

The Therapeutic Potential of Nitrated Fatty Acids in Acute Lung Injury

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Acute lung injury (ALI) is characterized by severe inflammation and damage to barrier function. ALI is caused by exposure to toxicants (e.g. air pollutants, chemotherapeutics, and radiation). 22 in 100,000 people are diagnosed yearly with ALI, however no effective pharmacological treatments exist. New studies have correlated lung tissue damage in ALI to the excess activity of pro-inflammatory macrophages. The electrophilic nature of nitro-oleic fatty acid (OA-NO₂) is a target for specific cysteine residues within DNA binding regions of transcription factors, including nuclear factor kappa-light chain-enhancer of activated B cells (NF-κB). OA-NO₂ modification of NF-κB is proposed to inhibit its function and thus reduce inflammatory responses within macrophages. In this study, we used the cell line RAW 264.7 induced with LPS to model pro-inflammatory activation of airway macrophages, similar to that seen in ALI. Cells were treated with OA-NO₂ or media control. A BCA Protein Assay, a Griess Assay, and Western Blotting were utilized to identify the presence of iNOS, a downstream signal of NF-κB activation, and IκB, an inhibitor of NF-κB. We determined OA-NO₂ reduces the production of iNOS after stimulation, implicating NF-κB inhibition, resulting in anti-inflammatory, pro-survival responses in the cell. OA-NO₂ decreased the IκB expression by 74% in control and 139% in LPS. We conclude OA-NO₂ modification of NF-κB decreased association with IκB, increasing its degradation. This supports the use of OA-NO₂ as a potential therapeutic for ALI. Funding NIH-R25ES020721, R01HL086621, P30ES005022, SOT Intern Program, ASPET SURF Program, and the Rutgers Office of Research and Economic Development.

