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Title: Slug can contribute to the phenotypic modulation of smooth muscle cells

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Body: Recently, we have found that remodeled pulmonary arteries have increased expression of slug, a transcription factor related with transitional changes in cell phenotype. Smooth muscle cells (SMC) may show high plasticity switching from a contractile (fully differentiated) to a proliferative phenotype (dedifferentiated). The aim of the study was to investigate in human pulmonary SMC the expression of slug during the phenotypic switching in an in vitro model of cell differentiation, and also after exposure to inflammatory cytokines. We analyzed the expression of slug and specific markers of mature SMC in three cell culture states: 70% confluence (dedifferentiated), 100% confluence (partially differentiated) and 4 days after reaching confluency (contractile/fully differentiated). In cytokine assays SMC were starved overnight and subsequently stimulated with TNFa, IL1-b and INF-g, 10ng/ml each. Slug expression decreased 30% and 50% (p<0.001) in partially and fully differentiated cells, respectively. Contractile SMC showed a significant upregulation (p<0.05) of the SMC markers myocardin (mycd), Sm22a and calponin. Treatment of contractile SMC with TNFa during 48h increased the expression of slug two-fold (p<0.05) whereas no changes were observed in this gene after treatment with IL1-b or INF-g. Fully differentiated SMC treated with TNFa, downregulated significantly mycd, sm22a and calponin. We conclude that slug expression might be associated with a SMC proliferative phenotype induced by inflammation. This SMC phenotype switching might contribute to the development and progression of vascular disorders. Supported by grants FIS 09/00536 and10/02175, and SEPAR-2009, MMM is recipient of a Sara Borrell grant from ISCiii.