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The Role of P2X7 Cytoplasmic Anchor in Inflammation

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Abstract : Purinergic P2X7 receptors (P2X7R) are ligand-gated non-selective cation channels involved in several physiological and pathological processes. They are particularly promising pharmacological targets as they are present in an increasing number of different cells types. P2X7R activation is triggered following elevated concentrations of extracellular ATP, similarly to those observed in tissues injury, chronic inflammation and T-cell activation, as well as in the scrambling of phospholipids leading to membrane blebbing and apoptosis. Another hallmark of P2X7 is cell permeabilization, commonly known as “macropore” formation allowing the passage of nanometer-sized molecules up to 900Da. Recently, full-length P2X7 Cryo-EM structures revealed unique functional sites, including two cytoplasmic domains - the cytoplasmic "anchor" and "ballast". To date, the molecular units/complex by which P2X7R exerts its pathophysiological functions are unknown. Using custom-made cell-penetrating HIV-1 TAT peptides, we show for the first-time potential implications of P2X7 cytoplasmic anchor in the regulation of caspase3/7 activation as well as TNFα regulation.

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