Conclusions: This study suggests that mean plaque size stabilizes at 4 weeks after carotid injury with no further increase at later time points. Furthermore, there appears to be a time-dependent decrease in activated macrophages in the neointima. Potential mechanisms for this observation are currently being investigated.

1200-143
Altered AP-1/Ref-1 Redox Pathway in INOS Deficient Vascular Smooth Muscle Cells: A Novel Involvement of INOS in Cellular Signaling

Kwang-Yuh Chyu, Xiaoxing Zhao, Paul C. Dobryga, Bajan Corcos, Predomin K. Chah, Cedars-Sinai Medical Center, Los Angeles, CA

Background: We previously showed injury-induced medial proliferation and neointimal formation in carotic arteries of normal oxoxo summarize knockout ( ctrl. KU) mice were significantly less compared to wild type (WT). INOS is a source of reactive oxygen species, which could modulate cellular growth and redox signaling molecules such as the AP-1, Ref-1, and the thioredoxin system. Therefore, we sought to determine the role of INOS in the vasculature.

Methods: CON: RAd36: MIEmCMV 4. Add-PREP-/lacZ RE, MIEmCMV, WPRE. Smo0 muscle myosm heavy chain promoter (RE) further increases expression of lacZ to 4 fold in vitro. We hypothesized that blockade of TGF-β by local delivery of an adenovirus expressing a soluble form of TGF-β type II receptor (AdTb-ExR) inhibits stent-induced neointima in porcine coronary arteries.

Results: Morphometric assessment of stented arteries after gene transfer displayed significantly less area (p=0.05 vs AdLacZ). Neither cell replication rate assessed by PCNA immunohistochemistry or cytosine incorporation was significantly different between the two groups. AdTb-ExR significantly inhibited neointima formation by inhibiting ECM accumulation in porcine coronary arteries. Arteries treated with AdLacZ displayed significantly increased neointima formation compared to control (AdPZ)

Conclusions: Blockade of TGF-β by local delivery of a soluble TGF-β receptor inhibits stent-induced neointima in porcine coronary arteries, and may provide a therapeutic potential to inhibit restenosis after stenting.

1201-111
Adenovirus Mediated Prostacyclin Synthase Gene Transfer Inhibits Neointimal Formation By Modulating Peroxisome Proliferator-Activated Receptors Expression

Hajime Imai, Yasushi Numaguchi, Yasuhito Nishimoto, Hideo Matsui, Toyoaki Murohara, Kenji Okumura, Nagoya University, Nagoya, Japan, Children's Hospital, Boston, MA

Peroxisome proliferator-activated receptors (PPARs) are nuclear hormone receptors which regulate cell growth and differentiation by modulating gene transcription. Many data demonstrate that PPARs are expressed in human atheroma/denudation, and their ligands like fibrates and troglitazone reduce neointimal formation after angioplasty. AdPPARs inhibit stent-induced neointima by inhibiting ECM accumulation in porcine coronary arteries. A stent (n=20) was deployed after gene transfer in each segment in 10 pigs. Localized expression of transgene was confirmed by reverse transcription-PCR and immunohistochemistry. Computer-based morphometric assessment was performed in stented arteries at 4 weeks after gene transfer.

Results: There were significantly less ratio of intima area (IA/medial area (MA)) and higher neointima cell density in stented arteries treated with AdTb-ExR compared with those with AdLacZ. Neither cell replication rate assessed by PCNA immunohistochemistry or cytosine incorporation was significantly different between the two groups. Overall, this study suggests that mean plaque size stabilizes at 4 weeks after carotid injury with no further increase at later time points. Furthermore, there appears to be a time-dependent decrease in activated macrophages in the neointima. Potential mechanisms for this observation are currently being investigated.

1201-120
Inhibition of Angiogenesis and Wound Healing by Adenovirus-Mediated Gene Transfer of a Soluble Form of Vascular Endothelial Growth Factor Receptor in Mice

Johnnie Jacobs, Betty Y. Tam, Uma Sundram, Calvin J. Kuo, John P. Cooke, Stanford University, Stanford, CA

Background: Vascular endothelial growth factor (VEGF) is an important angiogenic growth factor. Since angiogenesis plays a major role in wound repair, we hypothesized that adenovirus-mediated gene transfer of a soluble form of VEGF receptor D (Flt 1) might attenuate wound healing in mice.