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Title: Small-non coding YRNAs can regulate the plasticity of smooth muscle cells

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Body: Chronic obstructive pulmonary disease (COPD) is characterized by the increase of smooth muscle cells (SMCs) proliferating in the intima of pulmonary arteries. SMCs are highly plastic and can change from a contractile to a proliferative phenotype and vice versa in response to different stimuli. YRNAs are a class of small-non coding RNAs that are highly conserved in mammals. There are 4 YRNAs in human (hY1, hY3, hY4 and hY5). Several studies have suggested that YRNAs can be processed and the products were found to be increased in several tumors. YRNAs are known to be required for chromosomal DNA replication and for cell proliferation. However, an involvement of those RNAs in cell differentiation has not been reported yet. Our objective was to investigate the importance of YRNAs in SMCs phenotypic change. We used primary human pulmonary artery SMCs (HPASMCs) (Lonza). To block the expression of YRNAs, we transfected small interfering RNAs (siRNA) targeting the central loop of YRNAs using Lipofectamine RNAiMax. To inhibit the small products we transfected 2'Omethylated probes antisense to those fragments using Lipofectamine 2000. Expression of YRNAs and of specific markers of SMCs was measured by northern blot and real time PCR respectively. We were able to block the expression of hY1, hY3 and hY4 as well as their small products in SMCs. Blocking the expression levels of YRNAs had a significant effect on the expression of mature markers of SMCs indicating that these non-coding RNAs regulate cell differentiation. We conclude that YRNAs may have a key role in the regulation of SMC plasticity. Supported by grants 10/02175, and SEPAR-2009, MMM is recipient of a Sara Borrell contract from ISCiii.