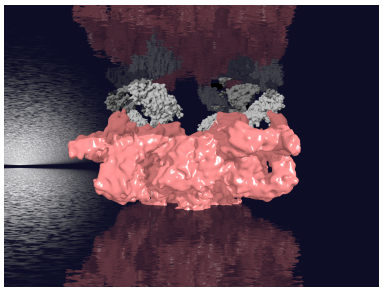
ASRC - City College of New York

Seminar in Biochemistry, Biophysics & Biodesign



THE SEMINAR WILL BE GIVEN VIA ZOOM:
Click here for Zoom link

THE ZOOM BROADCAST MAY ALSO BE VIEWED IN THE ASRC AUDITORIUM:

- *Current CUNY Cleared4 Pass required for entrance*
- *Masks are required*
- *Maximum occupancy: 30*

HOST:
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ADVANCED SCIENCE RESEARCH CENTER
THE GRADUATE CENTER
CITY UNIVERSITY OF NEW YORK

Wednesday, February 16, 2022

12:00 – 1:00 PM

Filip Van Petegem

Professor, Dept. of Biochemistry & Molecular Biology
University of British Columbia, Vancouver, Canada

Channelopathies at high resolution: Cryo-EM and crystallographic investigation of cardiac and skeletal muscle ion channels

ABSTRACT The contraction of skeletal and cardiac muscle is a tightly orchestrated event that starts with an electrical signal: a depolarization of the plasma membrane. Prior to contraction, this signal needs to be converted into a chemical signal: the release of calcium ions from the sarcoplasmic reticulum (SR). This process is mediated by two classes of ion channels: L-type voltage-gated calcium channels (CaVs), located in the T-tubular membrane, and Ryanodine Receptors (RyRs) in the SR membrane. Their close proximity allows for functional and mechanical interactions depending on the exact cell type. The process requires an array of auxiliary proteins that bind and modulate both channels. The various components are targets for mutations that have been linked to severe genetic disorders, including myopathies, cardiac arrhythmias, and malignant hyperthermia. Using X-ray crystallography and cryo-EM, we have been solving high-resolution structures of various components in wild-type and disease mutant forms. Making use of a natural pig model, we purified disease mutant RyRs and solved a range of cryo-EM structures, which explain the gain-of-function phenotype associated with malignant hyperthermia. Our results show that the exact effect is highly dependent on the roster of auxiliary proteins that are present in the complex. STAC proteins and junctophilins are essential proteins that organize the cross-talk between RyRs and CaVs. Their mutations have been linked to skeletal and cardiac myopathies, respectively. We explored their structure and how they mediate interactions with CaVs.