Dr. Filip Van Petegem
Professor, Department of Biochemistry & Molecular Biology
The University of British Columbia

Dr. Van Petegem is an Associate Professor of Biochemistry and Molecular Biology in the Family of Medicine. He received his license and Ph.D. in Biochemistry from Ghent University. His Ion Channel Lab research interests are in calcium signaling in health and disease, ryanodine receptors, and voltage-gate sodium channels, using a variety of complementary biochemical and biophysical techniques to investigate ion channels. Examples include x-ray crystallography to elucidate the 3D structure of individual subunits, domains, and their complexes with ligands, isothermal titration calorimetry (ITC) and surface plasmon resonance (SPR) to detect and quantify protein-ligand and protein-protein interactions, circular dichroism (CD) and differential scanning calorimetry (DSC) to analyze secondary structure and protein stability, and electrophysiology (two-electrode voltage clamp and Planar lipid bilayer electrophysiology) to measure the ionic conductance and gating properties. Dr. Petegem has over 50 publications and is the recipient of prestigious awards including the CIHR New Investigator award, the Michael Smith Career Investigator award, and the University of British Columbia Faculty of Medicine Distinguished Achievement Award for Basic Research. He is a CIHR new investigator and an MSFHR career investigator.

“From Epilepsy to Arrhythmia: High-resolution Structures of Ion Channel Disease Hot Spots”

Ryanodine Receptors (RyRs) are huge membrane proteins that govern the release of Ca2+ from the sarcoplasmic and endoplasmic reticulum. In doing so, they mediate multiple processes, but are mostly known for their role in muscle excitation-contraction coupling. Their importance is underlined by a range of severe conditions that result from point mutations in the ryr genes. Mutations in the skeletal muscle isoform (RyR1) result in malignant hyperthermia and central core disease, whereas variants in the cardiac isoform (RyR2) can trigger stress-induced arrhythmias. Our lab has been solving crystal structures of several domains in different RyR isoforms, including one of the mutational disease ‘hot spots’ in both RyR1 and RyR2. This has allowed us to map the positions of over 100 disease-associated mutations. Combining the crystal structures with cryo-electron microscopy images and FRET studies, we can define allosteric pathways and see how disease-causing mutations affect these. A direct comparison of disease-mutant and wild type structures shows that there are multiple ways in which mutations can result in overactive channels. RyRs are heavily regulated by a multitude of small molecules and auxiliary proteins. We have been able to map the exact binding determinants for FKBP12, a small protein that dampens RyR activity.