ENHANCED ANTIANGIOGENIC EFFICACY OF PRODRUG NANOPARTICLES QUANTIFIED WITH MAGNETIC RESONANCE IMAGING

ACC Poster Contributions
Ernest N. Morial Convention Center, Hall F
Tuesday, April 05, 2011, 9:30 a.m.-10:45 a.m.

Session Title: Vascular --Pathophysiology -- Basic/Angiogenesis/Gene Therapy
Abstract Category: 9. Vascular--Pathophysiology—Basic/Angiogenesis/Gene Therapy
Session-Poster Board Number: 1145-123

Authors: Dipanjan Pan, Ann Schmieder, Nibedita Sanyal, Xiaoxia Yang, Angana Senpan, John Allen, Huiying Zhang, Samuel Wickline, Gregory Lanza, Washington University School of Medicine, St Louis, MO

Background: \( \alpha v \beta 3 \)-fumagillin nanoparticles (NP) decrease angiogenesis in atherosclerotic rabbit models, but drug losses from NPs in circulation and chemical instability of fumagillin complicate translation. To develop a prodrug (PD) platform for improved chemical and circulatory stability of drugs in lipid-based NPs.

Methods: PD of fumagillin was coupled to the Sn-2 acyl position of phosphatidylcholine, which included removal of fumagillin light sensitivity. PD were formulated in perfluorocarbon NPs and studied in 2F2B endothelial cell proliferation assays. Efficacy of \( \alpha v \beta 3 \)-fumagillin-PD NP, nontargeted-fumagillin-PD NP, \( \alpha v \beta 3 \)-fumagillin NP and \( \alpha v \beta 3 \)-no drug NP were studied in a Matrigel mouse angiogenesis model. Mice (N=6/grp) were treated on days 6, 9, and 12 post-implantation and neovascularity imaged on day 16 with MRI and \( \alpha v \beta 3 \)-paramagnetic NP.

Results: \( \alpha v \beta 3 \)-PD NPs decreased (p<0.05) cell proliferation equal or better than equi-molar doses of free drug. \( \alpha v \beta 3 \)-fumagillin-PD NP decreased (p<0.05) Matrigel angiogenesis; no effects were measured in the other groups.

Conclusions: Sn-2 fumagillin PD offer improved chemical and circulatory stability in lipid-based NPs, facilitating translation of NP-based antiangiogenic treatment for atherosclerosis.