Histological Changes Subsequent Targeted Delivery of IL-1RA mRNA to ITB-Induced Acute Lung Injury Model

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Acute lung injury (ALI) occurs when there is damage to the lower lung portions from multiple insults, characterized by alveolar epithelial dysfunction and reduced gas exchange. Potential ALI treatments have limited bioavailability to lower lung regions and off-target effects in uninjured organs. A key component of ALI is inflammation mediated by pro-inflammatory interleukin-1 (IL-1). IL-1 binds to IL-1R on the surface of inflammatory cells. This activation results in epithelial injury in ALI. IL-1 signaling can be reduced by IL-1RA, which stops IL-1 from signaling inflammatory cells. We reasoned that increasing IL-1RA expression by delivering mRNA could reduce bleomycin-induced ALI. IL-1RA mRNA formulated with IAJD34 (known to target the lower lung) were administered i.v. to BALB/c mice exposed intratracheally to either PBS control or bleomycin (4 U/kg). Lung tissues were collected 3 days post-administration and stained with H&E. Morphological changes were imaged, using OlyVIA software (400x) and analyzed with Fiji. Nuclei count, white space, and alveolar wall thickness were measured to assess immune cell infiltration, tissue consolidation, and epithelial thickening respectively. Minimal morphological changes were observed between mice exposed with bleomycin treated with IL-1RA compared to control alone. IL-1RA treated mice displayed an increase in nuclei count, but no significant changes in white space and alveolar thickness. Notably, the bleomycin-induced injury was low in BALB/c mice. Our data show that IL-1RA appears to alter cell recruitment but further experiments are required to establish the effects on overall injury. Supported by NIH R25ES020721, T32-ES01984, and P30-ES005022.