CHINESE-AMERICAN LUNG ASSOCIATION

CALA Happy Friday Seminar

September 23rd, 2022

Time: EST 10:30 am; PST: 7:30 am; Beijing time: 10:30pm

Zoom: 849 9682 9273 (Password: 654321)

Vacuolar protein sorting 34 Activation Promotes Pulmonary Vascular Smooth Muscle Cell Proliferation in Pulmonary Hypertension

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Bio: Dr. Yuanjun Shen has training in both pharmaceutical and biomedical research. He obtained his Ph.D. from the University of Rhode Island. He then joined Dr. Elena Goncharova's Laboratory for the postdoctoral training, and started the research on the mechanisms of pulmonary hypertension. He has earned the VMI Postdoctoral Scholar Award (internal research grant from the University of Pittsburgh) and the American Heart Association Postdoctoral Fellowship. During the training, Dr. Shen has been awarded with several travel awards, Jane Morse Award for the best scored abstract in Pulmonary hypertension category (ATS 2022) and the President's Award (California Thoracic Society Annual Educational Conference 2022) for his presentations. His research has recently been published in Frontiers in Medicine, Circulation Research, Cellular and Molecular Gastroenterology and Hepatology, and Proceedings of the National Academy of Sciences. Dr. Shen is a member of ATS, AHA, PVRI, AAAS and CALA.

Abstract: My research focuses on understanding the mechanisms and development of pulmonary arterial hypertension (PAH). My current project aims to elucidate the status and mechanisms of regulation and function of Class III phosphatidylinositol 3-kinase vacuolar protein sorting 34 (Vps34) in PA vascular cells in PAH. Inhibitory Ser164 phosphorylation of Vps34 (P-Ser164-Vps34) was significantly decreased in smooth muscle alpha-actin (SMA)-positive areas of small remodeled PAs and PA vascular smooth muscle cells (PAVSMC) from PAH patients. Similar to human PAH, we detected a significant decrease of P-Ser164-Vps34 in SMA-positive areas of small remodeled PAs from mice and rats with SU5416/hypoxia-induced PH. Further, treatment of Akt inhibitor VIII or Akt-knockdown in PAH PAVSMC demonstrated that Vps34 activation is Akt-dependent, which is associated with TSC2 deficiency, Vps15 over-accumulation, and increased proliferation and survival. Pharmacological inhibition of Vps34 in PAH PAVSMC by selective inhibitors SAR405 and VPS34-IN1 significantly decreased proliferation and induced apoptosis. Two-week treatment of SAR405 in mice with SU5416/hypoxia-induced PH attenuated pulmonary vascular remodeling. The above results suggest a therapeutic potential of Vps34 inhibition to reduce PAH PAVSMC hyper-proliferation and attenuate pulmonary vascular remodeling in PAH. In conclusion, Akt-dependent Vps34 activation supports proliferation and survival of PAH PAVSMC. Further studies are needed to evaluate the therapeutic potential of Vps34 inhibition against PAH.