Characterization of the Role of Shikimic Acid in Vascular Smooth Muscle Cells

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Background: Vascular smooth muscle cell (VSMC) phenotypic modulation from a contractile to a synthetic state is central to the etiologies of multiple vascular wall diseases such as atherosclerosis, hypertension, and post-angioplasty restenosis. Shikimic acid (SA) is a chemical derived from a variety of plants and microorganisms and has been found to exhibit diverse pharmacological activities in multiple cell/tissue systems, such as antioxidant, anti-inflammatory, and pro-proliferative effects. However, the role of shikimic acid in the vascular system is unknown. The purpose of this study is to examine the effect of SA in regulating VSMC proliferation and migration.

Methods: Using human coronary artery smooth muscle cells (hCASMC), we investigated the effects of SA (10 mM) in vitro on (i) serum-induced VSMC phenotypic switching by immunoblotting or qRT-PCR analyses, (ii) platelet-derived growth factor-BB (PDGF-BB, 30 ng/ml) activation of proliferative signaling, (iii) serum- or PDGF-BB-induced VSMC proliferation by performing WST-1 and CyQUANT assays, and (iv) serum-induced VSMC migration by performing scratch wound assay.

Results: SA enhanced the expression of CCND1, a proliferation marker, at both mRNA and protein levels. Consistently, SA enhanced the effects of PDGF-BB on proliferative signaling, including ERK1/2, Akt, and mTORC1 signaling. Conversely, SA activated antiproliferative signaling components including the AMPK/autophagy pathway. Proliferation and migration assays revealed no significant differences after SA treatment as compared to PDGF-BB or serum.

Conclusion: Our findings indicate that SA activates both pro- and anti-proliferative signaling components in VSMCs and suggest that the net outcome of activation of these diverse signaling pathways has little effect on VSMC proliferation or migration.

