**ADAR1-MEDIATED RNA EDITING, A NOVEL MECHANISM CONTROLLING VASCULAR SMOOTH MUSCLE PHENOTYPIC MODULATION**

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Vascular smooth muscle (SMC) phenotypic modulation plays an essential role in the development and progression of several major human diseases such as atherosclerosis, hypertension, restenosis after angioplasty or bypass, diabetic vascular complications, and transplantation arteriopathy, asthma, and cancer. A hallmark feature of the phenotypic modulation is the down-regulation of SMC contractile genes. Platelet-derived growth factor-BB (PDGF-BB), a well-known stimulator of SMC phenotypic modulation, down-regulates SMC genes via posttranscriptional regulation. The underlying mechanisms, however, remain largely unknown. We found that SMC gene down-regulation was caused by abnormal RNA editing of their precursor mRNAs (pre-mRNAs), which was facilitated by adenosine deaminase acting on RNA (ADAR). ADAR converts adenosines to inosines (A to I editing). PDGF-BB induced ADAR1 expression while down-regulating smooth muscle myosin heavy chain (SMMHC) and alpha-actin (a-SMA). Knockdown of ADAR1 by shRNA restored PDGF-BB-blocked SMMHC and a-SMA expression, demonstrating that ADAR1 played an essential role in SMC phenotype modulation. Animal studies showed that SMMHC and a-SMA pre-mRNA was accumulated while their mature mRNA was decreased along with the expression of ADAR1 in media SMCs initially, and neointima SMCs subsequently in balloon-injured rat carotid arteries. Of importance, knockdown or heterozygous knockout of ADAR1 dramatically inhibited injury-induced neointima formation, demonstrating a critical role of ADAR1 in vascular remodeling in vivo. ADAR1 appeared to regulate SMC proliferation through RNA editing-mediated downregulation of p27kip1. Taken together, our study unraveled a novel molecular mechanism governing SMC phenotypic modulation.