Critical role of c-Abl in smooth muscle functions and asthma pathogenesis

Allergic asthma is a serious lung disease that affects nearly 25 million people in the United States and 250 million people worldwide. Allergic asthma is characterized by airway hyperresponsiveness (AHR) and airway remodeling. It is well accepted that AHR is largely attributed to airway smooth muscle hyperreactivity whereas airway remodeling stem from smooth muscle cell migration and proliferation. However, the mechanisms that control smooth muscle contraction, migration and proliferation are not fully understood. Our recent studies have demonstrated that c-Abl, a non-receptor tyrosine kinase is required for smooth muscle contraction. Knockdown of c-Abl by RNAi attenuates the activation of the adapter protein Abi1, which subsequently inhibits the activation of N-WASP and actin dynamics in smooth muscle. Thus, c-Abl regulates smooth muscle contraction by controlling the Abi1/N-WASP pathway. In addition, c-Abl knockdown diminishes smooth muscle cell migration. The actin-regulatory protein cortactin and profilin-1 are positioned at the leading edge of motile cells. c-Abl silencing also inhibits the localization of cortactin and profilin-1 at the tip of lamellipodia of motile smooth muscle cells. Furthermore, c-Abl regulates smooth muscle cell proliferation by affecting the Raf1-MEK1/2-ERK1/2 cascade. Finally, c-Abl protein expression is up-regulated in asthmatic smooth muscle cells/tissues. Conditional knockout of c-Abl in smooth muscle attenuates the allergen-induced AHR and airway remodeling in a model of asthma. These studies strongly suggest that c-Abl plays a critical role in regulating smooth muscle functions and asthma pathogenesis.

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 Center for Cardiovascular Sciences at Albany Medical College, New York, USA. He is the Director of Cytoskeletal Signaling and Asthma Research Program at the school. His research focuses on the role and mechanism of cytoskeleton-associated proteins in smooth muscle WW and the pathogenesis of asthma and hypertension in vivo. He has published more than 70 peer-reviewed articles in journals including the Journal of Biological Chemistry and Circulation Research. He is an Associate Editor of BMC Respiratory Research.

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