute. Proinflammatory diseases, including severe sepsis, diabetes, cardiovascular disease and cancer. In this review, we discuss recent findings on the inflammatory properties of polyp and propose a model to explain the molecular mechanism of proinflammatory effects of this molecule in different systems.

Recent studies suggest that in addition to modulation of coagulation, polyp can elicit potent proinflammatory responses in cellular and animal models. The proinflammatory signaling effect of polyp increases release of the proinflammatory mediator bradykinin, triggers vascular permeability, promotes leukocytes migration, activates the NF-κB pathway, induces expression of CAMs, amplifies proinflammatory signaling of nuclear cytokines (H4 and HMGB1) and links inflammation to activation of the metabolic regulatory mTOR signaling pathway. This review summarizes the proinflammatory functions of polyp, but the detailed mechanisms in this process have yet to be defined.