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Title: microRNAs are deregulated in pulmonary arteries from COPD patients

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Body: Pulmonary vessel remodelling in chronic obstructive pulmonary disease (COPD) is associated with changes in smooth muscle cell (SMC) phenotype. MicroRNAs (miRNAs) regulate the expression of many genes controlling cell growth and differentiation. The aim of the study was to evaluate miRNAs expression in pulmonary arteries (PA) from COPD and control patients. We studied 29 PA from COPD (n=12), smokers (S) with normal lung function (n=10) and nonsmokers (NS) patients (n=7) who underwent lung resection. MiRNAs expression was assessed after RNA isolation by RT-PCR using taqman low-density arrays card A Set v3.0 (Applied Biosystems). MiRNAs expression was additionally evaluated by Northern Blot (NB) in primary human pulmonary artery endothelial (HPAE) and in human pulmonary artery smooth muscle cells (HPASMC) (Lonza) with both proliferative and contractile phenotype. MiRNAs were also studied in PA-derived SMC from patients. Expression of markers was assessed by Real Time PCR. The results showed a significant upregulation of miR-146 and miR-139, whereas miR-204, miR-149, miR-197, miR-487b and miR-485 were downregulated in PA from COPD respect to NS ($p<0.05$). NB analysis showed that miRNA-139 was specifically expressed in HPAE; miR204 in HPAE and in contractile SMC while the other miRNAs were abundantly expressed in SMC. Some miRNAs had differential expression levels in proliferative respect to a contractile SMC, suggesting a role of those miRNA in the phenotypic switch of SMC. We conclude that vascular remodeling in COPD might be linked to an alteration of SMC miRNAs expression. Supported by grants FIS 09/00536 and 10/02175, SEPAR-2009 and 2010. MMM is recipient of a Sara Borrell grant from ISC III, Spain.