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**Title:** AXL receptor tyrosine kinase controls epithelial differentiation of human lung progenitor cells

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**Body:** Understanding the molecular mechanisms controlling differentiation of lung stem/progenitor cells may offer therapeutic opportunities for lung diseases. Studies of human lung progenitor cells indicated that inhibition of epithelial-to-mesenchymal transition (EMT) was important for differentiation towards alveolar epithelial type II cells (Fujino N, et al. Respir Investig 2012;50:110). However, it is not known what signalling pathway(s) controls the EMT and provokes the differentiation. The aim of this study was to identify molecular targets and pathways regulating differentiation from the progenitors towards alveolar epithelial cells. We conducted a phenotypic screen using human lung progenitor cells (Fujino N, et.al. Lab Invest 2011;91:363) and 220 known modulators for stem cell phenotypes. Immunofluorescence staining for pro surfactant protein-C (SP-C), to detect alveolar type II cell-differentiation, was quantified by ArrayScan. 41 out of the 220 compounds increased SP-C expression. These hit compounds included a variety of kinase inhibitors, e.g. AXL kinase, GSK3β, IκB kinase and PI3 kinase. However, only one of them, which had the inhibitory effect on AXL kinase, changed the shape of the progenitor cells to the epithelial-like morphology. Inhibition of AXL kinase also increased expression of other proteins for alveolar type II and type I cells, including surfactant protein-A, aquaporin 5 and T1α, and decreased expression of EMT-inducing transcription factors, e.g. Zeb1. These data indicate that the AXL kinase pathway may be important in controlling lung progenitor differentiation to alveolar epithelial type II and type I cells via suppression of the EMT.