Lung Biology Research & Trainee Day
June 7, 2021

Category: Postdoc
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Title: Essential role of MIRO1 in maintaining endothelial cell integrity
Abstract: Essential role of MIRO1 in maintaining endothelial cell integrity Rauf A. Najar, Michelle Millar, Mohammad Shadab, Fabeha Fazal, Arshad Rahman Departments of Pediatrics, Lung Biology and Disease Program, Rochester, New York MIRO-1, a mitochondrial Rho GTPase1, is an important regulator of trafficking and subcellular distribution of mitochondria to meet the local demands of energy, Ca2+, and redox balance to drive a number of cellular responses, particularly in cancer cells. However, the role of MIRO-1 in endothelial cells (EC), particularly in their quiescent state, is not known. To address this question, we used siRNA-mediated knockdown approach to impair the function of MIRO-1 in human pulmonary artery EC. The MIRO1-depeleted EC exhibited elongated cell shape, increased mitochondrial ROS generation, and reduced barrier function. These cells were also impaired in their ability to proliferate, migrate, and form capillary-like network on Matrigels. Consistent with the reduced barrier function and proliferative/migratory capacity, VE-cadherin and VEGFR2 levels were markedly decreased in MIRO1-depleted cells. In contrast, EC overexpressing wild-type MIRO-1 (MIRO1-WT) showed increased VE-cadherin and VEGFR2 levels. However, unlike MIRO1-WT, overexpression of a MIRO-1 mutant (MIRO-1 E208K/E328K) which is defective in its Ca2+-binding ability failed to increase VE-cadherin and VEGFR2 levels. These data establish the essential role played by MIRO-1 in maintaining EC integrity and the requirement of Ca2+ in driving MIRO-1's action in the endothelium. Supported by: NIH (GM130463, HL148695, and HL138538)