



Lysyl oxidase like 2 is increased in asthma and contributes to asthmatic airway remodelling

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Novel role for matrix cross-linking enzyme LOXL2 in asthmatic airway remodelling: LOXL2 is increased in #asthma but LOXL2 inhibition reduces matrix stiffness in airway smooth muscle cells and reduces remodelling *in vivo* <https://bit.ly/3FnzGb3>

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Abstract

Background Airway smooth muscle (ASM) cells are fundamental to asthma pathogenesis, influencing bronchoconstriction, airway hyperresponsiveness and airway remodelling. The extracellular matrix (ECM) can influence tissue remodelling pathways; however, to date no study has investigated the effect of ASM ECM stiffness and cross-linking on the development of asthmatic airway remodelling. We hypothesised that transforming growth factor- β (TGF- β) activation by ASM cells is influenced by ECM in asthma and sought to investigate the mechanisms involved.

Methods This study combines *in vitro* and *in vivo* approaches: human ASM cells were used *in vitro* to investigate basal TGF- β activation and expression of ECM cross-linking enzymes. Human bronchial biopsies from asthmatic and nonasthmatic donors were used to confirm lysyl oxidase like 2 (LOXL2) expression in ASM. A chronic ovalbumin (OVA) model of asthma was used to study the effect of LOXL2 inhibition on airway remodelling.

Results We found that asthmatic ASM cells activated more TGF- β basally than nonasthmatic controls and that diseased cell-derived ECM influences levels of TGF- β activated. Our data demonstrate that the ECM cross-linking enzyme LOXL2 is increased in asthmatic ASM cells and in bronchial biopsies. Crucially, we show that LOXL2 inhibition reduces ECM stiffness and TGF- β activation *in vitro*, and can reduce subepithelial collagen deposition and ASM thickness, two features of airway remodelling, in an OVA mouse model of asthma.

Conclusion These data are the first to highlight a role for LOXL2 in the development of asthmatic airway remodelling and suggest that LOXL2 inhibition warrants further investigation as a potential therapy to reduce remodelling of the airways in severe asthma.

