Gwangju Institute of Science and Technology
Official Press Release (https://www.gist.ac.kr/)

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Release Date	2018.11.1	

Professor Gwangrog Lee's joint research team identifies mechanism by which magnesium ions dynamically regulate the function of gene-degrading enzymes

☐ Korean researchers have identified the dynamic heterogeneity between enzyme activity and metal-ion interactions.

* Dynamic heterogeneity: the enzyme activity is different in each molecule even if the same enzyme is used

- GIST (President Seung Hyeon Moon) Professor Gwangrog Lee of the School of Life Sciences collaborated with KIAS (Director Yong-hee Lee) Professor Chang-bong Hyun to study how molecular metal ions, which are essential for enzyme function, activate gene hydrolytic enzyme cofactor ** by using single molecule fluorescence imaging. They have succeeded in discovering the mechanism of enzyme activation by observing the entire process in real time.

** Enzyme cofactor: The enzyme itself can not perform its function, but the enzyme can be activated by chemical reaction by binding with a metal ion.

☐ Magnesium, an essential mineral in bodies, activates enzymes by binding to the active site of the enzyme. Magnesium (Mg2+) is an essential cation before the activation of many enzymes in the cell (nucleic acid degrading enzyme, nucleic acid polymerase, helicase, integrase, ATPase, topoisomerase).

- In particular, magnesium is used to combine enzymes to repair genes when the DNA is damaged. It is known that if this process goes wrong, diseases such as cancer will occur. However, the concentration of intracellular magnesium does not depend on enzymes, and it was not known how different degrees of binding and dissociation affected the function and activity of enzymes.

☐ Magnesium also affects the rate of enzyme activity depending on the binding or binding time of the active site of the enzyme. Therefore, in order to understand the overall mechanism of enzyme activity, it is necessary to understand the stability or residence time of the metal ion bound to the enzyme active site. However, most studies, including theoretical studies, have focused only on the metal-to-enzyme bond mode or degradation step, and details of the role of metal ions such as magnesium during the complete enzymatic cycle have not been fully understood so far.

☐ Professor Gwangrog Lee's joint research team observed how two magnesium ions promote enzyme activity and how a combination of enzyme and magnesium ions affect the overall enzyme activity of the (λ-exonuclease) * model system. Single-molecule-FRET fluorescence and molecular dynamics simulation were used.

* Genetic enzymes (λ-exonuclease): Genes in living organisms are damaged or mutated by various chemical substances or UVs that occur in the process of cell metabolism, and these enzymes restores them to the original state.

☐ Professor Gwangrog Lee said, "This study revealed that two magnesiums (MgA2+ and MgB2+) bind to the active site of the enzyme with a similar thermodynamic binding constant *, but because of the asymmetric stability, the two magnesiums have different asymmetric velocity bonds and dissociations by up to 200 times."

* Binding constant: a constant that indicates how strong and long the two substances are combined

☐ This study by Professor Gwangrog Lee and Professor Chang-bong Hyun was supported by the Korea National Research Foundation, the Korean Health Technology R&D Project for Cancer Control, and Ministry of Health and Welfare. The results were published on October 23, 2018, in *Nature Communications* (IF 12.3).

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