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Meeting abstract

Store-operated calcium entry into rat basophil leukaemia cells: contribution of TRPC3 and Orai1

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Background

Before the discovery of STIM and Orai proteins, mammalian TRPC channels, including TRPC3, were considered as candidates for mediating store-operated Ca^{2+} entry (SOCE). This calcium entry pathway governs diverse cellular processes from exocytosis, cellular remodelling to gene transcription. Although a prominent role of Orai1 is now well established for immune cells, the role of TRPC proteins and the possible crosstalk between these two ion channels families to the overall store operated calcium entry into cells of the immune system is still elusive.

Results

Calcium imaging experiments with Fura2-AM-loaded rat basophil leukaemia (RBL) cells overexpressing either TRPC3, Orai1 or dominant negative mutants of these channel proteins sustain evidence for a complex interaction network between TRPC and Orai pathways. Overexpression of either wild-type protein (TRPC3 or Orai1) resulted in promotion of calcium entry as compared to controls. PYR3, a novel inhibitor of NFAT activation, which has recently been demonstrated as a selective inhibitor of TRPC3 channels [1], also suppressed thapsigargin-induced calcium entry into RBL cells, being most efficient in TRPC3-overexpressing cells. Expression of dominant negative mutations of either channels reduced SOCE to levels significant below controls, revealing a PYR3-resistant calcium entry component that was significantly larger in dominant negative Orai1-knock-out cells.

Conclusion

These results demonstrate a combined involvement of TRPC3 and Orai1 in SOCE of RBL cells. It remains to be clarified if a crosstalk between these channels exists. Investigation of down-stream signalling events such as NFAT activation and degranulation confirmed the activity of PYR3 as an inhibitor of mast cell function. In aggregate, our results support evidence for a complex interaction network of TRPC and Orai channels in immune cells.

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