Abstracts - Angelography & Interventional Cardiology

68A

POSTER SESSION

1102

Restenosis: Basic Research I

Monday, March 08, 2004, 3:00 p.m.-5:00 p.m.
Morial Convention Center, Hall G
Presentation Hour: 3:00 p.m.-4:00 p.m.

1102-01

Important Species Differences of Sirolimus, Paclitaxel, and Tacrolimus on Porcine and Human Coronary Smooth Muscle and Endothelial Cells

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Background: Implantation of drug coated stents shows clinical efficacy for the prevention of restenosis, but large animal studies have not shown any long term benefit with the use of Sirolimus (SIR) and Paclitaxel (PAC). Despite this the possible interspecies differences have not been investigated.

Methods: Porcine (p) and human (h) smooth muscle (SMC) and endothelial cells (EC) were serum deprived for 48h until addition of drugs.

Results: SMC from both species responded to SIR and PAC with a similar inhibition of proliferation. The concentration of SIR and PAC that reduced cell growth by 50% (IC50) was 0.019 â&mu;M (n=6) and 0.016 â&mu;M (n=4), respectively. 2) E5555 inhibited rat SMC proliferation induced by thrombin with an IC50 value of 0.16 â&mu;M (n=4), but did not inhibit that induced by basic fibroblast growth factor or platelet-derived growth factor. 3) The area of neointima in the vehicle-treated group (n=23) was 0.13±0.01 mm² (meansSEM), while that in the group treated with E5555 at 10 mg/kg (n=24) and 30 mg/kg (n=24) were 0.11±0.007 mm² (ns vs. vehicle) and 0.07±0.009 mm² (p<0.001), respectively. The ratio of neointimal to medial area was significantly decreased in the group treated with E5555 at 50 mg/kg (0.86±0.092 vs. 1.49±0.091 in vehicle, p<0.001) without affecting the medial area.

Conclusion: E5555, a potent and orally active PAR-1 antagonist, may be beneficial for the treatment of restenosis after percutaneous coronary intervention.