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[ATS] L-Carnitine Supplementation Attenuates Elastase-Induced Emphysema Progression

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Introduction

We have previously described a progressive emphysema following the oropharyngeal application of porcine pancreatic elastase (PPE) into C57BL/6 mice, characterized by a decline in lung function and progressive airspace enlargement.

Targeted metabolomic analysis of lung tissue from these mice revealed a reduction in the concentration of a number of Acylcarnitines, with the greatest reduction in free L-carnitine, a metabolite critical for transporting long chain fatty acids into the mitochondria for their subsequent β-oxidation and a reported anti-oxidant.

We therefore **hypothesized** that supplementation with L-carnitine can impair the development of PPEinduced emphysema.

Methods

The progression of emphysema was examined in C57BL/6 mice that were treated i.p. every other day with 500mg/kg L-carnitine following a single oropharyngeal application of PPE, compared to mice that were not supplemented with L-carnitine and PBS treated controls. Lung function and histology were analyzed 28 days later. Alveolar epithelial type II-like murine LA-4 cells were treated with L-carnitine and analyzed for apoptosis development following PPE and H2O2 exposure, as well as wound healing ability.

Resultados

PPE-treated mice demonstrated impaired **lung function** compared to PBS treated controls (lung compliance of 0.067 ± 0.008 ml/cmH20 vs 0.035 ± 0.005 ml/cmH20, respectively SD $p<0.01$), which improved following supplementation with L-carnitine (lung compliance of 0.051 ± 0.006 ml/cmH20, $p<0.01$ compared to mice only treated with PPE).

Lung histology also revealed that supplementation with L-carnitine reduced the airspace enlargement caused by PPE-treatment.

Interestingly, L-carnitine significantly inhibited the development of both H2O2 and PPE induced apoptosis in **cultured LA-4 cells** as determined by Annexin V staining. However, culturing LA-4 cells in the presence of increasing concentrations of L-carnitine did not improve the wound healing ability of these cells in a scratch assay.

Conclusions

Our results indicate that supplementation of mice with **L-carnitine attenuates the severity of PPE-induced emphysema, and that this may in part be due to reduced levels of apoptosis**.

We therefore suggest that L-carnitine supplementation, which is used clinically for the treatment of neonates with congenital metabolic diseases, may be beneficial to COPD patients.