Farnesoid X Receptor Regulates Immune Cell Activation and Recruitment following Mustard-Induced Pulmonary Injury

Tanvi Banota, Alexa Murray, Amanda Sowinski, Debra L. Laskin
Rutgers, The State University of New Jersey

Nitrogen mustard (NM) is a cytotoxic vesicant known to cause acute lung injury which progresses to fibrosis. This is accompanied by a robust immune cell response, including activation of resident macrophages, and infiltration of neutrophils and myeloid-derived macrophages. Infiltrating macrophages sequentially accumulate in the lung as pro-inflammatory/cytotoxic M1 macrophages and anti-inflammatory/pro-fibrotic M2 macrophages. Previous experiments in our lab showed that expression of farnesoid X receptor (FXR), along with two of its targets, ApoA and ApoE, were also upregulated in lung macrophages following NM exposure. FXR is a bile-acid activated nuclear receptor involved in lipid homeostasis and has been shown to increase anti-inflammatory M2 macrophage activity. To analyze the role of FXR in regulating immune cell activation and recruitment, male and female wild type (WT) and FXR-/- mice were treated with PBS (control) or NM (0.08 mg/kg) via intratracheal instillation. Lung tissue and bronchoalveolar lavage (BAL) fluid were collected 3, 14, and 28 days later. Immune cells from digested lung tissue and BAL were analyzed by flow cytometry. Flow cytometric analysis revealed that both pro- and anti-inflammatory macrophages accumulate in the lung following NM exposure. Pro-inflammatory macrophages were most abundant in BAL and lung tissue 3 days post NM; this was exacerbated in FXR-/- mice. Conversely, anti-inflammatory macrophages peaked 14 days later; this increase was more significant in WT mice. By day 28, both pro- and anti-inflammatory macrophages in WT and FXR-/- mice returned to levels of their control counterparts. These findings demonstrate that FXR modulates immune cell response following NM exposure and may be useful in the development of therapeutics aimed at mitigating lung injury and inflammation. Supported by NIH ES020721, AR055073, ES004738, ES005022