PIEZO1 as Mechanosensor for Protecting Vascular Cells from Fibrosis

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Background

Blood vessels are composed of endothelial cells that can regulate arterial vasodilation and blood pressure. Ion channels are expressed in nearly all mammalian cell types, including endothelial cells. In smooth muscle cells, PIEZO1 is critical for maintaining vascular architecture, and is involved in myogenic remodeling during hypertension; however, vascular structure is altered during endothelial-to-mesenchymal transition (EndoMT), or fibrosis. Transient potential channel (TRP) has been shown to be essential for TGF- β 1-induced fibrogenesis. The miRNA-103a was reported to play a role in an artery disease (Abdominal aortic aneurysm). Mechanistically, the role of PIEZO1 during EndoMT is unknown. We hypothesize that PIEZO1 function is affected by miRNA-103a, and PIEZO1 has protective function for the endothelial cells against fibrosis. Thus, we will investigate PIEZO1 function, and how miRNA-103a can modulate PIEZO1 function in fibrotic endothelial cells.

Methods

We used mechanical stretch 15%, 1Hz for 6, 24h to instigate fibrosis in the human mammary vascular endothelial cells (HMVECs). We determined the PIEZO1, CD31, α -SMA, collagen I protein level using western blot. We will use calcium green fluorescence probe to detect calcium transduction. We will perform Phospho-kinase array to identify candidate phosphorylated proteins in the A) control (No stretch), and B) stretched groups. We will apply inhibitors for the candidate proteins to confirm the potential signaling pathway by western blot, analyze calcium by calcium green, and knockdown PIEZO1 to further examine any correlation with miRNA-103a in the fibrotic endothelial cells. If the level of PIEZO1 and miRNA-103a are inversely-related to each other, we will silence miRNA-103a to analyze PIEZO1 protein level and calcium transduction.

Results

After stretching for 6, and 24h at 15%, 1Hz, the HMVECs attained fibroblastic morphology compared to that No stretch, and PIEZO1 protein level was down-regulated, accompanied with up-regulated α -SMA. At present, the investigation of PIEZO1 as mechanosensor in vascular fibrosis this is an ongoing project.

Conclusions

Preliminary data shows that PIEZO1 was affected by cyclic stretch as fibrosis was observed. Therefore, it is worthwhile to further study the protective function of PIEZO1 as a mechanotransducer in the endothelial cells.

Keywords

Mechanotransducer, fibrogenesis, artery disease