# A Topologically Unique, Highly Selective $F^-$ Channel

**The Governor's Academy SMART Team**

L Bailey, W Campbell, J Cerniglia, S Chigier, K Cho, J Gustafson, M Liapin, Z Liu, B Zhan
J Rokous

**PDB**: 5A41

**Primary Citation:** Stockbridge, R.B., Kolmakova-Partensky, L., Shane, T., Koide, A., Koide, S., Miller, C., Newstead, S. (2015). Crystal Structures of a Double-Barrelled Fluoride Ion Channel. *Nature* 525: 548-552.

**Abstract:**

Fluoride's ubiquity has led to the evolution of transporters to export the toxic anion from organisms. Due to the weak acid accumulation effect, these anions build up within the cell and inhibit phosphoryl-transfer enzymes critical for glycolysis and nucleotide synthesis. Two phylogenetically unrelated protein families have been discovered that combat this effect: the CLC superfamily's strictly bacterial $CLC^F$ $F^-/H^+$ antiporters and the Fluc family's small-membrane channel proteins. An understanding of Fluc structure and function may lead to development of antibiotic treatments targeting membrane transport proteins. Fluc is an ion channel with unprecedentedly high selectivity for $F^-$ over $Cl^-$. Monobodies, synthesized to stabilize the protein for crystallization, were found to inhibit $F^-$ current. The solved structure revealed that each subunit comprises four transmembrane helices with the third broken into TM3a and TM3b. Near the break, evidence suggests a presumed $Na^+$ ion coordinated by four backbone carbonyl groups residues, serving a crucial structural role. Each channel contains two electron densities, suspected fluoride ions, potentially interacting with induced electropositive phenylalanine rings. Lining TM4 are electropositive $H^+$-donating sidechains that may assist in dehydrating $F^-$ as it enters the channel. The Governor's Academy SMART team 3D-printed the Bpe Fluc transporter to elucidate its dimer assembly, $F^-$ ion permeation and high selectivity for $F^-$ over Cl-, as well as to explore its evolutionary relationship to other membrane transporters.