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Molecular physiology of lipid scrambling in the brain

Lipid Scrambling & Ion Transport in Brain

Ions and lipids can move through cellular membranes dynamically. While ion transport mediated by channels or pumps is well studied, the molecular mechanism, cellular functions, and physiological roles of lipid transport are still poorly understood. Recently, independent groups suggested that TMEM16 protein family includes both ion channels and lipid scramblases. These findings raise new questions to tackle the lipid transport phenomenon. Phospholipids undergo dynamic redistribution when the lipid scramblases are activated. The collapse of asymmetric lipid distribution can change the local/global lipid composition spatiotemporally and alter the various signaling cascades. By using a combination of biochemical experiment, electrophysiology and imaging techniques, I will facilitate the understanding of TMEM16 proteins at the molecular level, which helps to reveal their physiological functions and provide insights to develop new therapeutics to prevent and treat neurological disorders.

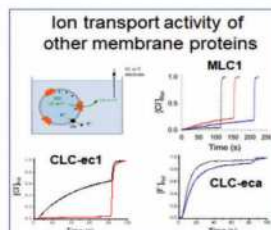
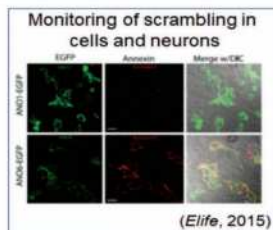
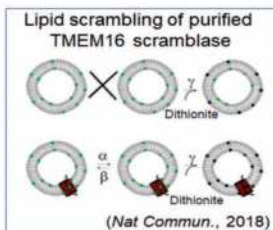
Aim

Investigation of structure–function relationship of membrane proteins in brain

Tool

Membrane protein biochemistry + Liposome-based functional assays + Cellular imaging + Electrophysiology

TARGET



Curriculum Vitae

2018~Present : Principal Investigator, KBRI
 2014~2018 : Postdoctoral Associate,
 Weill Cornell Medical College, USA
 2013~2014 : Postdoctoral Fellow, Gwangju Institute of
 Science and Technology (GIST), Korea

Academic Credential

2013 : Ph.D., Life Science, GIST
 2007 : M.S., Life Science, GIST
 2005 : B.S., Bioinformatics, Soongsil University

Awards/Honors/Memberships

2019~2022 : Grant from Young Researcher Foundation of Korea(NRF)
 grant funded by the Korea government(MSIT)
 (grant 2019R1C1C1002699)
 2014 : Fellowship from Basic Science Research Program through the
 National Research Foundation of Korea (N.R.F.) funded by the
 Ministry of Education, Science and Technology
 (grant 2013R1A6A3A03064407)
 2007~Present : Member, Biophysical Society

Research keywords

Membrane protein, Ion transport, Lipid scrambling, Electrophysiology.

Key techniques

Membrane protein biochemistry, Liposome-based ion transport assay (w/ion-specific electrode or ion-specific fluophore), Lipid scrambling assay and patch-clamp recording.

Research Interests/Topics

- Structural and functional studies on the brain-specific TMEM16 scramblases.
- Structure-function relationship of chloride transporting membrane proteins.

Research Publications (Latest 5)

- Falzone ME, Rheinberger J, **Lee BC**, Peyear T, Sasset L, Raczkowski AM, Eng ET, Di Lorenzo A, Andersen OS, Nimigean CM, Accardi A. Structural basis of Ca^{2+} -dependent activation and lipid transport by a TMEM16 scramblase. *Elife*, 8:e43229, 2019.
- **Lee BC**, Kelashvili G, Falzone M, Menon AK, Weinstein H, Accardi A. Gating mechanism of the extracellular entry to the lipid pathway in a TMEM16 scramblase. *Nat Commun.*, 9:3251, 2018.
- Malvezzi M, Andra KK, Pandey K, **Lee BC**, Falzone M, Brown A, Iqbal R, Menon AK, Accardi A. Out of the groove transport of lipids by TMEM16 and GPCR scramblases. *Proc Natl Acad Sci.*, 115:E7033-E7042, 2018.
- Falzone M, Malvezzi M, **Lee BC**, Accardi A. TMEM16 scramblases and channels: known structures, unknown mechanisms. *J Gen Physiol.*, 150:933-947, 2018.
- **Lee BC**, Menon AK, Accardi A. The nhTMEM16 Scramblase Is Also a Nonselective Ion Channel. *Biophys J.*, 111:1919-1924, 2016.

Patents

Screening Methods of a Ion Channel Modulator Using a Mutated BK_{Ca} Channel. 1015996860000 (2016.02.24)