In vivo self-assembled siRNA as a modality for combination therapy of ulcerative colitis

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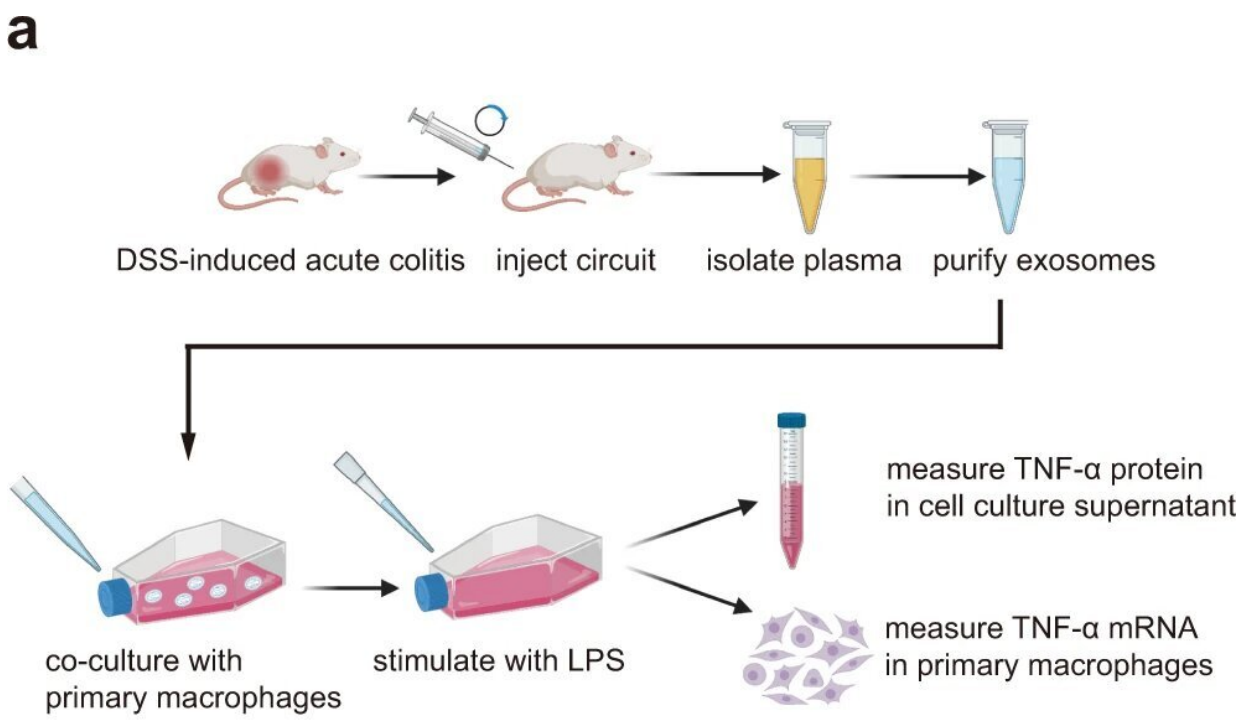

Evaluation of the activity of TNF-α siRNA-encapsulating sEVs in an ex vivo model. **a** Schematic of the experimental design. Acute UC was induced in male BALB/c mice by replacing their drinking water with a 2.5% DSS solution for 7 days. DSS mice were intravenously injected with 5 mg/kg CMV-scrR or CMV-siR$^{TNF-\alpha}$ circuit every day for a total of 7 times, and then the sEVs were purified from the plasma of each mouse and dissolved in 50 μL PBS. BCA method was employed to quantify total protein content in sEVs, and the isolated sEVs had a total protein concentration of ~0.8 μg/μL. Subsequently, the sEV solution (50

μL) was incubated with 1×10^5 primary macrophages. After stimulating macrophages with 50 ng/mL LPS, the suppression of TNF-α expression by TNF-α siRNA were examined in this ex vivo model. **b** Quantitative RT-PCR analysis of the relative expression levels of TNF-α mRNA in primary macrophages (n = 6 in each group). Created with BioRender.com. **c** Determination of the levels of secretory TNF-α protein in cell culture supernatant by ELISA (n = 6 in each group). Values are presented as the mean ± SEM. Significance was determined using one-way ANOVA followed by Dunnett's multiple comparison. ***p*