

Development of Retrievable Molecular Target Drug using Intelectin

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Intelectin-1 (ITLN) is a secretory protein that exists in blood, thoracic, and gut lumen. ITLN doesn't induce obvious physiologic and immunological reaction. Therefore, ITLN would induce no harmful effect when it injects into the body. In previous study, we found that ITLN specifically bound to 1,2-diol residues. The 1,2-diol residue is chemically stable, low-toxic, and is not bound with almost other proteins. Accordingly, we hoped that we could develop a retrievable molecular target drug by combining an ITLN-fused antibody and a blood purification device with a diol-coated resin.

In this study, we used ITLN-fused TNF receptor (TNFR-ITLN) instead of antibody because it doesn't need humanization. TNFR-ITLN is a soluble TNF receptor replacing Fc of etanercept with ITLN. TNFR-ITLN bound and neutralized to TNF- α as well as etanercept. In addition, TNFR-ITLN was specifically eliminated from the blood with a diol-silica gel column. On an apheresis model using LPS-treated rats (sepsis model), we measured the concentration of plasma TNF- α . When the TNFR-ITLN-injected LPS-treated rats were treated by apheresis using diol column, the transient increase of TNF- α was clearly suppressed in the blood. Furthermore, these rats were prevented from death by endotoxin shock.

According to these results, we considered that the apheresis using TNFR-ITLN plus diol column could selectively remove plasma TNF- α . A Fab-fused ITLN may specifically eliminate any pathogenic antigen from the body. This medical technology can be applicable to various autoimmune diseases and it is expected to have clinical application for a new blood purification method.