GS3-5 **Creation of TNF receptor I-specific antagonist, and its therapeutic efficacy for autoimmune disease**

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In the onset and exacerbation of disease, hundreds of proteins change in quality and quantity and identification of drug target proteins has been attracted a great deal of attention by exploring these disease-related proteins. Because the functions of protein are regulated with the manner binding to several receptors, unexpected side-effects would happen with complete inhibition or activation of the receptor signaling such as cytokines. Thus, it is essential to develop a novel drug developing technology, which regulates the functions of bio-molecule definitely for therapeutic purposes. In this regard, we have aimed to create the protein drugs focusing on the tumor necrosis factor (TNF), which binds two kinds of TNF super-family receptors (TNFR1 and TNFR2) and regulates the onset and exacerbation of autoimmune diseases such as rheumatoid arthritis and multiple sclerosis. Recently, we have succeeded to create several TNF receptor-selective agonists and antagonists by phage display techniques which can substitute aimed amino acids to the other, randomly. In this study, we introduce about the unique TNFR1-selective antagonist, which can only inhibit the function via TNFR1 correlating with the onset and exacerbation of autoimmune disease. This TNFR1-selective antagonist doesn't inhibit the host defense function via TNFR2, therefore, it can overcome the risk of infectious disease, which is a major side-effect of anti-TNF therapy. These results suggest that the approach of regulating protein function in molecular level is attractive to create safe and effective medical drug reducing side-effects.