

ORAI channels in lactation and in breast cancer

G.R. Monteith, The School of Pharmacy, The University of Queensland, The Pharmacy Australia Centre of Excellence, Woolloongabba, QLD 4102, Australia.

The molecular components responsible for the refilling of depleted intracellular calcium stores were identified in 2006 and 2005. These proteins were Orai1, a protein responsible for the formation of a Ca^{2+} permeable ion channel, and STIM1, an endoplasmic reticulum store Ca^{2+} sensor. Recent studies suggest that the basolateral entry of Ca^{2+} across epithelial cells of the mammary gland during lactation is Orai1-mediated. Assessment of Orai1 in breast cancer, suggests that Orai1 expression and alterations in the relative levels of the calcium store sensors and Orai1 activators STIM1 and STIM2 are a characterizing feature of some breast cancer subtypes with poor prognosis. Silencing of Orai1 reduces store operated calcium entry and the proliferation, migration and invasion of some breast cancer cell lines. However, the role of other Orai isoforms and non STIM1-mediated mechanisms of Orai1 activation in breast cancer cells is still not fully understood. The use of high throughput methods for the assessment of store operated Ca^{2+} entry, as well as the assessment and identification of regulators of Orai-mediated Ca^{2+} influx in breast cancer cells, may help identify therapeutics for the treatment of breast cancers associated with a remodeling of store operated Ca^{2+} entry.