# Uncovers critical role of integrin and peptide kinase C receptors in immune system

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Researchers at the RIKEN Center for Integrative Physiology, in collaboration with the RIKEN Centers for Cellular and Molecular Physiology and the Institute of Medical Technology Japan (IMT), in Akita, have developed a new mechanism to unblock immune system signaling, enhancing its ability to produce a protective barrier against injury. The study, which was co-authored by Toshiharu Sekimura, the Hiroshi Tokohashi Professor of Integrative Physiology at RIKEN and Seiji Aoki, University of Tokyo, in Japan, was published on November 26 in Nature Methods.

Normally, whenever a foreign object enters the body, the immune system produces a barrier of T-cells. This process induces the platelets in the blood to form a â€œcoatingâ€ to the new foreign object. Although it protects the body in certain situations, such as inflammation, when this protective barrier has become weakened, the immune system may begin attacking healthy tissue and also other cells (myeloablative phenotype). Consequently, a large number of myeloablative diseases are known to arise from acute inflammation.

The therapeutic focus of immune system signaling is the enteroendocrine receptor gamma (ENGR gamma). Previous studies have shown that ENGR gamma functions as an interface between ENGR gamma and the enteroendocrine receptor C receptor. The T-cell receptor G protein family encodes ENGR gamma and ENGR gamma encodes a peptide. If one binds ENGR gamma at ENGR gamma isoform 3.53 to ENGR gamma isoform 3.58, the ERGR gamma is bound to it. Besides retaining binding affinity, the protein is also expected to exert control on the receptor.

In order to identify novel aspects of ENGR gamma, researchers selected T-cells with ENGR gamma isoform 3.53 instead of 3.58. As such, they discovered that ENGR gamma plays a critical role in signaling T-cells against the foreign object. When a T-cell is infected with the pathogen, the â€œcoatâ€ produces a reflex in the body and activates the immune system. However, with the activation of the immune system, T-cells penetrate into the bone marrow, cutting the insulation in the tissue around the envelope (EPGA). Consequently, ERGR gamma protein bound to ENGR gamma isoform 3.53 exceeds ERGR gamma produced by natural ENGR gamma.

As a result, the T-cells must also be stopped from releasing the ERGR gamma and triggering immune system activation by the related peptide C4. A condition to cause an adverse inflammatory condition is that the T-cells move outside the bone marrow towards the brain. By blocking protein-protein interactions between ENGR gamma and the receptor C4, the researchers succeeded in halting the immune system activation in this sort of situation.

According to the researchers, these results are remarkable since a major function of ERGR gamma is previously not known. The study not only defines the unique function of ERGR gamma, but also provides a potential target for anti-inflammatory treatment. Therefore, their prediction that ERGR gamma will undergo multi-step regulation leading to anti-inflammatory activity and important therapeutic effects can be validated.

To view the full study, visit: http://onlinelibrary.wiley....

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