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Title: Translocation of β-catenin into cytoplasm during TGFβ-induced EMT is negatively regulated by phosphorylation of the PTEN C-terminus in lung cancers

Dr. Naozumi 315 Hashimoto hashinao@med.nagoya-u.ac.jp MD [1], Dr. Daisuke 316 Aoyama aoyamada@med.nagoya-u.ac.jp MD [1], Dr. Masaaki 317 Kusumose kusunose@med.nagoya-u.ac.jp MD [1] and Prof. Yoshinori 318 Hasegawa yhasega@med.nagoya-u.ac.jp MD [1]. [1] Department of Respiratory Medicine, Nagoya University Graduate School of Medicine, Nagoya, Japan .

Body: Rationale: Transforming growth factor β (TGFβ)-induced translocation of β-catenin into cytoplasm is a critical step to induce de novo transcription of epithelial-mesenchymal transition (EMT) target genes. Although we demonstrate that modulation of phosphorylation sites in the PTEN C-terminus blunt TGFβ-induced EMT in lung cancers, whether TGFβ can induce translocation of β-catenin via phosphorylation of the PTEN C-terminal tail remains elusive. Objective: We determined the underlying mechanisms, by which modulation of phosphorylation sites in the PTEN C-terminus tail could rescue EMT. Methods: Immunofluorescence of β-catenin was performed for the lung cancer cells with mutation of phosphorylation sites in the PTEN C-terminal tail (PTEN4A). Main Results: H358ON cells with either GFP or GFP-PTENWt protein showed TGFβ-induced β-catenin translocation into the cytoplasm when treated by Doxycycline. In contrats, only de novo GFP-PTEN4A protein completely inhibited β-catenin translocation induced by TGFβ stimulation. This finding was supported by the data that ectopic PTEN4A, not PTENWt, protein in H1299 cells completely inhibited β-catenin translocation induced by TGFβ stimulation. Conclusion: Our data suggest that modulation of phosphorylation sites in the PTEN C-terminus inhibits TGFβ-induced EMT via blockade of β-catenin translocation. Our study is first to demonstrate the underlying mechanisms, by which phosphorylation sites in the PTEN C-terminal tail might be a promising therapeutic target to negatively regulate TGFβ-induced EMT in lung cancers.