Identification of TBX3 as a Novel Regulator of Lung Angiogenesis

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The T-box transcription factor TBX3 is highly expressed within the lung endothelium, yet the effect of its expression is unknown. This study aimed to overcome present limitations by determining the specificity of TBX3 expression to the lung endothelium through RNA-seq of lung, liver, kidney, and heart endothelial cells (CD144+ CD31+), along with lung, liver, and heart non-endothelial cells (CD144- CD31-). Subsequently, the amount of capillary tube formation and TBX3 expression within endothelial cells post co-culture with lung stromal cells was evaluated through fluorescence microscopy and western blotting, respectively. RNA-seq identified that TBX3 expression was highest within lung endothelial cells, with minimal expression in both non-lung endothelial cells and non-endothelial cells, signifying that TBX3 is specific to the lung endothelium. Additionally, endothelial cells in both contact and non-contact co-cultures with lung stromal cells displayed significant tube-formation and yielded average vessel lengths of 60mm and 35mm, respectively. Observed tube-formation in endothelial cell populations correlated with increases in TBX3 expression; contact and non-contact co-cultures resulted in 4.4-fold and 2.6-fold increases in TBX3 expression, respectively, suggesting that TBX3 regulates endothelial cell tube formation, and consequently lung angiogenesis. Future investigations must be performed to identify the upstream and downstream targets of TBX3 during its regulation of angiogenesis. In a clinical setting, TBX3 expression can either be targeted within the tumor endothelium to prevent cancer angiogenesis or augmented in transplantable endothelial cells for more efficient tissue regeneration in the treatment of chronic lung diseases.

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