

# Nitrated Fatty Acids Reduces the Presence of Matrix Metalloproteinase 9 in Bleomycin-Induced Lung Inflammation

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Acute lung injury leads to an increase in infiltrating cells. Matrix Metalloproteinase 9 (MMP9) is a zinc dependent endopeptidase that degrades the extra cellular matrix and increases the porosity of the lung. Nitro-oleic fatty acid (OANO2) is an electrophile that has been studied in reducing cardiovascular system inflammation. OANO2 modifies cysteine residues via Michael addition leading to altered protein function. We hypothesized that OANO2 administration would modify the active cysteine (position 87) in MMP9, reducing the number of infiltrating cells in acute lung injury. To test our hypothesis we used an intratracheal bleomycin acute lung injury model. 2 groups of 6 C57BL/6J mice were treated intratracheally, one with bleomycin (3U/kg) and one with PBS (50uL). A further 2 more groups of 6 mice were treated in a similar manner but each group was also administered OANO2 (50mg) via the same installation 3 days later. The lungs were collected 7 days post bleomycin treatment. Expression of CD11b positive cells (marker for migratory macrophages) and MMP9 positive cells was determined by immunohistochemistry. Bleomycin injured mice displayed increased levels of CD11b positive cells compared to PBS mice. The 2 groups treated with OANO2 resulted in a marked decrease of CD11b positive cells most notably in bleomycin injured animals. It can be concluded that OANO2 can reduce the presence of CD11b positive infiltrating cells. The bleomycin group also displayed an increase in the amount of MMP9 positive cells compared to PBS mice. However, both groups of mice treated with OANO2 showed an increase in the amount of MMP9 positive cells; this was confirmed by the use of a western blot which showed high densities in PBS + OANO2 and bleomycin + OANO2. We speculate that increased MMP9 expression results from reduced self-degradation as a consequence of OANO2 mediated enzyme inhibition. Supported by ASPET SURF and NIH R25ES020721.

## OANO2 ALTERS THE PRESENCE OF MMP9 IN BLEOMYCIN INDUCED LUNG INJURY

