Life Sciences / IBB
Faculty Candidate Seminar

"Structural insights into gating mechanism of ion channel proteins and their modulation by tarantula toxins"

[Chanhyung Bae, Ph.D.]
Postdoctoral Fellow, National Institutes of Health

A wide range of physiological processes including the perception of external stimuli, transmission of signals and release of hormones depends upon the activity of ion channels, integral membrane proteins which selectively control the permeation of ions across cellular membrane. Disrupting the regulatory function of theses ion channels can cause adverse consequences in nerves and neuromuscular junctions. As a result, ion channels are frequently the target of peptide toxins produced by venomous creatures, and in this talk I will describe how we can use these toxins to learn about ion channel function and structure.

The first toxin I will discuss is the double-knot toxin (DkTx) from the venom of Chinese bird spider, which binds to and activates the transient receptor potential vanilloid 1 (TRPV1) channel, a non-selective cation channel expressed by sensory neurons which perceive noxious stimuli including heat, inflammation and acidosis. DkTx has an unusual bivalent structure in which two structurally similar domains (K1 and K2) are joined by a short linker. Using solution NMR spectroscopy, electrophysiology, molecular dynamics simulations and fluorescence spectroscopy experiments, I found that although the K1 and K2 domains are structurally similar, they evolved for distinct functions with K1 and K2 tuned for membrane partitioning and TRPV1 activation, respectively. In addition, the DkTx/TRPV1 channel complex structure revealed the toxin modulates interactions at the aqueous-membrane interface of a cluster of hydrophobic residues in the pore domain, a region later found to contribute to sensing temperature.

My second example concerns the voltage-activated potassium (Kv) channels expressed in excitable cells such as neurons and muscle cells. Kv channels control membrane voltage by permeating potassium ions through the pore domain of the channel upon activation and by closing the pore domain through inactivation mechanism, whose structural basis remains unclear. I will present a 3.3 Å resolution single-particle cryo-electron microscopy (cryo-EM) structure of Kv1.2 channel in lipid nanodisc, which provides the glimpse of slow inactivated structure of Kv channels in lipid membranes, involving subtle structural changes in the outer pore region. Finally, I will present unpublished biochemical results demonstrating the interaction between the Kv channel in nanodisc and peptide toxins that modulate key domains of the channel. Cryo-EM specimens prepared using the Kv channel and toxins will be imaged to solve the toxin/Kv channel complex structure, which will elucidate the structural basis for inhibition mechanism of the toxins and the structure of Kv channel in different conformations.

- **Date: 4:00PM/Nov. 19(Mon.)/2018**
- **Venue: Auditorium(1F), Postech Biotech Center**
- **Contact: Department of Life Sciences (Tel. 279-2721)**

*** This seminar will be given in English.**
please refrain from taking photos during seminars. *