**MICRORNA AS KEY TARGETS OF MEF2 TRANSCRIOPTION FACTOR IN THE ENDOTHELIUM: ROLE IN THE PATHOGENESIS OF PULMONARY ARTERIAL HYPERTENSION**

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Pulmonary arterial hypertension (PAH) is a fatal disease characterized by the vascular remodeling of the pulmonary arterioles, including formation of plexiform and concentric lesions comprised of proliferative vascular cells. Clinically, PAH leads to increased pulmonary vascular resistance resulting in right ventricular failure. The existing therapies have improved outcome but mortality remains exceedingly high. Given the high rate of mortality and limited modalities of treatment, identifying novel targets of therapy remain of utmost importance. Our recent identification of a key signaling paradigm in PAECs involving apelin, microRNAs (miRNAs) 424 and 503, and FGF2/FGFR1 demonstrate the importance of crosstalk among these molecules in maintenance of pulmonary vascular homeostasis. Here we demonstrate that the transcription factor myocyte enhancer factor 2 (MEF2) is a cis-acting factor that regulates miR-424 and miR-503 expression downstream of apelin in PAECs. MEF2 transcriptional activity was found to be significantly decreased in PAH PAECs. This is mediated by increased nuclear localization of two class IIa histone deacetylases (HDACs) in PAH PAECs, namely HDAC4 and HDAC5, which negatively regulate MEF2 function. Selective inhibition of class IIa HDACs led to restoration of MEF2 transcriptional targets, decreased PAH PAEC migration and proliferation, and amelioration of experimental pulmonary hypertension (PH) models. These studies demonstrate that restoration of endothelial MEF2 activity, achieved by selective inhibition of class IIa HDACs, is a promising therapeutic strategy in PAH.