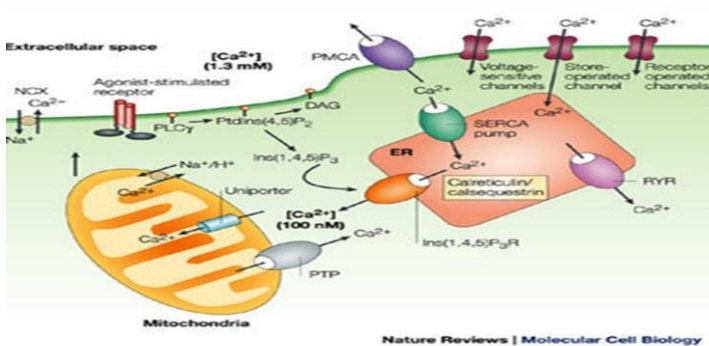


Calcium as a third messenger

Crucial aspect of calcium signalling is that the intracellular concentration of calcium always remains low in order to allow for a sudden rise.

The ER/SR is a major intracellular store of calcium

- Allows for calcium to be sequestered from the rest of the cell
- Allows for rapid release of that calcium
- The ER has specialised calcium store areas called **calciosomes**.
- **SERCA pumps** (Smooth endoplasmic reticulum calcium ATPase) pump the calcium through the ER membrane just as channels would do so in the plasma membrane
- SERCA pumps make up approximately 80% of the integral proteins of the SR
- In the ER the calcium channels are made up of two similar channels which have low sequence similarity
- They form homotetramers
 - IP3R
 - Ryanodine receptor (RyR)



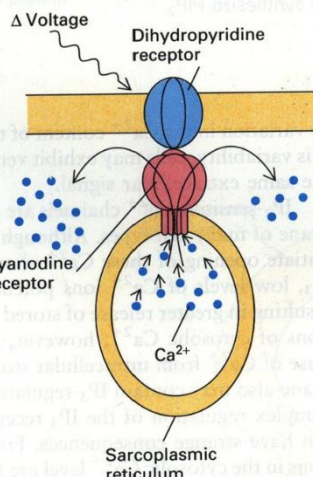
Activation of RyR

- Voltage sensitive receptor is present on the plasma membrane.
- Ryanodine receptor is present on the sarcoplasmic reticulum. Those are closely related, as such when the voltage sensitive receptor is activated, it directly interacts and activates RyR.
- This opens the channel and allows Calcium ions to move down their concentration gradient (from within the Sarcoplasmic reticulum, to the cytoplasm).

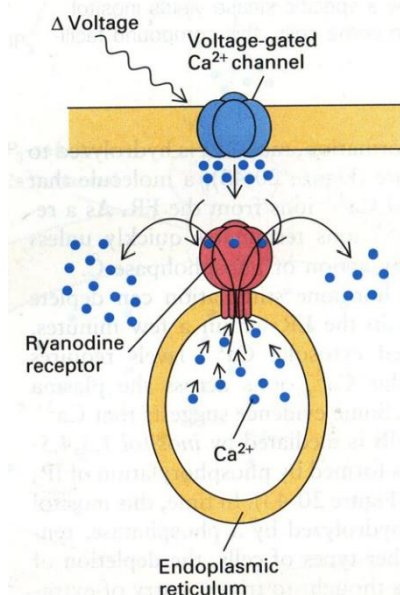
In skeletal muscles

- Tripartite protein complexes bring a **voltage sensitive receptor (PM)** in contact with **RyR (SR)**
- Voltage changes result in conformational change of the receptor that is detected by RyR and results in opening of channel

(a) Voltage-sensitive RYR (skeletal muscle)



(b) Ca²⁺-sensitive RYR (cardiac muscle, neurons)



In Cardiac Muscle

- **Voltage gated Ca²⁺ channels** will result in a small influx of Ca²⁺
- This will be detected by RyR and result in its activation