miR 19a

The dysfunction of human pulmonary arterial smooth muscle cells (HPASMCs) has been suggested to participate in the pathophysiology of pulmonary arterial hypertension (PAH). This study determined miR-19a expression in hypoxia-induced HPASMCs and explored the mechanistic actions of miR-19a in hypoxia-induced HPASMC proliferation and migration.

METHODS: QRT-PCR and western blot assays respectively determined the mRNA and protein expression of miR-19a, phosphatase and tensin homolog (PTEN) and hypoxia-inducible factor-1 alpha (HIF-1α). In vitro functional assays determined HPASMC proliferation and migration, respectively. Luciferase reporter assay determined interaction between miR-19a and PTEN. The knockdown effects of miR-19a on PAH were confirmed in in vivo mice model.

RESULTS: Hypoxia treatment time-dependently up-regulated miR-19a expression and enhanced cell proliferation in HPASMCs. MiR-19a overexpression increased cell proliferation and migration of HPASMCs, while repression of miR-19a reduced cell proliferative and migratory potentials of hypoxia-treated HPASMCs. Bioinformatics analysis and luciferase reporter assay showed that PTEN 3' untranslated region was targeted by miR-19a, and miR-19a repressed the mRNA and protein expression of PTEN in HPASMCs. Further rescue studies revealed that miR-19a regulated proliferative and migratory potentials of hypoxia-treated HPASMCs via suppressing PTEN expression. In addition, HIF-1α was identified as one of the mediators for the hypoxia-induced aberrant expression levels of miR-19a and PTEN. MiR-19a overexpression enhanced PI3K/AKT signaling, which was attenuated by enforced expression of PTEN in HPASMCs. More importantly, knockdown of miR-19 attenuated the chronic hypoxia-induced PAH in in vivo mice model.

CONCLUSION: This study presented a novel mechanistic action of miR-19a-mediated cell proliferation and migration of HPASMCs [1)].

1)
Zhao M, Chen N, Li X, Lin L, Chen X. MiR-19a modulates hypoxia-mediated cell proliferation and migration via repressing PTEN in human pulmonary arterial smooth muscle. Life Sci. 2019 Nov 1:116928. doi: 10.1016/j.lfs.2019.116928. [Epub ahead of print] PubMed PMID: 31682848.