

P020 11β -hydroxysteroid dehydrogenase type 1 activity limits inflammation following bleomycin lung injury by augmenting active glucocorticoids

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Glucocorticoids are potent anti-inflammatory agents. Endogenous glucocorticoid action is modulated by 11β -hydroxysteroid dehydrogenase (11β -HSD) which interconverts active (cortisol) and intrinsically inert glucocorticoids (cortisone). 11β -HSD type 1 regenerates active glucocorticoids and is highly expressed in the lung but its role is little explored. Immunohistochemical staining of mouse lung localised 11β -HSD1 to interstitial fibroblasts in wild type (WT) mice and staining was increased in alveolar walls following intratracheal instillation of 0.025U bleomycin. Comparison of 11β -HSD1 deficient (KO) and WT mice showed worse inflammation and greater fibroblast response in KO 14d after bleomycin. Real-time PCR results showed significantly greater induction of Haemoxygenase-1 and collagen I α 2 in KO mice (WT: 1.52 ± 0.5 vs KO: 2.26 ± 0.13 , and WT: 1.38 ± 0.16 vs KO: 1.82 ± 0.21 , respectively, Arbitrary Units; $p < 0.05$) We suggest that glucocorticoid regeneration by 11β -HSD1 in lung fibroblasts limits fibroblast proliferation and/or collagen synthesis, and its deficiency or inhibition might lead to greater fibrosis following lung injury.