【別紙２】

論文名：

Specific overexpression of tumour necrosis factor-α-induced protein (TNFAIP)9 in $CD14^{+}CD16^{-}$ monocytes in patients with rheumatoid arthritis: comparative analysis with TNFAIP3.

新潟大学大学院医歯学総合研究科　生体機能調節医学専攻　内部環境医学
氏名　高井　千夏

Objective: The TNFα-induced proteins TNFAIP9 and TNFAIP3 play an important pathogenic role in murine arthritis. To clarify their pathophysiological roles in patients with rheumatoid arthritis (RA), we examined their expression and localization in peripheral blood mononuclear cells (PBMC).

Methods: TNFAIP9 and TNFAIP3 mRNA expression was determined in peripheral blood mononuclear cells (PBMC) of RA patients and healthy subjects (control). Flow cytometry was used to analyze the main TNFAIP9- and TNFAIP3-expressing cell populations. TNFAIP9 and TNFAIP3 mRNA expression levels were examined *in vitro* on $CD14^{+}$ cells stimulated with TNFα and lipopolysaccharide (LPS). The expression levels of TNFAIP9 and TNFAIP3 mRNAs were also measured before and 3 months after treatment with tocilizumab and abatacept.

Results: TNFAIP9 expression was significantly higher while TNFAIP3 expression was lower in PBMC of RA (n=36) than the control (n=24) ($p<0.05$, each). TNFAIP9 was expressed on $CD14^{+}$cells, especially in HLA-$DR^{+}CD14^{bright}CD16^{-}$cells, while TNFAIP3 was mainly expressed on $CD3^{+}$ T cells. TNF□ and LPS induced TNFAIP9 and TNFAIP3 in human $CD14^{+}$monocytes *in vitro*. Treatment with tocilizumab (n=13), but not abatacept (n=11), significantly reduced TNFAIP9 mRNA expression in PBMC, which was associated with reduction in the number of circulating $CD14^{bright}$ monocytes.

Conclusion: The expression of TNFAIP9 in $CD14^{+}$ cells was specifically elevated in patients with RA, regulated by TNFα and LPS, and suppressed by tocilizumab, while TNFAIP3 in PBMC showed different localization and induction patterns.