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ORIGINAL ARTICLE

A critical role for *miR-142* in alveolar epithelial lineage formation in mouse lung development

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Abstract

The respiratory epithelium arises from alveolar epithelial progenitors which differentiate into alveolar epithelial type 1 (AT1) and type 2 (AT2) cells. AT2 cells are stem cells in the lung critical for the repair process after injury. Mechanisms regulating AT1 and AT2 cell maturation are poorly defined. We report that the activation of the glucocorticoid pathway in an in vitro alveolar epithelial lineage differentiation assay led to increased AT2 marker Sftpc and decreased *miR-142* expression. Using *miR-142* KO mice, we demonstrate an increase in the AT2/AT1 cell number ratio. Overexpression of *miR-142* in alveolar progenitor cells in vivo led to the opposite effect. Examination of the KO lungs at E18.5 revealed enhanced expression of *miR-142* targets *Apc*, *Ep300* and *Kras* associated with increased β-catenin and p-Erk signaling. Silencing of *miR-142* expression in lung explants grown in vitro triggers enhanced *Sftpc* expression as well as increased AT2/AT1 cell number ratio. Pharmacological inhibition of Ep300-β-catenin but not Erk in vitro prevented the increase in *Sftpc* expression triggered by loss of *miR-142*. These results suggest that the glucocorticoid-*miR-142*-Ep300-β-catenin signaling axis controls pneumocyte maturation.

Keywords Alveolar epithelium · microRNA-142 · Lung · EP300 · Beta-catenin

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