

# European Respiratory Society Annual Congress 2013

**Abstract Number:** 1343

**Publication Number:** 1812

**Abstract Group:** 3.3. Mechanisms of Lung Injury and Repair

**Keyword 1:** ALI (Acute Lung Injury) **Keyword 2:** No keyword **Keyword 3:** No keyword

**Title:** Lung epithelial pten controls epithelial barrier integrity in vitro and in vivo

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**Body:** Exploration of the mechanisms of alveolar epithelial cells (AECs) integrity is important for understanding the pathogenesis of acute lung injury. The tight junctions (TJs) of AECs provide intercellular sealing and are integral to the maintenance of the integrity of the alveolar-capillary barrier. However, the mechanisms regulating AEC barrier integrity are not fully understood. We explored the role of epithelial Pten in lung injury by using lung-epithelium specific Pten-deficient (SOPten) mice. We also investigated the function of Pten by using stably introduced lentivirus encoding either wild-type PTEN (lenti-PTEN-WT) or dominant-negative mutant of PTEN (lenti-PTEN-CS) in BEAS-2B. SOPten lungs after bleomycin or lipopolysaccharide injury exhibited extensive intralveolar edema and increased alveolar permeability. SOPten lungs demonstrated loss of TJs morphology and dissociation of cell-cell contacts after injury. Levels of TJs protein were decreased in SOPten lungs after injury. Exogenous expressions of PTEN were observed in the lenti-PTEN-WT and lenti-PTEN-CS transfected cells. Expression of WT PTEN abolished Akt phosphorylation, whereas that of PTEN-CS increased pAkt levels in BEAS-2B cells. After treatment with transforming growth factor (TGF)-beta1, monolayers of the lenti-PTEN-WT cells showed retained transpeithelial electrical resistance (TER) levels compared with those of untreated cells. In contrast, monolayers of the lenti-PTEN-CS cells exhibited a substantial reduction of TER after TGF-beta1 treatment. Levels of TJs protein were severely attenuated in the TGF-beta1-treated lenti-PTEN-CS cells. These findings reveal that epithelial Pten is crucial guardian controlling AECs barrier integrity.