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Title: Effect of hypoxia and cigarette smoke on hypoxia-inducible factor 1α (HIF-1α) and heat shock protein 72 (HSP72) system of alveolar epithelial cells

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Body: Smoking is the main risk factor of alvolar destruction in emphyseama/COPD. In COPD airway obstruction causes hypoventilated areas in the lung leading to alveolar hypoxia. HIF-1 α plays a key role in the defense against hypoxic cellular damage. The inducible HSP72 has a central role in the maintenance of cell integrity, apoptosis and cellular immunity. It is unknown, what role HIF-1α and HSP72 play in cell damage caused by hypoxia and cigarette smoke. HIF1α and HSP72 mRNA expression using RT-PCR of immortalized alveolar epithelial cells (A549) was analyzed using hypoxia (FiO2 20,9% (control); 13±1%; 6±1%; 1±1%) and treatment with cigarette smoke extract (CSE). Under hypoxic conditions cell count grew significantly (FiO2 13±1%: 13,33x105; FiO2 6±1%:13,2x105; FiO2 1±1%: 12,86x105 vs. normoxia FiO2 20,9%: 7,73x105; p<0.01), whereas treatment with CSE decreased cell number compared to control. Mild hypoxia significantly increased HIF-1α mRNA, while atmospheric oxygen tension resulted in unchanged expression. Severe hypoxia and CSE treatment significantly lowered HIF-1α mRNA expression in A549 cells (CSE: 4,30±0,60, FiO2 1±1%: 3,24±1,03 vs. control: 11,671±0,70 arbitrary unit, p<0,05). HSP72 mRNA expression increased using FiO2 20,9%, in contrast decreased in all hypoxic and CSE treated cells. Dexamethasone treatment of CSE treated cells dose-dependently increased HIF-1 α and HSP72 mRNA expression. Hypoxia increases, whereas CSE treatment decreases alveolar epithelial cell count. HSP72 mRNA decreases following hypoxic or CSE induced cellular stress, while severe hypoxia and CSE treatment decreases HIF-1α mRNA expression of A549 cells.