Effects of anti-TNFα Antibody on Sulfur Mustard-Induced Lung Injury in Rats

Talia Seymore, Chenghui Jiang, Helen Abramova, Rama Malaviya, Debra Laskin
Pennsylvania State University and Rutgers, The State University of New Jersey

Sulfur mustard (SM) is a vesicating chemical warfare agent that causes severe lung injury when inhaled. Acute sulfur mustard-induced toxicity is due, in part, to persistent accumulation of macrophages in the lung and the release of inflammatory mediators including cytokines, chemokines, eicosanoids and growth factors. The proinflammatory cytokine, tumor necrosis alpha (TNFα), is released from activated macrophages; it has been shown to contribute to lung injury by promoting inflammatory cell accumulation in tissues and stimulating the release of other inflammatory mediators. This leads to oxidative and nitrosative stress, airway hyperresponsiveness, and tissue remodeling. Previous studies have shown that SM-induced injury is associated with increased numbers of galectin-3+ macrophages in the tissue, which are involved in tissue remodeling. In this study, we tested the hypothesis that anti-TNFα antibody therapy will mitigate mustard induced lung inflammation and injury, as assessed by expression of TNFα and galectin-3. Male Wistar rats were exposed to SM vapors (0.4 mg/kg) or air control and treated with either monoclonal anti-TNFα antibody (15 mg/kg) or vehicle 15-30 min later. Animals were euthanized 3 days after exposure and lung tissue collected and fixed in paraformaldehyde. Paraffin embedded lung sections were analyzed for expression of TNFα and galectin-3 using immunohistochemistry.

Treatment of rats with SM resulted in increased expression of TNFα, relative to lungs from control rats, which had little to no expression. This was reduced by anti-TNFα antibody treatment. SM also caused an increase in galectin-3 expression in the lung. However, anti-TNFα had no effect on this response. Additional studies to assess the effects of anti-TNFα on other markers of lung injury are needed to determine if TNFα targeting agents offer a promising way to attenuate mustard-induced pulmonary injury. Supported by the SOT Intern Program, NIH R25ES020721, and NIH U54AR055073.