Triamcinolone acetonide induces the autophagy of fibroblasts in tracheobronchial stenosis due to tuberculosis via mediation of SIRT1/FOXO3 pathway

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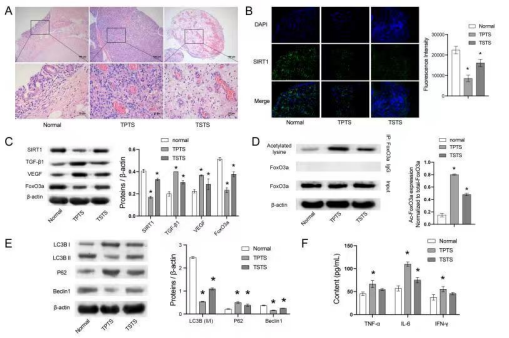
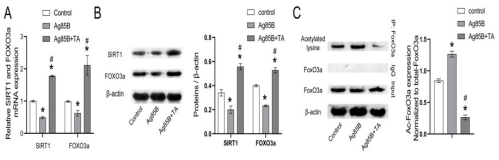
Purpose

Tracheobronchial stenosis due to tuberculosis (TSTB) seriously threatens the health of patients with tuberculosis. In addition, the inflammation and autophagy of fibroblasts could lead to the progression of TSTB. It has been reported that triamcinolone acetonide (TA) could inhibit the autophagy of fibroblasts. Nevertheless, the mechanism underlying the impact of TA on TSTB remains not explored.



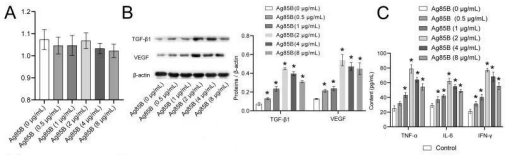
Methods

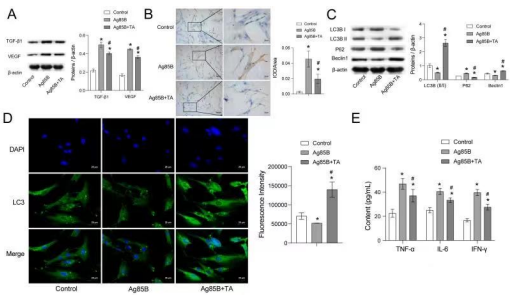
In order to mimic TSTB in vitro, WI-38 cells were exposed to Ag85B. In addition, CCK8 assay was applied to assess the function of TA in WI-38 cells. RT-qPCR was applied to detect the mRNA level of SIRT1 and FOX3a, and autophagy-related proteins were evaluated by western blot. VEGF level was investigated by IHC staining. ELISA was applied to detect the secretion of inflammatory cytokines. Furthermore, H&E staining was applied to observe the injury of tissues.



Results

Ag85B limitedly affected the WI-38 cell viability, while TA notably suppressed Ag85B-treated WI-38 cell viability. TA dose-dependently induced the apoptosis of Ag85B-treated WI-38 cells. In addition, Ag85B-induced upregulation of IL-6, TNF-α, IFN-γ and fibrotic proteins (TGF-β and VEGF) was significantly abolished in the presence of TA. Meanwhile, TA reversed Ag85-induced inhibition of cell autophagy via mediation of p62, LC3 and Beclin1. Furthermore, silencing of SIRT1/FOXO3a pathway could reverse the effect of TA on autophagy of Ag85B-treated cells.





Conclusions

TA significantly induced the autophagy of fibroblasts in TSTB via mediation of SIRT1/FOXO3 pathway. Thus, TA might act as a novel agent against TSTB.