**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
- T-tubule foot 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

#### 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