

## Shear stress and cell cycle stretch role on isolated smooth muscle cells of chronic thromboembolic pulmonary hypertension

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### Objective:

Chronic thromboembolic pulmonary hypertension (CTEPH) is one of pulmonary hypertension (PH) type which caused by chronic persistent obstruction of thromboembolic material. The importance of this disease has been recognized recently by both of clinician and researcher, however the mechanism is still unclear. Blood vessels have shear stress and cell cycle stretch controls which can prevent proliferation, migration, and apoptosis. We hypothesize that these mechanisms are blunted in CTEPH. Therefore, we introduced shear stress (SS) and cell cycle stretch (CCS) to the isolated smooth muscle cell of CTEPH (CTEPH-SMC) patients to investigate whether these mechanisms have a role in CTEPH.

### Method:

We isolated CTEPH-SMC (n=4) from pulmonary endarterectomy (PEA) tissues of CTEPH patients. For SS condition, those cells were exposed to low shear stress (1dyne/cm<sup>2</sup>) or high flow stress (10dyne/cm<sup>2</sup>) for 24 hours by using our established shear stress machine. For CCS condition, those cells were given 10% and 20% stretch for 24 hours by using stretch culture system. Several phenotypes and angiogenesis markers were investigated by Real time PCR.

### Results:

We observed that  $\alpha$ SMA mRNA expression of CTEPH-SMC was decreased after either SS or CCS treatment. We found that there are no significant response of CTEPH-SMC subjected to either SS or CCS condition for several angiogenesis marker such as endothelin-1 (ET-1), endothelin-1 converting enzyme (ECE1), S100A4, and Vimentin.

### Conclusion:

This preliminary study shown that several angiogenesis marker of such as ET-1, ECE1,

S100A4, and Vimentin response to SS or CCS are blunted in CTEPH-SMC. We also found that laminar flow SS and CCS decreased CTEPH-SMC  $\alpha$ SMA expression which could be important for CTEPH process. Further study is needed to compare these CTEPH-SMC response to SS and CCS with normal pulmonary SMC.