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Title: Klotho: An important protein in the formation and development of emphysema

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Body: Objective: Klotho is an anti-aging protein which also possesses anti-inflammatory actions and modulates the cellular responses to oxidative stress. Knock out of klotho in the mouse caused the formation of emphysema. The aim of this study is to investigate the expression of klotho in human emphysema and factors affecting its expression and activity in human bronchial epithelial cells. Methods: Lung tissue from 5 COPD patients, 8 smokers without COPD and 13 non-smoking, non-COPD. Klotho expression was determined by quantitative real-time PCR, Western blotting and immunohistochemistry. Human bronchial epithelial cells (HBE) were treated with tumor necrosis factor (TNF)-α and hydrogen peroxide (H_2O_2), and the expression of klotho mRNA in cells and protein in cell supernatants was detected by RT-PCR and enzyme-linked immune sorbent assay (ELISA) respectively. Exogenous klotho was also added to HBE and A549 cell cultures and MTT assays were used to detect cell apoptosis. Results: Klotho was detected in human lung tissue with a clear localization to airway epithelial cells. The level of klotho mRNA and protein in smokers with normal lung function was similar to that in non-smokers but was reduced in COPD patients The level of klotho expression was similar in COPD patients with emphysema compared with that in non-emphysematous COPD patients. In addition, we found that both TNF-α and H_2O_2 could significantly inhibit the expression and release of klotho in HBE cells. Exogenous klotho inhibited apoptosis in HBE) and A549 cells). Conclusions: Klotho may play an important role in the formation and development of emphysema in COPD. However, further research is needed to explore the underlying mechanism.