Orai3: Oncochannel with therapeutic potential for several cancers

Current review by scientists at DBT’s Regional Centre for Biotechnology (RCB), Faridabad retrospect the evidences supporting Orai3 as an oncochannel. Authors have discussed the potential of therapeutically targeting Orai3 for better management and treatment of certain specific cancer subtypes. Most importantly, key outstanding questions have been highlighted in the field that demand urgent attention and further studies.

Orai channels are responsible for Ca\(^{2+}\) influx across the plasma membrane in response to decrease in Endoplasmic Reticulum (ER) Ca\(^{2+}\) stores. STIM1/STIM2 proteins sense the reduction in ER Ca\(^{2+}\) levels and activate Orai channels for restoring ER Ca\(^{2+}\) as well as for driving the other cellular functions. Although Orai1 is the ubiquitous SOCE channel protein, Orai2 and Orai3 mediate SOCE in certain specific tissues. Further, mammalian specific homolog Orai3 forms heteromultimeric channel with Orai1 for constituting arachidonic acid regulated Ca\(^{2+}\) (ARC) channels or arachidonic acid metabolite Leukotriene C4 (LTC4) regulated Ca\(^{2+}\) (LRC) channels.

Earlier work by the authors has highlighted a key role for Orai3 channel in different types of cancers. Ion channels in particular calcium (Ca\(^{2+}\)) channels play a critical role in physiology by regulating plethora of cellular processes ranging from cell proliferation, differentiation, transcriptional regulation and programmed cell death. One of the most ubiquitous and highly regulated cellular Ca\(^{2+}\) influx pathways is *Store Operated Calcium Entry* (SOCE) mediated by Orai1-3 channels.
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