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Calcium and Signal Transduction

Edited by John N. Buchholz and Erik J. Behringer

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Chapter 1

Regulation of Calcium Signaling by STIM1 and ORAI1

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Abstract

STIM1 and ORAI1 proteins are regulators of intracellular Ca^{2+} mobilization. This Ca^{2+} mobilization is essential to shape Ca^{2+} signaling in eukaryotic cells. STIM1 is a transmembrane protein located at the endoplasmic reticulum, where it acts as an intraluminal Ca^{2+} sensor. The transient drop of intraluminal Ca^{2+} concentration triggers STIM1 activation, which relocates to plasma membrane-endoplasmic reticulum junctions to bind and activate ORAI1, a plasma membrane Ca^{2+} channel. Thus, the Ca^{2+} influx pathway mediated by STIM1/ORAI1 is termed store-operated Ca^{2+} entry (SOCE). STIM and ORAI proteins are also involved in non-SOCE Ca^{2+} influx pathways, as we discuss here. In this chapter, we review the current knowledge regarding the role of SOCE, STIM1, and ORAI1 in cell signaling, with special focus on the modulation of the activity of kinases, phosphatases, and transcription factors that are strongly influenced by the extracellular Ca^{2+} influx mediated by these regulators.

Keywords: calcium, signaling, SOCE, STIM, ORAI

1. Introduction

Cell signaling is the network of reactions and interaction of molecules that allow cells to react to a wide range of stimuli. In this response, many pathways are involved, so cells are able to adapt to changing conditions. One of the mechanisms to respond to external stimuli is mediated by receptors, that is, proteins located at the plasma membrane that communicate the extracellular and the intracellular medium. A significant strategy that cells acquired early in their evolution was the modification of the composition of the intracellular milieu, so the ionic

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