Editorial

Molecular determinants of airway smooth muscle cells in health and disease

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The review article entitled "*A narrative review of research advances in the study of molecular markers of airway smooth muscle cells*" by Yu *et al.* (1) aims to summarize the molecular markers for airway smooth muscle cells (ASMCs) in the pathophysiological condition of airway remodeling in asthma. Identification and characterization of the molecular markers, especially related to ASMCs hold a novel gateway for early prognosis of airway remodeling during asthma progression. The current review provides a thorough compilation of smooth muscle specific markers during the different phases of ASMCs growth. Further, identification of these markers holds the key to the ASMCs phenotypic changes like contractile to non-contractile, non-proliferative to proliferative, and smooth-muscle to fibroblast (2), which altogether provides a cellular environment for the management of asthma pathophysiology.

It is a well-recognized fact that ASMCs present as a circular shape to the bronchial tree, plays a very crucial role in regulating airway structure and function, by controlling bronchomotor tone and airway caliber (3-5). Further, as mentioned in this review during airway remodeling it is very hard to identify the origin of the thickened airway and its properties. However, the recent research development in the field of airway remodeling shows that ASMCs from asthmatics proliferate faster compared to non-asthmatics (6-10). This is further supported by *in vivo* studies using a mouse model of asthma showed an increased airway smooth muscle (ASM) layer thickness (11-13). Further, increased ASM mass due to increased ASMC proliferation, hypertrophy, and migration observed in asthmatics (6,14,15). All these evidences conflicts with the sentence mentioned in this review, "*bronchial biopsies from asthmatic and non-asthmatic patients have no significant difference in ASMCs proliferation*".

α-smooth muscle actin (α-SMA), appears to be a very important molecular marker for the identification of the ASMCs (16). The notable caveat with considering α-SMA as a specific smooth muscle marker is that during the phenotype changes of ASMCs to fibroblast the expression levels of α-SMA are shown to be significantly higher (17). Accordingly, the α-SMA as ASMCs marker may lead to misdiagnosis during airway remodeling with pulmonary fibrosis and carefully investigated.

This review elaborates on numerous molecular markers which are favorable for the comprehensive study of the increased ASMCs in asthmatic airway remodeling. This information is supported by the bench studies establishing the markers of ASMCs through semi-quantitative studies like western blotting, immunofluorescence staining, and northern blot analysis with conjunction by using primary cultures of myocytes (18). Amongst the multiple ASMCs markers, MYH11 is considered a molecular marker for mature SMCs, and TAGLN is an early marker for differentiation. A rare variant of *MYH11*, *R247C*, has been shown to alter the myosin contractile function and smooth muscle cells (SMCs) phenotype, leading to

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increased proliferation *in vitro*. Similarly, the mutation in the corresponding amino residue in *MYH7*, *R249Q*, causes familial hypertrophic cardiomyopathy (19). Myh11, which is a very important contractile protein expressed only in SMCs gained importance in generating smooth muscle-specific knockout animals using the Cre-loxP recombinant technique (20). This review comprehensively provided information on all the primary molecular markers (Myosin heavy chain 11, Transgelin, Calponin 1, α-SMA, h-caldesmon, Smooth muscle cell differentiation-specific protein, Desmin and Cysteine- and glycine-rich protein 1) of ASMCs. Further, we wish to point out that Tropomyosin (Tm), which is also one of the major components of smooth muscle phenotype (21) and can be used as a marker of mature differentiated ASMCs. Further, we would like to add a note that, Ki67 is reported as an important proliferative marker in ASMCs in asthmatic conditions (22,23). Additionally, Ki67 is also identified as a crucial marker for mitosis because of its involvement in various phases of the cell cycle (15,24).

Overall, this article provides valuable information regarding the different molecular markers for the identification of stages of ASMCs differentiation. Further, this review will significantly increase the knowledge about molecular markers of ASMCs, which can enhance our knowledge of the phenotypic behavior of ASM and assist in easy diagnosis and management of asthma.

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