

# Combination therapy of anti-TNF nanobody and PGE2 elevated therapeutic effect in experimental colitis via regulating Treg/Th17 balance

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## Abstract

**Abstract Backgrounds and purpose:** Anti-TNF therapy have gained great success in autoimmune disease. However, insufficient efficacy and safety of high dosage anti-TNF agents are exposed in amounts of clinical cases. Aiming at improving therapeutic of anti-TNF therapy, an anti-TNF nanobody V19 and combination therapy with PGE2 was introduced. **Experimental Approach:** DSS-induced colitis mice was used for evaluating therapeutic effect of V19 and combination therapy. Variation of Treg/Th17 balance was raised as the criterion for comparing therapeutic with combination therapy and mono-therapy. **Key Results:** V19 expressed by *Escherichia. coli* showed therapeutic effect on DSS-induced colitis mice by inducing the increase of treg via up-regulating tm-TNF- $\alpha$  and TNFR2 in peripheral blood. However, cell apoptosis (treg, Dendritic Cells and CD8 T cells) was induced in peripheral blood under high dose of V19 accompanied with up-regulated tm-TNF- $\alpha$ . Besides, Th17 cells in colons from DSS-induced mice were induced by V19 accompanied with up-regulation of IL-6. Combination therapy presented better therapeutic effect than mono-therapy. After combination therapy, Th17 cells were significantly decreased in colons and vitro assay demonstrated that PGE2 reduced Th17 cells by down-regulating IL-6 in colons via EP4. Although PGE2 showed no influence on cell apoptosis and can not induce treg generation, it enhanced the ability of V19 in inducing treg by up-regulating TNFR2 via EP4 in peripheral blood. **Conclusion:** This combination therapy presents good clinical significance that combination of PGE2 can expand drug delivery window and enhanced therapeutic effect during the anti-TNF clinical treatment.

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