**A NOVEL MECHANISM CONTROLLING SMOOTH MUSCLE PHENOTYPE AND VASCULAR REMODELING**

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Smooth muscle cell (SMC) proliferation in injured artery is a common process occurring in a number of vascular diseases such as atherosclerosis, post-transplant vasculopathy, and restenosis after angioplasty, etc. Molecular mechanisms controlling SMC proliferation, however, is not completed understood. The objective of this study is to determine the role and mechanism of Janus kinase 3 (JAK3) in SMC proliferation and vascular remodeling. Platelet-derived growth factor (PDGF)-BB, a SMC mitogen, induces JAK3 expression and phosphorylation while stimulating SMC proliferation. JAK3 kinase inhibitor Janex-1 or its shRNA inhibits the SMC proliferation. Conversely, forced expression of JAK3 promotes SMC proliferation. Mechanistically, JAK3 promotes the phosphorylation of signal transducer and activator of transcription 3 and c-Jun N-terminal kinase in SMC, two signaling pathways known to regulate SMC proliferation and vascular remodeling. Blockade of these two signaling pathways by their inhibitors impeded the JAK3-mediated SMC proliferation. In vivo, knockdown of JAK3 attenuates injury-induced neointima formation with attenuated neointimal SMC proliferation. Knockdown of JAK3 also induces neointimal SMC apoptosis in rat carotid artery balloon-injury model. Our results demonstrate that JAK3 mediates SMC proliferation and survival during injury-induced vascular remodeling, which provides a potential therapeutic target for preventing neointimal hyperplasia in proliferative vascular diseases.