Ferreira TPT; Arantes ACS, Nascimento CVM, Olsen PC, Trentin PG, Rocco PRM, Hogaboam CM, Puri RK, Martins MA & Silva PMR. (2013). IL-13 immunotoxin accelerates resolution of lung pathological changes triggered by silica particles in mice. *Journal of Immunology*, 191: 5220-5229.

Instillation of silica into the lungs of rodents results in pathological changes that strongly mimic human silicosis, an occupational lung disease marked by restrictive airway obstruction, inflammation, and fibrosis. Because IL-13 is a pivotal proinflammatory and fibrogenic cytokine, we examined whether a recombinant immunotoxin comprised of human IL-13 and a mutated form of Pseudomonas exotoxin (IL-13-PE) might affect pathological features of experimental silicosis. Mice received a single intranasal instillation of silica particles and were treated with intranasal IL-13-PE every other day from days 21 to 27 postsilica. The sensitivity of putative cell targets to IL-13-PE was also assessed in in vitro settings. Upregulation of IL-13, its receptor subunits IL-13Rα1 and IL-13Rα2, and shared receptor IL-4Rα were associated with development of granulomatous lung inflammation triggered by silica. IL-13-PE inhibited silica-induced granuloma and fibrotic responses noted at 24 h and 15 d after the last treatment. Upregulation of TNF-α, TGF-β, and chemokines, as well as increased collagen deposition and airway hyperreactivity to methacholine were all clearly sensitive to IL-13-PE. In addition, IL-13-PE inhibited both IL-13-induced proliferation of cultured lung fibroblasts from silicotic mice and silica-induced IL-8 generation from A549 cells. In conclusion, our findings show that therapeutic treatment with IL-13-PE can reverse important pathological features caused by inhalation of silica particles, suggesting that this recombinant immunotoxin is a promising molecular template in drug discovery for the treatment of silicosis.