

Increased expression and activity of the ligand-gated ion channel TRPV1 has been shown to block cell division and induce apoptosis in human cells. The structure of the TRPV1 protein consists of several transmembrane domains that are embedded in the membrane as well as a carboxy-terminus and an amino-terminus that are located inside the cell (Figure 1).

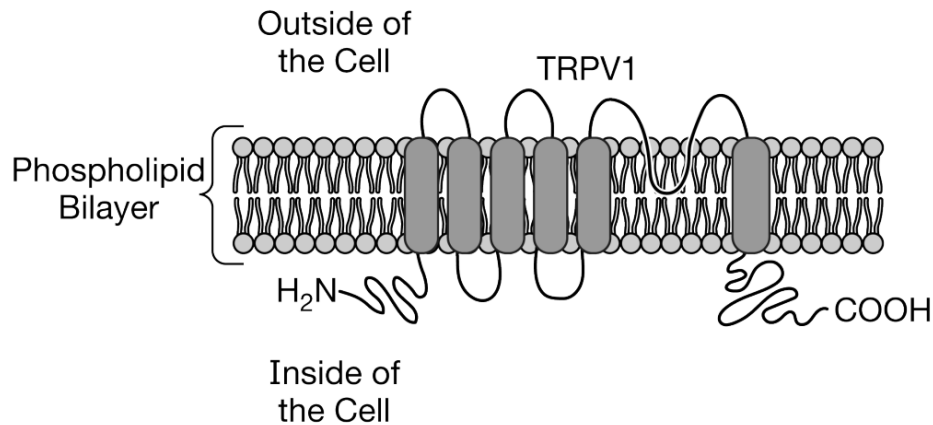


Figure 1. Structure of the TRPV1 protein channel in the membrane

TRPV1 is activated by several stimuli, including the binding of capsaicin, a chemical found in chili peppers. Capsaicin enters the cell by simple diffusion and then binds to one of the transmembrane domains of TRPV1, which opens the ion channel.

The opening of the TRPV1 channel allows Ca^{2+} ions to enter the cell, leading to the activation of the enzyme calcineurin. Calcineurin removes phosphate groups from the phosphorylated form of the transcription factor NFAT2, which is typically found in the cytoplasm. Once dephosphorylated, NFAT2 moves into the nucleus, where it blocks the transcription of another protein, ATF3. ATF3, when active, prevents the cell cycle regulatory protein pGoG from inducing apoptosis and blocking cell division (Figure 2).

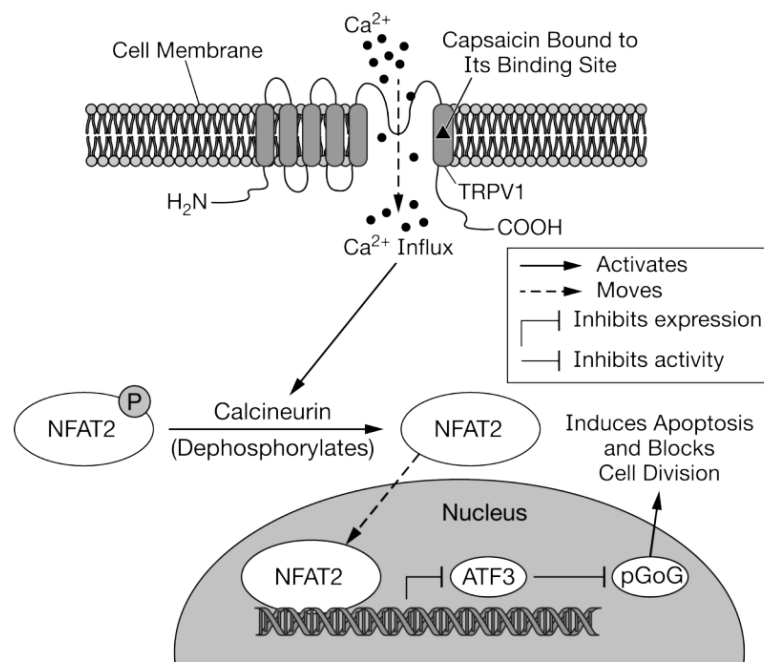


Figure 2. Capsaicin-activated TRPV1 signaling pathway in human cells

- a) **Describe** the characteristics of capsaicin that allow it to enter the cell before binding to the transmembrane domain of TRPV1.
- b) **Identify** the type of signal transduction receptor required for the “downstream” activation of calcineurin.
- c) **Describe** what prevents NFAT2 from inhibiting ATF3 expression in the absence of calcineurin.
- d) Researchers discover a mutation that results in the constant expression of ATF3 regardless of the presence of NFAT2. **Predict** the effect of this mutation on the cell cycle of cells treated with capsaicin. Provide reasoning to **justify** your prediction.
- e) Researchers claim that capsaicin could be used as a potential treatment for melanoma, a type of skin cancer. **Support** the researchers’ claim.