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Professor Inchan Kwon's research team combines lipids in a new way to improve the effectiveness of drugs for gout

☐ Drug injection is one way to treat illnesses. However, since drugs quickly decomposes in the body, injections should be repeated periodically until the disease is completely cured. Therefore, developing a long-lasting treatment in the patient's body is very important to reduce the patient's pain and medical costs.

- Gwangju Institute of Science and Technology (GIST, President Kiseon Kim) School of Materials Science and Engineering Professor Inchan Kwon's research team was the first to discover how a large-sized therapeutic system can last for a long time by combining lipids that were only applicable to small-sized therapeutic agents.

☐ The research team developed a new method for gout therapy by combining lipids with urate oxidase * , a large therapeutic protein, so that it can last up to eight times longer than before. This technique not only increases the effective duration of gout treatment, but it can be applied to various therapeutic proteins in the future and is expected to dramatically reduce the duration of treatments as well as the cost and pain to patients.

* urate oxidase: an enzyme that convert toxic uric acid (an organic acid that is produced by the breakdown of the nucleic acid in a cell when it dies) into substances that are harmless to the body

- The short half-life * of therapeutic proteins is due to filtration in the kidneys, uptake into cells, and degradation by proteolytic enzymes *in vivo*. Among the ways to increase the half-life of therapeutic proteins is to combine them with lipids, which has been applied only to therapeutic peptides or small proteins.

  * half-life in the body: the time it takes for the concentration of proteins, drugs, etc. to drop by half in the body

□ The researchers systematically identified a large protein attached to serum albumin that prevents half-life augmentation by lipid bonds and then hypothesized that it is caused by collision with FcRn *.

  * FcRn: a special receptor in cell membranes

- To resolve these collisions, linkages of various lengths were introduced between large therapeutic proteins and lipids to measure changes *in vivo* half-life and the formation of complexes with therapeutic proteins, albumin and FcRn bound to lipids. As a large therapeutic protein, urate oxidase with a molecular weight of about 140 kDa and used for gout treatment.

- As a result, as the length of the linker increased, the degree of complex formation of lipoprotein-bound uricase, albumin and FcRn increased, and the half-life increased. In addition, when a linkage of more than a certain length was introduced, there was no difference in the degree of complex formation and the increase in half-life.

□ GIST Professor Inchan Kwon said, "This study is the first of its kind to show that the efficacy of half-life augmentation techniques using lipids was affected by the size of therapeutic proteins. In the future, this technique may be used to increase the half-life *in vivo* by binding lipids to various therapeutic proteins as well as uric acid enzymes."

□ This research was led by School of Materials Science and Engineering Professor Inchan Kwon (corresponding author) and was conducted SMSE graduate student Jinhwan Cho, and by Department of Biomedical Science and Engineering Ph.D. student Junyong Park and was supported by the National Research Foundation of Korea funded by the Ministry of Science and ICT. Their research was published on Januray 30, 2020, in the *Journal of Controlled Release*, a global journal for drug delivery.

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