# ABSTRACT

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| **TITLE:** | Overexpression of the Klotho Protein in Human Epithelial Lung Cells and the Effect on AKT and P38 MAPK Concentrations in the IGF-1 Signaling Pathway: Investigating the Mechanisms of COP |
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**ABSTRACT:** Chronic obstructive pulmonary disease (COPD) is the 3rd leading cause of death in the U.S., with symptoms that include worsening cough and shortness of breath, followed by successive lung damage. Recently, the klotho gene has gained attention for exhibiting anti-aging properties at the cellular level. This gene encodes a soluble and a secreted form of the protein, which inhibit the AKT transduction pathway. Activation of AKT prevents transcription of vital detoxification genes that encode proteins to neutralize reactive oxygen species (ROS) produced during cell metabolism. Accumulation of ROS induces the activity of p38 MAPK, a kinase that promotes inflammation and apoptosis. KLOTHO inhibition of the AKT pathway may be the key to future efforts to prevent lung damage in smokers. We hypothesize that cells, which overexpress klotho will have significantly lower levels of AKT and p38 proteins versus unaltered cells. Human epithelial lung cells that overexpress klotho as well as control cells were treated with 200 g/mL CSE for 6, 12 and 24 hours. RNA was isolated, and the klotho gene was amplified and quantified using RT-qPCR. Proteins were isolated and subjected to Western Blot. AKT and p38 levels were quantified using densitometry. Klotho mRNA levels were significantly higher in CSE treated cells versus controls at 12 hours post-CSE exposure. Basal levels of AKT and p38 were significantly increased in klotho overexpressing cells. AKT and p38 protein levels were significantly higher in CSE treated cells versus controls in cells that overexpress klotho only. Future experiments should focus on quantifying levels of active (phosphorylated) AKT and p38 proteins. This would provide more insight into whether activities of AKT and p38 are lowered, despite increased levels of total proteins, in response to klotho overexpression.