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Impromptu Seminar

Calcium microdomains and NAADP signaling

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Ca^{2+} signaling is the major intracellular signaling system found in almost all cell types. Ca^{2+} signals occur globally or locally via Ca^{2+} microdomains, which are platforms with high Ca^{2+} concentration that localize near open Ca^{2+} channels at the plasma or organellar membrane. Mechanisms involved in the formation of Ca^{2+} microdomains, extensively studied in mammalian T-lymphocytes, revealed that nicotinic acid adenine dinucleotide phosphate (NAADP) evokes the initial local Ca^{2+} signals observed upon T cell activation. These Ca^{2+} microdomains occur within hundreds of milliseconds up to approx. 15 to 25 s following directed T cell receptor ligation. NAADP acts via its receptor/binding protein HN1L/JPT2 which partially co-localizes with the ryanodine receptor (RYR), demonstrating a major role of RYR1 as Ca^{2+} release channel, responding to NAADP via HN1L/JPT2. The very close co-localization of RYR1 and ORAI1 (at approx. 40 nm resolution) suggests that ER - plasma membrane junctions are the hub for the first Ca^{2+} microdomains close to the immune synapse.

Surprisingly, in addition to store-operated Ca^{2+} entry (SOCE) operated by STIM2 and ORAI1, a second amplification system for Ca^{2+} microdomains consisting of ATP release and purinergic activation of P2X4 and P2X7 was discovered recently.

Keywords: immunology, inflammation research, cell signaling, calcium signaling, T cell activation

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