IL-10 alleviates lipopolysaccharide-induced skin scarring via IL-10R/STAT3 axis regulating TLR4/NF-ϰB pathway in dermal fibroblasts

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Abstract

Background and Purpose: Hypertrophic scar (HS) is a serious fibrotic skin disease. The roles of bacterial contamination and prolonged inflammation in wound were considered to be significant. IL-10 plays a pivotal role in wound healing and scar formation. Here, we investigate whether IL-10 alleviates lipopolysaccharide (LPS)-induced inflammatory response and skin scarring, explore the possible mechanism in scar formation. Experimental Approach: RT-qPCR, Western blotting, histochemistry, immunostaining, ELISA array, electron microscope, fibroblast-populated collagen lattice (FPCL) and a rabbit ear scar model were used to investigate and validate the effect of IL-10 on LPS-stimulated scar formation. Key Results: Our results showed that the expression of TLR4 and pp65 was higher in HS and HS-derived fibroblasts (HSFs) than their counterpart normal skin (NS) and NS-derived fibroblasts (NSFs). LPS could upregulate the expression of TLR4, pp65, Col I, Col III and ∝-SMA in NSFs, but IL-10 could downregulate their expression in both HSFs and LPS-induced NSFs. Blocking IL-10 receptor (IL-10R) or the phosphorylation of STAT3, their expression was upregulated. In addition, in vitro and in vivo models results showed that IL-10 could alleviate LPS-induced fibroblast-populated collagen lattice (FPCL) contraction and scar formation. Conclutions and Implications: Our study suggests that IL-10 may improve LPS-induced harmful to wound healing, reduce scar contracture and scar formation via IL-10R/STAT3 axis regulating TLR4/NF-ϰB pathway in dermal fibroblasts by reducing ECM proteins deposition and the conversion of HSFs to NSFs. Therefore, the downregulation of inflammation may be a better option for improving scar quality, and become potential therapeutic targets for scarring.

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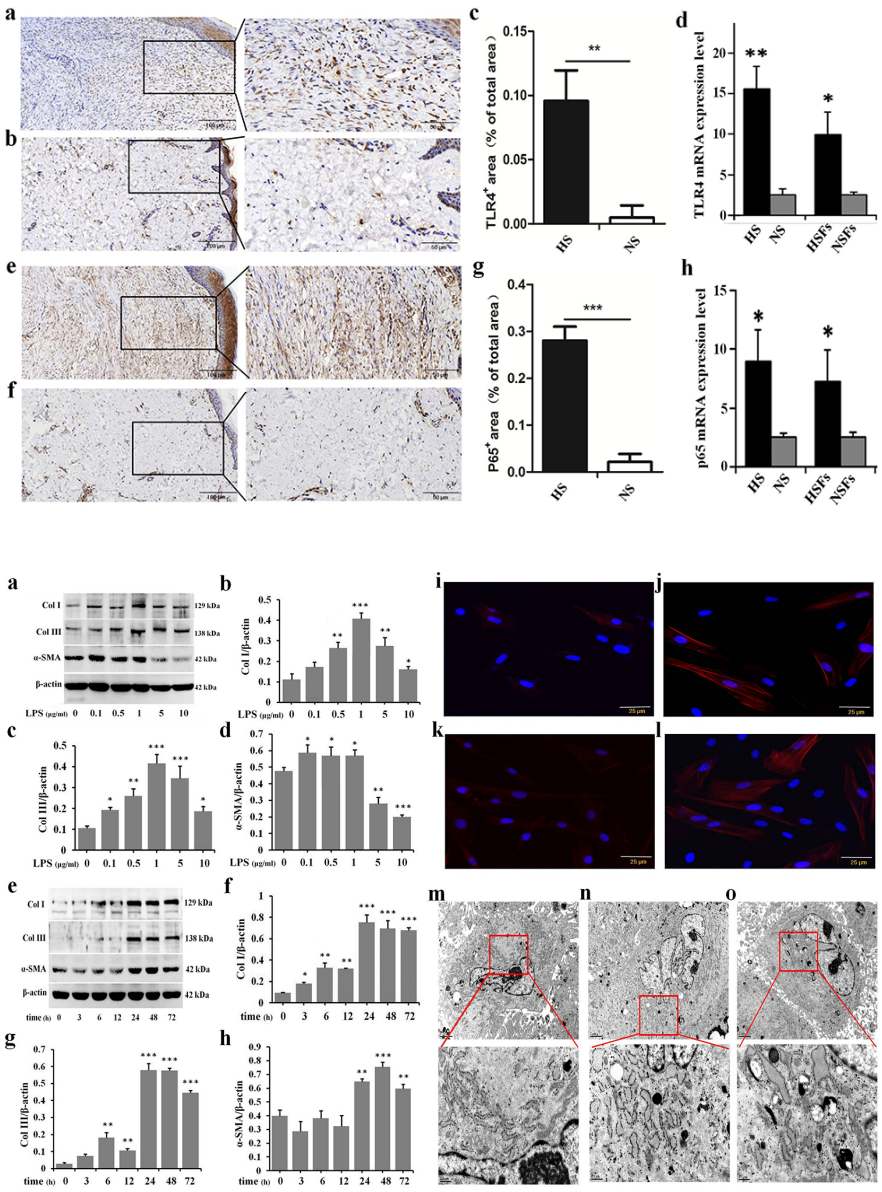

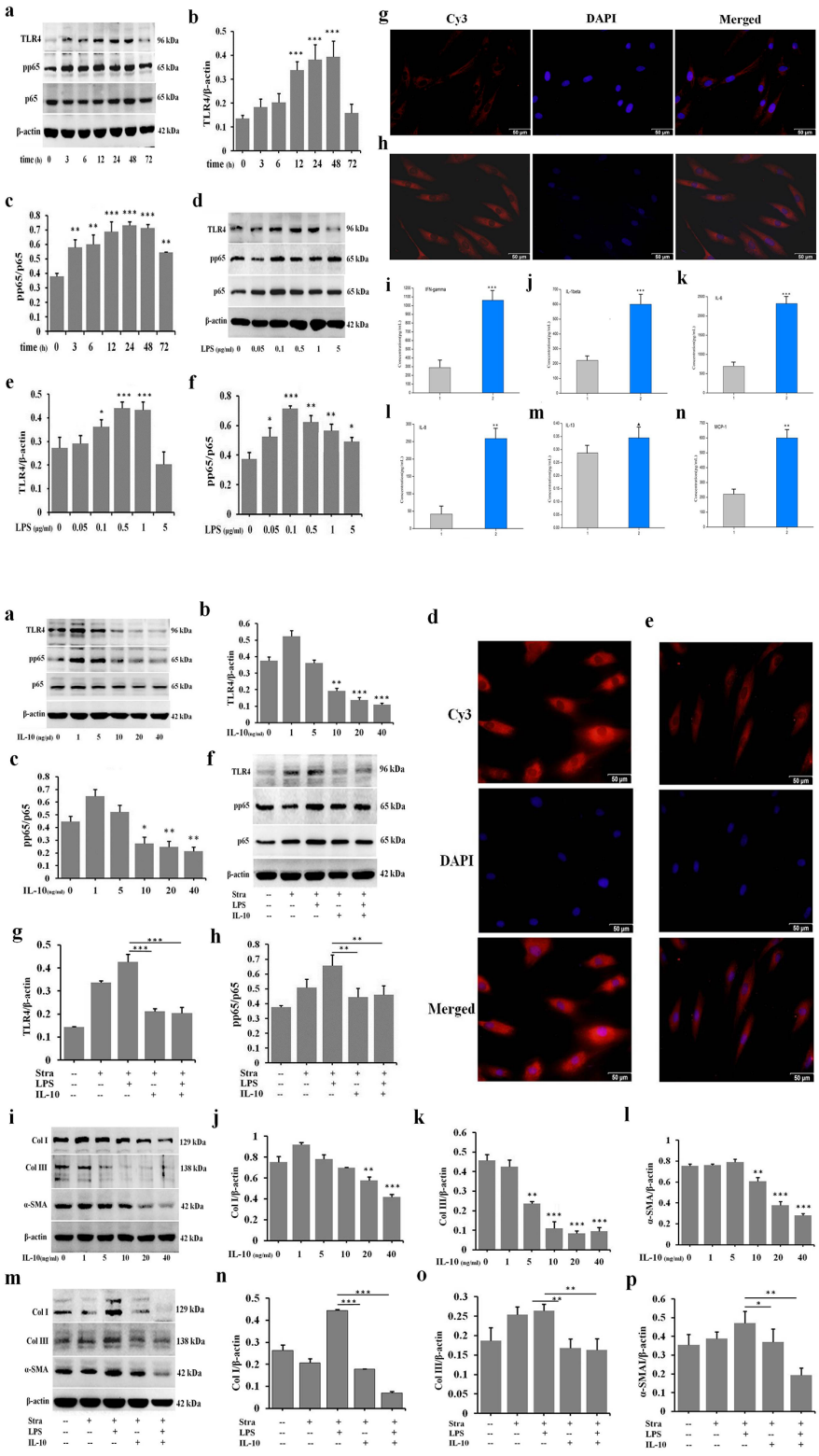

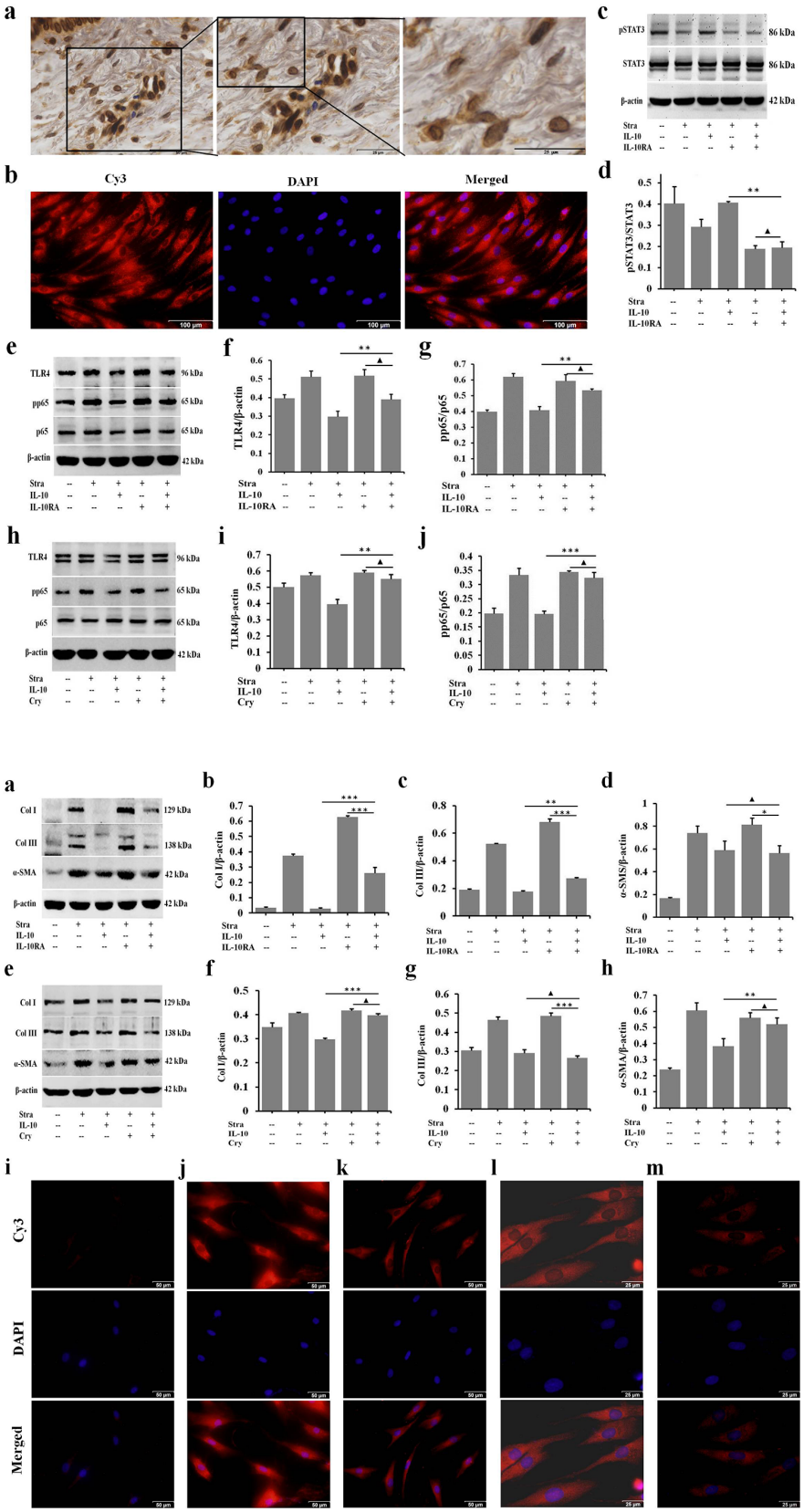

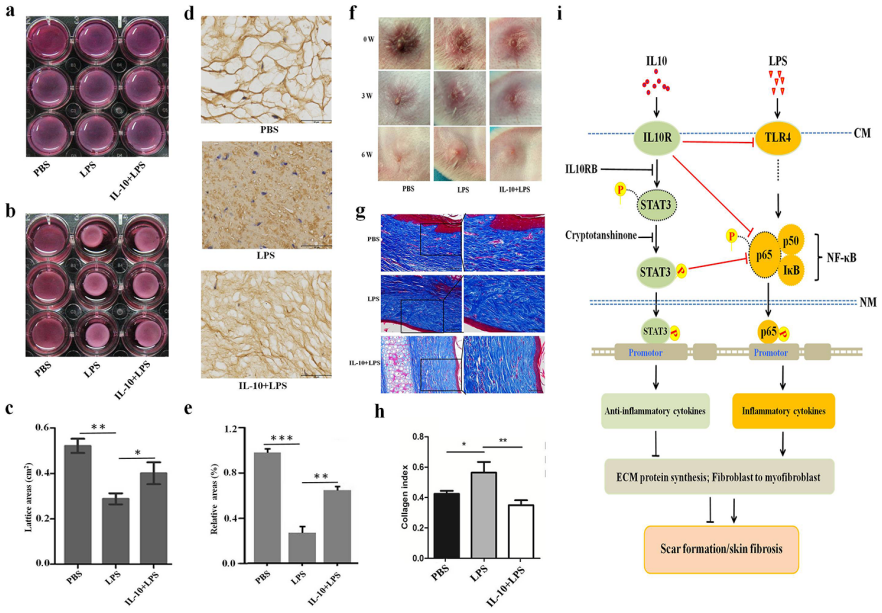

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Table 1 The profile of each samples.doc available at https://authorea.com/users/350674/articles/475460-il-10-alleviates-lipopolysaccharide-induced-skin-scarring-via-il-10r-stat3-axis-regulating-tlr4-nf-%CE%BAb-pathway-in-dermal-fibroblasts

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Table2 Sequences of primers for RT.docx available at https://authorea.com/users/350674/articles/475460-il-10-alleviates-lipopolysaccharide-induced-skin-scarring-via-il-10r-stat3-axis-regulating-tlr4-nf-%CE%BAb-pathway-in-dermal-fibroblasts