Mechanisms of Sulfur Mustard-Induced Lung Injury

Zakiyah Henry, Yilin Wang, Rama Malaviya, Debra L. Laskin
Winston-Salem State University and Rutgers, The State University of New Jersey

Sulfur Mustard (SM) is a chemical warfare agent known to target the respiratory tract. It is a cytotoxic vesicant with a lipophilic nature that quickly penetrates tissues and cells causing acute injury that progresses over time into chronic lung injury. Evidence suggests that macrophages play a role in both acute and chronic lung pathologies. During acute injury, proinflammatory macrophages (M1) release inflammatory mediators to promote injury whereas later anti-inflammatory/wound repair macrophages (M2) release mediators that promote fibrosis. Since SM causes acute lung injury which progresses overtime, we examined the role of macrophages in SM-induced injury in rat lung. Male Wistar rats were treated intratracheally with SM (0.4 mg/kg) or air (control) by vapor inhalation. The rats were euthanized 3, 7, 16, and 28 days post-exposure, lungs lavaged with PBS, and bronchoalveolar lavage (BAL) and lung tissue collected. SM exposure resulted in increased expression of antioxidant heme oxygenase (HO-1) at 3 days indicating oxidative stress. Expression of cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS), which are both proinflammatory enzymes, were also upregulated at 3 days. At this time, the M2 macrophage marker Ym-1 was also upregulated. These findings show that SM induces inflammation, oxidative stress, and induces fibrogenesis in the lung early after exposure. Supported by MARC U*STAR Scholar Program, NIH U54AR055073 and P30ES005022.