Lecture 1: “Dynamics of intracellular calcium fluxes”

Abstract:

Calcium is an essential element that build our skeleton and teeth. However, inside the cell, calcium represents a key second messenger implicated in a broad range of cellular functions including cell cycle, cell metabolism, cell migration and apoptosis. Calcium ions are stored in intracellular organelles including endoplasmic reticulum (ER) and mitochondria and are constantly trafficking between these compartments.

Mitochondria have a central role in the control of the intracellular Ca2+ levels and signaling; they constantly uptake Ca2+ ions under physiological conditions, to ensure their proper functions. These organelles can rapidly uptake substantial amounts of Ca2+ though the existence of Ca2+ hot spots localized at the interface between the mitochondria and the ER. Recent characterization of the mitochondrial Ca2+ uptake machinery, including the mitochondrial Ca2+ uniporter (MCU) and associated regulators, shed new light on the molecular mechanisms underlying mitochondrial Ca2+ buffering and homeostasis. The mitochondrial Ca2+ uptake capacities have been also linked to an efficient Store-Operated Ca2+ Entry (SOCE). Interestingly, the role of the SOCE process, which is regulated in part by the ER-resident Stromal Interacting Molecule 1 (STIM1) and Calcium release-activated calcium channel protein 1 (Orai1), has been highlighted in the actomyosin contractility and breast tumor cell migration. At the molecular level, these effects are mediated by the reduction of the ER and cytosolic Ca2+ pools, which led to a decrease in the Rho-GTPases and the Ca2+-dependent Calpain activities. Together, these results highlight the fundamental role of the mitochondrial Ca2+ homeostasis in cytoskeleton dynamics and cell migration.

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