

ABSTRACTS

Abstracts of Original Contributions: Young Investigators Awards Competition

The purpose of the Awards is to find and encourage the Young Investigators of promise on whom the future of cardiology depends. Any physician/scientist who is currently in a residency or fellowship training program or who has been in such a program within the past three years is eligible to submit an original investigation. Medical students and Ph.D. candidates are also eligible for the competition.

The Judging Committee will select a first and second place winner and three honorable mentions for each of the following categories: a) Clinical Investigations; b) Physiology, Pharmacology and Pathology; and c) Molecular and Cellular Cardiology. The Awards will be presented at the 45th Annual Convocation Cere-

mony on Wednesday, March 27, at 6:00 p.m. The Young Investigator of the Year (first place) for each category will receive a plaque, a certificate and \$2,000. Second place winners each receive a certificate and a check for \$1,000. The three honorable mentions each receive a certificate and a check for \$500. The American College of Cardiology Young Investigators Awards Competition is supported by grants from Searle and Boehringer Mannheim Pharmaceuticals Corporation.

Timothy J. Gardner, MD, FACC
 Chair
 1996 Young Investigators Awards Committee

407 Young Investigators Awards Competition - Physiology, Pharmacology, and Pathology

Monday, March 25, 1996, 10:30 a.m.-Noon
 Orange County Convention Center, Room 231

10:30

407-1 Accelerated Re-Endothelialization and Reduced Neointimal Thickening Following Catheter Transfer of phVEGF₁₆₅

Takayuki Asahara, Donghui Chen, Marianne Kearney, Susan Rossow, Jonathan Passeri, James F. Symes, Jeffrey M. Isner. *St. Elizabeth's Medical Center, Boston, MA; Tufts University School of Medicine, Boston, MA*

We investigated the hypothesis that an endothelial cell (EC) mitogen could serve as the basis for a novel gene therapy strategy designed to facilitate reendothelialization (rET), reduce neointimal thickening, and promote recovery of EC dysfunction following balloon injury. New Zealand white rabbits underwent simultaneous balloon injury and gene transfer of one femoral artery with phVEGF₁₆₅, encoding the 165-amino acid isoform of vascular endothelial growth factor (VEGF); or LacZ. In each animal transfected with phVEGF₁₆₅ or LacZ, the contralateral femoral artery was also subjected to balloon injury, but not gene transfer.

For LacZ, rET remained incomplete at 4 wks post-transfection; in contrast, phVEGF₁₆₅ produced prompt rET which was 95% complete by 1 wk. Moreover, rET in the contralateral, balloon-injured, non-transfected limb of the VEGF group was similarly accelerated. Intimal thickening (intima to media area ratio) was correspondingly reduced (0.14 vs 0.69), as was the frequency of thrombotic occlusion (3.1% vs 21.9%), and the vasomotor response to EC-dependent agonists was preserved as normal in VEGF transfected vs controls. A similar benefit was observed for the contralateral, balloon-injured, non-transfected limb.

These experimental findings thus establish proof of principle for the concept that catheter-mediated, mitogen-accelerated rET can be achieved by arterial gene transfer, with a consequent inhibition of neointimal thickening, reduction in thrombogenicity, and restoration of endothelium-dependent vasomotor reactivity.

407-2 The Doppler Effect as a Cause for Irregular Electrocardiograms in Reentrant Ventricular Arrhythmias

Richard A. Gray, José Jalife, William T. Baxter, Candido Cabo, Jorge M. Davidenko, Arkady Pertsov. *SUNY Health Science Center at Syracuse, Syracuse, NY*

Reentrant excitation of the myocardium is thought to be the underlying mechanism for the most dangerous cardiac arrhythmias including ventricular tachycardia and ventricular fibrillation. The relationship between the spatio-temporal patterns of electrical activity in the heart and the clinically useful electrocardiograms remain unclear. To study this relationship we utilized a combination of high-resolution video imaging, numerical simulations, electrocardiography and image processing. We recorded the patterns of wave propagation on the surface of the isolated Langendorff-perfused rabbit heart during ventricular arrhythmias in which a single reentrant source was observed. To complement these studies we performed computer simulations of reentrant waves in a realistic three-dimensional heart geometry. Our results indicate that the speed of the reentrant source was related to the irregularity of the electrocardiogram through the Doppler mechanism. If the dimensionless ratio of the speed of the reentrant source divided by the wave speed was small (less than 5%) the electrocardiogram was monomorphic, if this ratio was intermediate (5 to 30%) the electrocardiographic pattern was polymorphic, and if this ratio was large (greater than 30%) the electrocardiograms were indistinguishable from fibrillation. Quantitative comparisons using Doppler equations were successful in predicting the width of the frequency spectra of electrocardiograms (a measure of irregularity) and the ratio of periods ahead and behind the moving reentrant source. The Doppler phenomenon provides a robust mechanistic explanation for the irregularity of electrograms recorded during reentrant arrhythmias.

407-3 Mathematics of Systolic Pulmonary Vein Flow: a Closed Form Analytical Solution Incorporating Fundamental Principles and Key Variables

Randall Y. Grimes, Ajit P. Yoganathan, Robert A. Levine. *Georgia Institute of Technology, Atlanta, GA*

Systolic pulmonary venous (PV) flow is becoming part of the non-invasive assessment of left atrial function and pressure. However no unifying model of the determinants of systolic PV flow exists. A mathematical model of atrium and

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11:00