学会/受賞報告書

第32回日本炎症・再生医学会
Travel award
受賞

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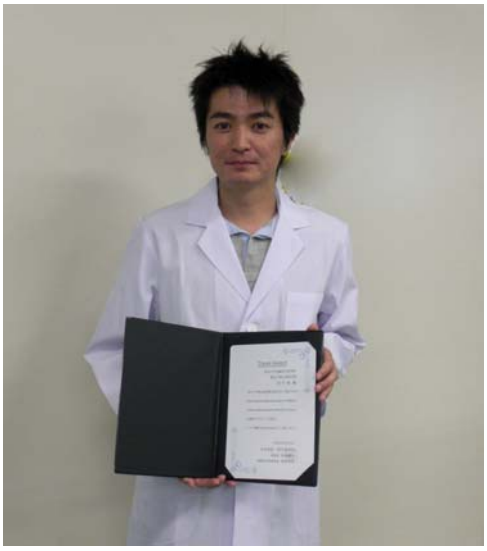

今回、日本再生・炎症医学会より「JSIR Travel Award」に採択頂き、大変光栄に思います。本研究を行うに際しまして、ご指導頂きました高井教授をはじめ遺伝導入研究分野の方々に心より感謝を申し上げます。

現在、私は自己免疫疾患に対する静注用免疫グロブリン製剤の作用機序解明の研究を行っております。今回は、その一環と致しまして、活性化B1細胞からの自己抗体産生に対する静注用免疫グロブリン製剤の抑制機序の解明における研究成果を10th World Congress on Inflammationで発表するにあたり、日本炎症・再生医学会より若手研究者支援の一環としまして採択頂きました。この受賞に慢心することなく、これからも研究に精進していきたいと思います。

受賞研究：

INTRAVENOUS IMMUNOGLOBULIN INHIBITS AUTOANTIBODY PRODUCTION BY B-1 CELLS

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抄録：
Many autoimmune diseases (ADs) are characterized by the production of autoantibodies (autoAbs) specific for self-antigens. However, the precise mechanism for the pathogenesis of autoimmunity is unknown. On the other hand, Intravenous Immunoglobulin (IVIg) exhibits therapeutic effects in the treatment of variety of ADs in clinical practice, while the precise mechanisms have also been left unclear. Innate B cells or B-1 cells, which produce mainly natural antibodies including weakly autoreactive antibodies, have a distinct lineage different from conventional B cells or B-2 cells. Recently, B-1 cells are shown to play a role in development of ADs when they are activated, and the class-switch is induced upon stimulation of their toll-like receptor (TLR)9 with unmethylated CpG oligonucleotide. Here we show that IVIg treatment in mice injected with CpG inhibits the proliferation and activation of B-1 cells. Upon stimulation of B-1 cells with CpG *in vitro*, IVIg attenuated the autoantibody production as well as the IL-10 production that is necessary to induce CSR, while it did not reduced the IL-6 production. The inhibitory effect of IVIg was dependent on the $F(ab')_2$ but independent on the Fc. In addition, IVIg upregulated the expression of CD22, a B cell inhibitory receptor, on B-1 cells. However, IVIg treatment exhibited a comparable inhibitory effect on B-1 cells from wild-type and CD22-knockout mouse. Inspections of IVIg-induced modulation of intracellular signaling revealed that the IVIg attenuated several TLR9-initiated signaling pathways, such as phosphorylation of TAK1, NF-kB and ERK, but not IRAK-1 and p38 MAPK. We propose a novel inhibitory mechanism of IVIg in ADs, in which IVIg inhibits TLR9 signaling that leads to production of autoreactive antibody in a $F(ab')_2$-dependent manner.