

## **The muscle model for intracellular calcium signalling: cross-talk between the calcium release channel and calcium buffer in the intracellular calcium store**

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Cellular signalling in many animal tissues depends on calcium released from intracellular calcium stores. The efficiency of this calcium release depends both on the calcium binding capacity of the store proteins and the activity of calcium release channels in the store membrane. The calcium store in striated muscle, the sarcoplasmic reticulum (SR), is pivotal to the vital functions of movement, respiration and heart beat. It provides a template for all calcium stores since the key store proteins are homologous with those in other stores (in e.g. blood vessels, neurones and lymphocytes). The key calcium binding protein in muscle is calsequestrin (CSQ) and the calcium release channel is the ryanodine receptor (RyR). CSQ not only binds calcium but also regulates calcium release by communicating with the RyR *via* two other key proteins, triadin and junctin. Calcium release from the SR and RyR activity are strongly dependent on the calcium load within the SR: both parameters increase as the total calcium within the store increases and decrease to conserve calcium when the store is depleted. Changes in RyR activity reflect the calcium release data only when CSQ is bound to the luminal side of the RyR and only when the CSQ bound to the RyR exists as a polymer. As a result of these observations, we have developed a hypothesis that: (a) the ryanodine receptor recruits the CSQ polymer as a luminal calcium sensor; and (b) CSQ is an ideal calcium sensor because its conformation is exquisitely sensitive to changes in calcium concentration. Data consistent with CSQ polymer association and dissociation during EC coupling have been obtained in intact muscle fibre studies (Launikonis & Rios, 2006).

Launikonis, B.S. & Rios, E. (2006) *Proceedings of the Australian Physiological Society*, **37**: 25P