In Situ Gene Transfer for Restenosis

Stephen N. Oesterle, MD
Associate Professor of Medicine, Harvard Medical School
Director, Interventional Cardiology Services, Massachusetts General Hospital

Background:

Rationale for gene therapy as an anti-restenosis strategy

Nitric oxide (NO) is a key molecule for mediating vessel wall homeostasis

- Physiologic regulator of vascular function
- Anti-proliferative effects
- Anti-atherogenic effects
- Inhibits platelet aggregation

Extensive animal literature supports the concept of NOS gene transfer for inhibition of neointima
van der Leyen & Dzau, PNAS, 1995 92, 1137

Liposomes as a vehicle for gene delivery

- Non-viral vector
- Already used in clinical trials
- No apparent toxicity

Local drug delivery: Infiltrator™ Catheter:

- Enables targeting of the medial cells
- Currently used for local drug delivery (EtOH delivery-Beaumont)

REGENT Phase 1 Trial (Safety and Efficacy)

- Massachusetts General Hospital (S. Oesterle)
- Brigham and Women's Hospital (R. Kuntz)
- Beth Israel Hospital (J. Carrozza)

Dose escalation study: 0.5, 2.0, 5.0, 10 υg
48 patients

Endpoints: Clinical safety, angiography at 6 weeks
IND submission 9/2000
RAC hearing 12/15/2000 with unanimous approval