

New study uncovers the interaction of calcium channels

October 25 2018

A

Wildtype Ca_v β -subunit

N—SH3 HOOK GK—C

Translocatable Ca_v β -subunit (β -FG)

—SH3 HOOK GK—FKBP—GFP

Target organelle markers

> PM: Lyn₁₁-FRB (LDR)

Lyn₁₁—FRB

> Mito: Tom20-mCherry-FRB (Tom20-MR)

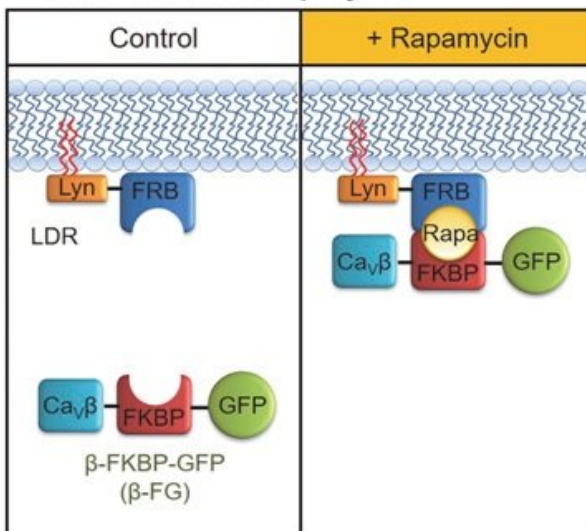
Tom20—mCh—FRB

> ER: mCherry-FRB-Cb5 (MR-Cb5)

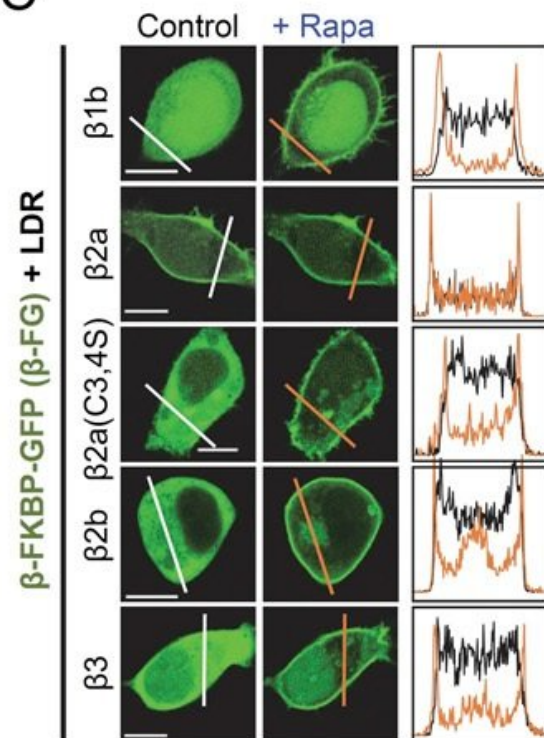
mCh—FRB—Cb5

B

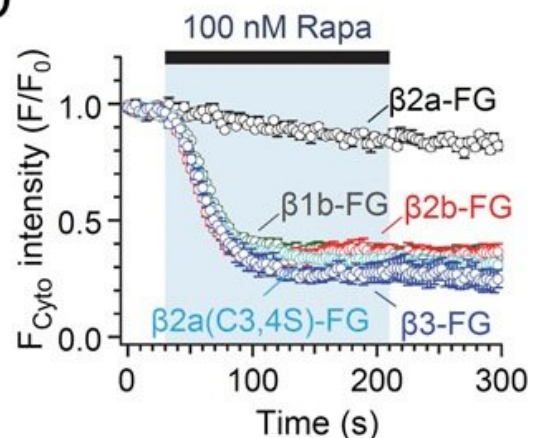
PM translocatable β system



C



D



Subcellular translocation of CaV β subunits on the addition of rapamycin in intact tsA-201. Credit: Daegu Gyeongbuk Institute of Science and Technology (DGIST)

Korean researchers have identified the interactions of the combinants among calcium channel proteins that exist in nerve and heart cells. The result opened a new path of developing treatments for high blood pressure and brain diseases.

A research team led by DGIST Professor Byung-Chang Suh at the Department of Brain and Cognitive Sciences has observed in real-time and identified the interaction of calcium channel complexes existing in nerve and heart cells inside cells.

Calcium channel complexes consist of alpha 1 ($\alpha 1$), beta (β), and alpha 2 gamma ($\alpha 2\delta$) subunits, which play important roles for calcium channels to control the inflow of [calcium ion](#) inside cells. Despite many scientists' efforts into identifying and analyzing the interactions of complexes, there has been no significant research achievements so far due to difficulties in verifying them in real-time.

Professor Suh's research team first modified and applied the 'Rapamycin-inducible FKBP-FRB dimerization technique', inducing calcium channel β subunits to move to organelle, a specialized subunit contained inside a cell membrane, mitochondria, or an endoplasmic reticulum, to create an environment that can be observed by eyes in real-time. Using the patch-clamp, the team could identify not only the interactions among various subunits inside calcium channels but also among subunits which could not been researched before.

β subunit is combined stably with $\alpha 1$ subunit if it is expressed by itself inside a calcium channel. However, if more than 2 β subunits of different types exist inside the same channel, β subunits of the existing $\alpha 1$ and β combined subunits are replaced by another single β subunit due to a competition among β subunits, reducing stability. This has been identified by the research team.

This is considered as opening a new horizon in the related research by enabling to observe in real-time the dynamic combination of $\alpha 1$ and β subunits in the calcium channel of a live cell due to the competition of subunits. In addition, such interaction among subunits mean more precise control of the calcium ion inflow inside cells, showing the importance of the close interaction among subunits.

Furthermore, the researchers also discovered new phenomena caused by subunits' interactions such as a decrease in [calcium](#) inflow into a channel caused by the separation of $\alpha 1$ and β combined subunits, decline in the [channel](#) blocking speed, and decreased activity of [calcium channels](#) caused by the phosphatide of cell membrane.

Professor Byung-Chang Suh said "Since this research was carried out on nerve and [heart cells](#), it is expected to open a path for the development of new treatment on [high blood pressure](#) and various [brain diseases](#). The research technique used in this research is also expected to greatly influence the research of various proteins inside [cells](#) that have interactions among proteins".

This study has been published on the latest issue of a world-renowned international journal, *Proceedings of the National Academy of Sciences (PNAS)*.

More information: Jun-Hee Yeon et al. Translocatable voltage-gated Ca_2^+ channel β subunits in $\alpha 1$ - β complexes reveal competitive

replacement yet no spontaneous dissociation, *Proceedings of the National Academy of Sciences* (2018). [DOI: 10.1073/pnas.1809762115](https://doi.org/10.1073/pnas.1809762115)

Provided by DGIST

Citation: New study uncovers the interaction of calcium channels (2018, October 25) retrieved 23 June 2024 from <https://phys.org/news/2018-10-uncovers-interaction-calcium-channels.html>

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