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# Involvement of smooth muscle cell specific iPLA2β in the initiation and early progression of vascular inflammation and neointima formation

**Zhenheng Guo**
University of Kentucky School of Medicine, USA

Neointima formation is a common feature of restenosis after angioplasty and atherosclerosis. However, the persistent occurrence of restenosis after vascular interventions indicates that the current understanding of the mechanisms responsible for neointima formation is incomplete. Here we report that calcium independent phospholipase A2beta (iPLA2β) expression increases in the vascular tunica media upon carotid artery ligation and that neointima formation is suppressed by genetic deletion of iPLA2β or by inhibiting its activity or expression via perivascular delivery of bromoenol lactone (BEL) or of antisense oligonucleotides, respectively. To investigate whether smooth muscle-specific iPLA2β is involved in neointima formation, we generated transgenic mice in which iPLA2β is expressed specifically in smooth muscle cells (SM-iPLA2β -Tg), and demonstrate that smooth muscle-specific expression of iPLA2β exacerbates ligation-induced neointima formation and enhanced both production of proinflammatory cytokines and vascular infiltration by macrophages. With cultured vascular smooth muscle cell (VSMC), angiotensin II (Ang II), arachidonic acid (AA), and TNF-β markedly induce increased expression of IL-6 and TNF-β mRNAs, all of which were suppressed by inhibiting iPLA2β activity or expression with BEL, antisense oligonucleotides, and genetic deletion, respectively. Similar suppression also results from genetic deletion of 12/15-lipoxygenase or inhibiting its activity with nordihydroguaiaretic acid (NDGA) or luteolin. Our studies thus illustrate that smooth muscle cell-specific iPLA2β participates in the initiation and early progression of vascular inflammation and neointima formation, and suggest that iPLA2β may represent a novel therapeutic target for preventing cardiovascular diseases.

## Biography

Zhenheng Guo has completed his Ph.D. from University of Virginia in 1999 and postdoctoral studies in University of Kentucky from 1999 to 2004 when he became an independent investigator. Currently, he is an Assistant Professor of Medicine, University of Kentucky. His research has focused on dysfunction of vascular smooth muscle cells in hypertension, restenosis, and aortic aneurysm. His research has been funded by American Heart Association (AHA), National Institutes of Health (NIH), and Kentucky Diabetes Research Trust Fund (DRTF). He has published 22 papers in reputed journals and serving as a member of AHA and other study sections.

zguo2@uky.edu