Maresin-1 Regulates Epithelial To Mesenchymal Transition And Wound Healing Processes In Bronchial Epithelial Cells

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Rationale: In the airway epithelium, epithelial to mesenchymal transition (EMT) can be a reparative or pathologic process, depending on the activation stimulus and regulatory cues governing the process. Pro-resolving lipid mediators have recently been implicated as both positive and negative regulators of EMT-related pathways. We sought to determine how the pro-resolving lipid mediator maresin-1 (MaR1) regulates the EMT response to pro-inflammatory stimuli in bronchial epithelial cells.
Methods: Primary human bronchial epithelial cells or the transformed bronchial epithelial cell line BEAS-2B were stimulated with 5 ng/mL TGF-β1 in the presence or absence of 1 – 100 nM MaR1. Cultures were assessed over 96 hours to ascertain how MaR1 treatment altered TGF-β1-induced EMT. Western blotting and gel zymography were performed to ascertain protein expression and protease activities, and confluent cultures were wounded and wound closure was monitored.
Results: TGF-β1-treated cultures exhibited morphological changes of mesenchymal transition by 72 hr following treatment. These changes correlated with loss of E-cadherin expression and increased fibronectin, MMP-2 and MMP-9 release. However, TGF-β1-induced loss of E-cadherin expression was repressed by 1 nM MaR1 treatment, and 100 nM MaR1 reduced TGF-β1 induction of fibronectin production. TGF-β1 increased MMP-2 protein expression and protease activities nearly two-fold, while cultures treated with MaR1 exhibited MMP-2 protease activities similar to controls. Despite inhibiting E-cadherin loss and MMP-2 protease activities, MaR1 did not impair TGF-β1-mediated increased wound healing capacity, and MaR1 treatment alone increased wound healing as compared to untreated, wounded cultures.
Conclusions: Our results suggest the pro-resolving lipid mediator MaR1 regulates the bronchial epithelial response to inflammation and wounding, encouraging maintenance of epithelial programing during non-injurious inflammatory insults, and speeding healing following wounding.

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