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INVITED SYMPOSIUM V

Platelets: Intracellular Control Mechanisms.

EVIDENCE FOR A CENTRAL ROLE FOR CALCIUM IONS IN REGULATION OF PLATELET FUNCTION.
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It is generally believed that calcium ions play a key role in regulation of platelet function. This is based on 3 types of evidence.

1. Analogies with other cells. Calcium ions are known to trigger secretion and contraction in many cells, possibly reflecting a general role for calcium in all secretion and contraction.
2. Indirect evidence. Platelet aggregation and secretion are induced by divalent cation ionophores. The response to the ionophore A23187 is identical to that induced by other potent stimuli.
3. Direct evidence. Platelet activation can be blocked by drugs (e.g., certain local anaesthetics) that block release of calcium ions from sarcoplasmic reticulum; the inhibition can be overcome by addition of extracellular calcium in the presence of a calcium ionophore.

While this does not constitute definitive proof, the central role for calcium ions remains an attractive hypothesis that justifies attempts to further define calcium pools and fluxes in platelets.

MOVEMENTS OF CALCIUM IONS AND THEIR ROLE IN THE ACTIVATION OF PLATELETS.
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The increase of the cytoplasmic Ca-concentration plays a central role in the initiation of platelet activation. Four kinds of movements of Ca-ions are presumed to occur during this process: (a) Ca-ions liberated from membranes induce the rapid shape change. (b) Vesicular organelles release Ca-ions into the cytoplasm which initiate the release reaction. (c) The storage organelles, called dense bodies, secrete their contents including Ca-ions to the outside during the release reaction. (d) At the same time a rearrangement of the plasma membrane occurs, resulting in an increase in its permeability for Ca-ions as well as in an increase in the number of Ca-binding sites.

Since most processes occurring during platelet activation are reversible the platelet must be equipped with a mechanism which removes Ca-ions from the cytoplasm. A vesicular fraction of platelet homogenate indeed accumulates Ca actively. This Ca-pump is stimulated by cyclic AMP and protein kinase; it might be involved in the recovery of platelets after activation.