Bronchial thermoplasty decreases airway remodelling by blocking epithelium-derived heat shock protein-60 secretion and protein arginine methyltransferase-1 in fibroblasts

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ABSTRACT Bronchial thermoplasty (BT) is to date the only therapy that provides a lasting reduction in airway wall remodelling. However, the mechanism of action of BT is not well understood. This study aimed to characterise the changes of remodelling regulating signalling pathways by BT in asthma.

Bronchoalveolar lavage fluid (BALF) was obtained from eight patients with severe asthma before and after BT. Primary bronchial epithelial cells were isolated from 23 patients before (n=66) and after (n=62) BT. Epithelial cell culture supernatant (Epi.S) was collected and applied to primary fibroblasts. Epithelial cells obtained from asthma patients after BT proliferated significantly faster compared with epithelial cells obtained before BT. In airway fibroblasts, BALF or Epi.S obtained before BT increased C/EBPβ expression, thereby downregulating microRNA-19a. This upregulated extracellular signal-regulated kinase-1/2 (ERK1/2) expression, protein arginine methyltransferase-1 (PRMT1) expression, cell proliferation and mitochondrial mass. BALF or Epi.S obtained after BT reduced the expression of C/EBPβ, ERK1/2, peroxisome proliferator-activated receptor-γ coactivator-1α (PGC1α), PRMT1 and mitochondrial mass in airway fibroblasts. Proteome and transcriptome analyses indicated that epithelial cell-derived heat shock protein-60 (HSP60) is the main mediator of BT effects on fibroblasts. Further analysis suggested that HSP60 regulated PRMT1 expression, which was responsible for the increased mitochondrial mass and α-smooth muscle actin expression by asthmatic fibroblasts. These effects were ablated after BT. These results imply that BT reduces fibroblast...
remodelling through modifying the function of epithelial cells, especially by reducing HSP60 secretion and subsequent signalling pathways that regulate PRMT1 expression.

We therefore hypothesise that BT decreases airway remodelling by blocking epithelium-derived HSP60 secretion and PRMT1 in fibroblasts.