

## ABSTRACT

### **The Inhibitory Mechanism of Limbal Mesenchymal Stem Cells Transplantation with Fibrin Glue Scaffold in Fibrosis Post Trabeculectomy**

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**Objective:** to analyze the inhibitory effect of limbal mesenchymal stem cells (LMSCs) with fibrin glue (FG) scaffold on fibrosis formation after trabeculectomy in rabbits.

**Materials and methods:** This experimental study was conducted under local ethical review board. A total 40 rabbits with 10 rabbits in control group (group 1), 10 rabbits underwent trabeculectomy without any therapy (group 2), 20 rabbits underwent trabeculectomy and received subconjunctival transplantation of FG scaffold and LMSCs with FG scaffold (group 3 and 4 respectively). They were terminated on day 21 post-operation. Histology and immunohistochemistry were performed to evaluate fibrosis area, EGF, bFGF, TGF- $\beta$ , and MMP-9 expression within macrophage in subconjunctival area.

**Results:** The fibrotic area was significantly lower on LMSCs with FG group ( $3.70 \pm 0.829$ ,  $p=0.000$ ) compared to group 2 ( $28.60 \pm 10.985$ ). TGF- $\beta$  were significantly lower in group 4 ( $1.556 \pm 0.543$ ,  $p=0.019$ ) compared to group 2 ( $2.210 \pm 0.513$ ), suggesting repressive effect of LMSCs on TGF- $\beta$  as key regulator in tissue fibrosis. EGF ( $3.77 \pm 1.11$ ,  $p=0.97$ ) and bFGF ( $4.111 \pm 0.660$ ,  $p=0.028$ ) were higher in group 4 compared to group 2. EGF and bFGF have significant positive effect on fibrosis formation, suggesting effect on regulation of bleb integrity. MMP-9 has significant negative effect on fibrosis formation ( $b=-1.171$ ,  $p=0.026$ ), suggesting a proteolytic enzyme in inhibiting fibrosis formation role.

**Conclusion:** TGF- $\beta$  may play a central role in wound healing after trabeculectomy. LMSCs may exert inhibitory effect in fibrosis after trabeculectomy through paracrine effect that modulate wound microenvironment resulting in proteolytic activity of MMP-9.

**Keywords:** limbal mesenchymal stem cell, fibrin glue, trabeculectomy, wound healing, fibrosis