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Characterization and Comparison of Vertebrate Voltage Sensing Phosphatases

The voltage sensing phosphatase (VSP) is a transmembrane protein which regulates the phosphatidylinositol phosphate (PIP) signaling pathway in a voltage dependent manner. The membrane potential is an important signal in normal cellular processes controlling neuronal signaling, muscle contractions, and immune responses while PIPs regulate many different processes in the cell, including membrane trafficking, promoting cell death, and cell growth. When either pathway is compromised, many serious diseases can occur, including autism, epilepsy, and cancer.Interestingly, VSP has been found to be expressed in non-small cell carcinoma and hepatobiliary cancers, suggesting it may also play a role in cancer and could indicate an unexplored role of voltage in cancer cell propagation. The majority of VSP research has focused on the tunicate Ciona intestinalis (sea squirt) species of the protein (Ci-VSP) and very little is known about the vertebrate VSPs. I have been studying the vertebrate VSP species Gallus gallus (chicken, Gg-VSP) and Danio rerio (zebrafish, Dr-VSP) in order to compare the functions of these vertebrate species to Ci-VSP, focusing on the 210 and 212 equivalent sites of Ci-VSP. Dr-VSP has been successfully mutated for voltage clamp fluorometry (VCF) experiments. VCF is a technique that allows us to monitor protein motions through a fluorescent tag on the VSP, all in a live cell. Several of the Dr-VSP mutations have expressed and display voltage-dependent fluorescence changes that vary from the equivalent Ci-VSP mutation suggesting that the different species of VSP do not all function similarly. The rest of the vertebrate species being studied are still being mutated to include labeling sites.