Crosstalk between signaling pathways involved in the regulation of airway smooth muscle cell hyperplasia

ABSTRACT

Increased ASM mass, primarily due to ASM hyperplasia, has been recognized as a hallmark of airway remodeling in asthma. Increased ASM mass is the major contributor to the airway narrowing, thus worsening the bronchoconstriction in response to stimuli. Inflammatory mediators and growth factors released during inflammation induce increased ASM mass surrounding airway wall via increased ASM proliferation, diminished ASM apoptosis and increased ASM migration. Several major pathways, such as MAPKs, PI3K/AKT, JAK2/STAT3 and Rho kinase, have been reported to regulate these cellular activities in ASM and were reported to be interrelated at certain points. This article aims to provide an overview of the signaling pathways/molecules involved in ASM hyperplasia as well as the mapping of the interplay/crosstalk between these major pathways in mediating ASM hyperplasia. A more comprehensive understanding of the complexity of cellular signaling in ASM cells will enable more specific and safer drug development in the control of asthma.

Keyword: Airway remodeling; ASM hyperplasia; ASM cell proliferation; ASM cell migration; ASM cell apoptosis