KBRI 한국뇌연구원

Press Release

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Mechanism of epilepsy causing membrane protein is discovered.

- The team lead by Dr. Lim Hyun-Ho of Korea Brain Research Institute published its paper in Proceedings of the National Academy of Sciences (PNAS).
- A new structure of membrane protein is discovered and the principle of ion exchange transport identified.

□ On August 21, Korea Brain Research Institute (**KBRI, President Pann-Ghill Suh**) announced that a team led by **principal researcher Lim Hyun-Ho** discovered **a new 3D structure and mechanism** of membrane protein which causes epilepsy and muscle problems.

○ The study results were published in the August issue of Proceedings of the National Academy of Sciences (PNAS), an international journal with the paper name and authors as follows.

* Paper name: Mutation of external glutamate residue reveals a new intermediate transport state and anion binding site in a CLC Cl-/H+ antiporter

* Authors: Kunwoong Park (first author), Byoung-Cheol Lee, and Hyun-Ho Lim (corresponding author)

□ Neurons control physiological phenomenon such as delivery of electrical signals and secretion of signal transduction materials by exchanging chloride (Cl^-) ions and hydrogen ions (H^+) in the cell membrane. If there is a problem with the **CLC transporter** protein that is involved in this process, muscle problems, epilepsy, hearing loss and blindness can develop.

□ **The research team led by Dr. Lim Hyun-Ho, succeeded in identifying a new structure of external glutamate residue, which plays a critical role in the ion exchange of single CLC transporter proteins, for the first time in the world.**

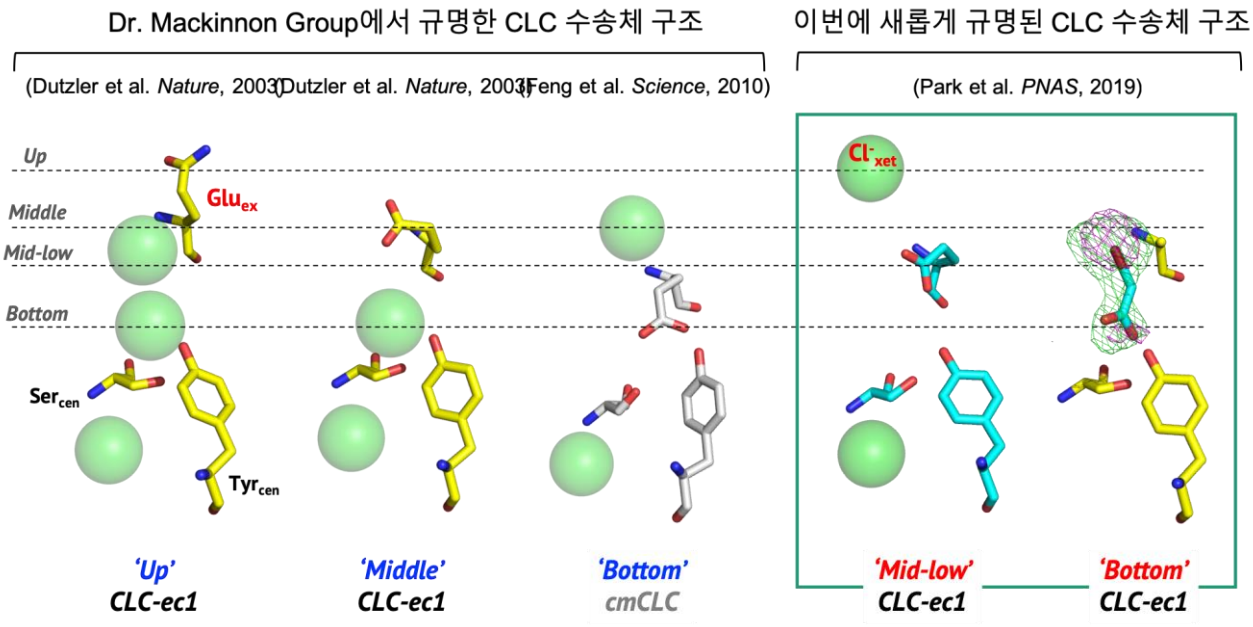
○ The research team produced mutated CLC proteins, where external glutamate residue is changed, and identified a 3D structure under 9 different conditions. In addition, the team found new areas where chloride ions (Cl^-) are combined in a transporter. Based on this, the team **found that a single CLC protein can have four different structures in the ion exchange process for the first time in the world**.

□ Dr. Mackinnon of Rockefeller University, who won the Nobel Prize for Chemistry in 2003 by identifying CLC protein structure for the first time, predicted there would be more than 3 kinds of structural diversity of this protein but less than two types of structure have been reported for the same species.

□ This research is meaningful in that **a new structure and functions are**

identified in membrane protein, for which structural determination is difficult, and the principle of material transport is identified. It is expected that this study will lead to the development of technologies that control various physiological phenomenon and diseases by controlling various functions based on membrane protein.

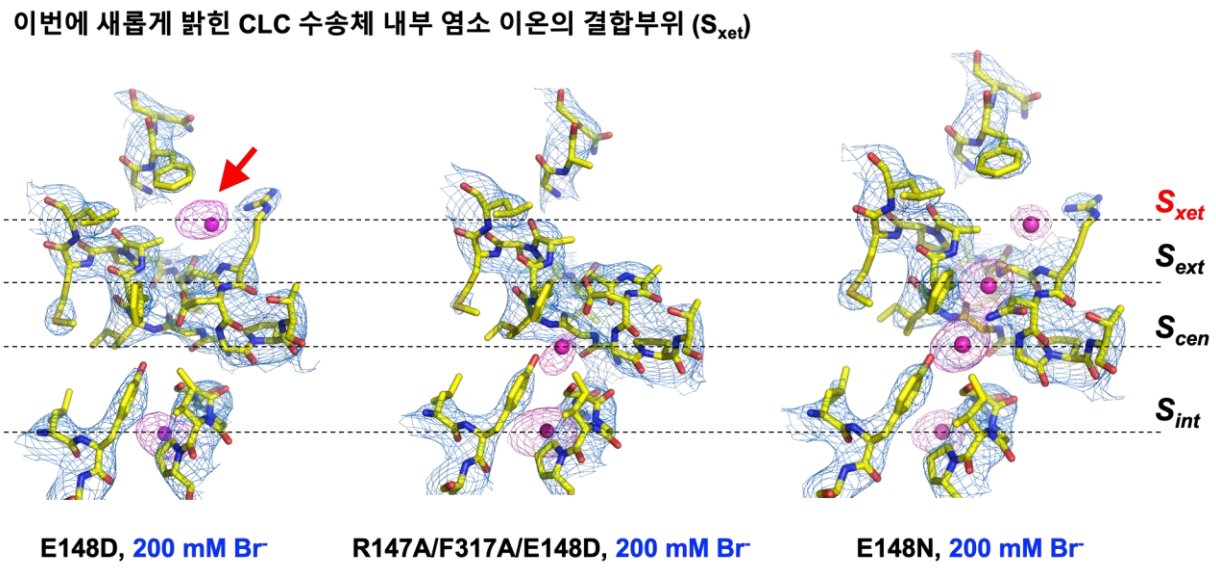
□ Dr. Lim Hyun-ho said “Our team could achieve good results thanks to KBRI which provided long-standing support for the systemic research that integrates structure and function even though the results could not be achieved immediately.” He added that “Our team will continue our research on membrane protein, which is essential to maintaining the physiological function of a brain.”



[Figure 1] Structural diversity of CLC transporter in the process of exchange and transport of chloride ions and hydrogen ions

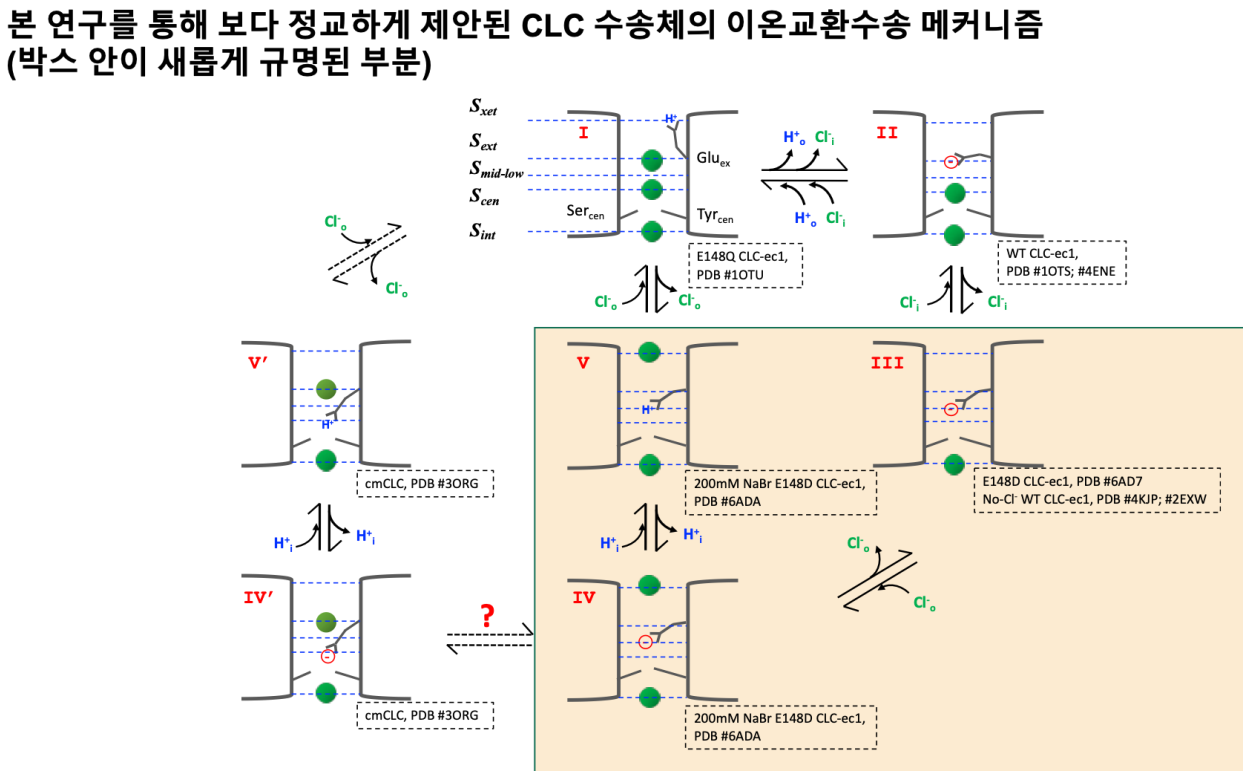
(Left) CLC transporter structure identified by the Dr. Mackinnon Group

(Right) CLC transporter structure newly identified in this study



[Figure 2] Area where chloride ions are combined within a CLC transporter

Area where chloride ions are combined within a CLC transporter, which is newly found in this research (S_{xet})



[Figure 3] The ion exchange transport mechanism of the CLC transporter, which is newly identified by Korea Brain Research Institute

The ion exchange transport mechanism of the CLC transporter, which is presented in a more elaborate manner in this study.