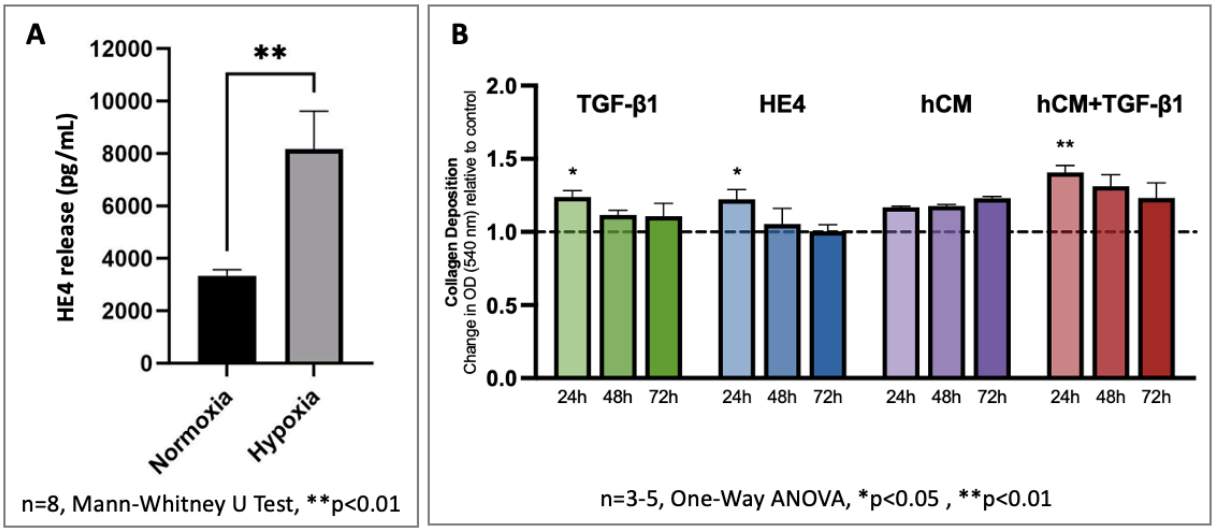
4.07 Hypoxia-stimulated Human Epididymis Protein 4 (HE4) Secretion by Bronchial Epithelial Cells and its Effect on Pulmonary Fibroblasts



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Background: Human Epididymis Protein 4 (HE4), a biomarker of ovarian cancer, has been implicated in fibrotic lung diseases. Here we aim to assess the hypoxia-stimulated secretion of HE4 by bronchial epithelial cells and investigate its effect on pulmonary fibroblasts.

Methods: Hypoxia-stimulated (6h 1% O_2, 18h 21% O_2) HE4 secretion was assessed using ELISA and confirmed with Western Blot in bronchial epithelial (16HBE14o-) cells. Pulmonary fibroblasts (CCD-11Lu) were exposed to recombinant human HE4 (rHE4), TGF-beta1 and hypoxia-conditioned medium (hCM). Collagen deposition was quantified using Sirius RED staining. The expression of collagen and inflammatory markers, including IL-6 and IL-8, was assessed using qRT-PCR and confirmed by ELISA.

Results: Hypoxia induced significant HE4 secretion in 16HBE14o- (Figure A). Collagen deposition was significantly increased in pulmonary fibroblasts following rHE4 and TGF-beta1 exposure. Collagen deposition was more gradual but sustained after hCM exposure (Figure B). rHE4-stimulated pulmonary fibroblasts also showed increased expression and secretion of IL-6 and IL-8.

Conclusions: HE4 is secreted by bronchial epithelial cells in response to hypoxia and has a fibrogenic and pro-inflammatory effect on pulmonary fibroblasts.

Keywords: HE4, interstitial lung disease, lung fibrosis

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