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Polo-like kinase 1 (Plk1) in smooth muscle and allergic asthma

Smooth muscle contraction and cell proliferation are critical for the pathogenesis of airway hyper-responsiveness and hyperplasia of allergic asthma. Polo-like kinase 1 (Plk1) is a serine/threonine protein kinase that has been implicated in mitosis and cytokinesis. The role of Plk1 in smooth muscle contraction and cell growth has not been previously investigated. Here, stimulation with acetylcholine induces Plk1 phosphorylation at Thr-210 (an indication of Plk1 activation) in smooth muscle. Contractile stimulation also activates Plk1 in live smooth muscle cells as evidenced by changes in fluorescence resonance energy transfer signal of a Plk1 sensor. Plk1 is necessary for smooth muscle force development. Plk1 regulates airway smooth muscle contraction by affecting vimentin phosphorylation at Ser-56, but without modulating myosin light chain phosphorylation. Plk1 phosphorylation is mediated by Ste20-like kinase (SLK), a serine/threonine protein kinase that has been implicated in spindle orientation and microtubule organization during mitosis. Moreover, Plk1 is indispensable for airway smooth muscle cell proliferation. Plk1 knockdown by lentivirus-mediated shRNA attenuates the growth factor-induced phosphorylation of MEK1/2 and ERK1/2. However, Plk1 knockdown does not affect the phosphorylation of Raf-1 or AKT. Finally, smooth muscle conditional knockout of Plk1 attenuates airway resistance, airway smooth muscle hyper-reactivity and hyperplasia in a murine model of allergic asthma. Taken together, these findings suggest that Plk1 is critical for the regulation of smooth muscle contraction and cell proliferation. Plk1 regulates smooth muscle contraction by controlling vimentin phosphorylation, whereas, it orchestrates cell proliferation by modulating the MAPK pathway. Plk1 contributes to the pathogenesis of allergic asthma. Plk1 may be a pharmacological target for the development of new therapy to treat asthma.

Biography

Dale D Tang has received training at the University of Texas Southwestern Medical Center at Dallas in 1990s. He is a Professor of the Department of Molecular and Cellular Physiology at Albany Medical College, New York, USA. He is Director of Cytoskeletal Signaling and Asthma Research Program at the school. He is an Associate Editor of *BMC Respiratory Research* and an Editorial Board Member of *Nature Scientific Reports*. His research focuses on the role and mechanism of cytoskeleton-associated proteins in smooth muscle in vitro and the pathogenesis of asthma and hypertension in vivo. He has published >70 peer-reviewed articles in journals including the *Journal of Biological Chemistry* and *Circulation Research*.

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