

Secretome of apoptotic peripheral blood cells (APOSEC) attenuates microvascular obstruction in acute myocardial infarction

- (I) Role of platelet aggregation
- (II) Role of vasodilation

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MEDICAL UNIVERSITY OF VIENNA

www.meduniwien.ac.at/applied-immunology

The following relevant financial relationships exist related to this presentation:

Medical University of Vienna/APOSCIENCE has claimed financial interest

WO2010070105-A1

WO2007121495A2

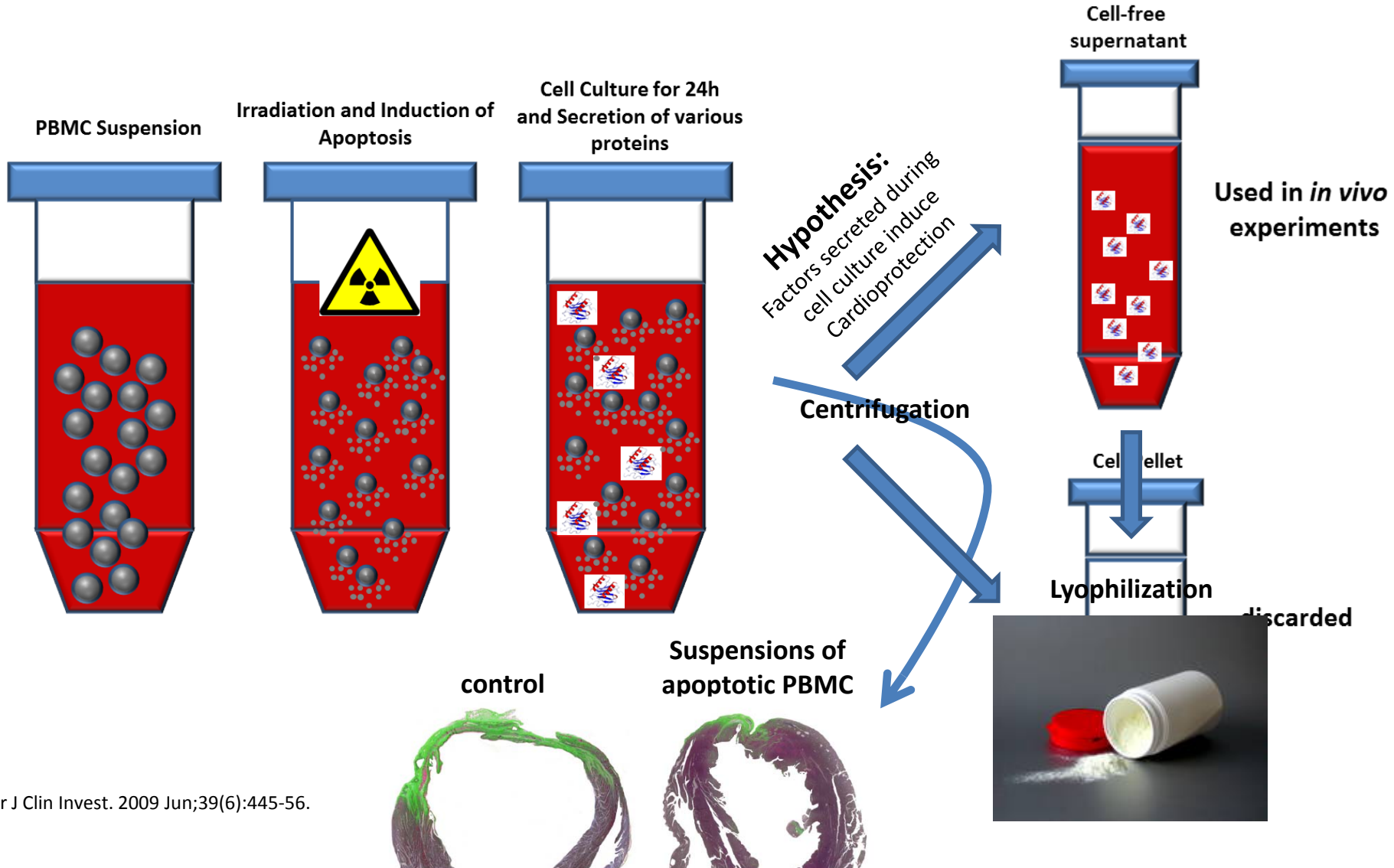
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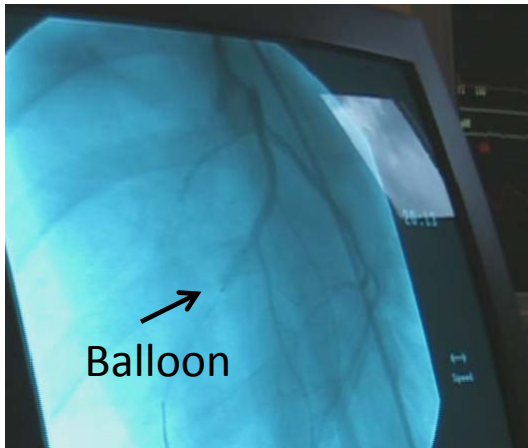
Ankersmit HJ: APOSCIENCE AG, shareholder , Vienna based Start Up



APOSEC Reperfused AMI Large Animal Model



Pigs (~30kg)



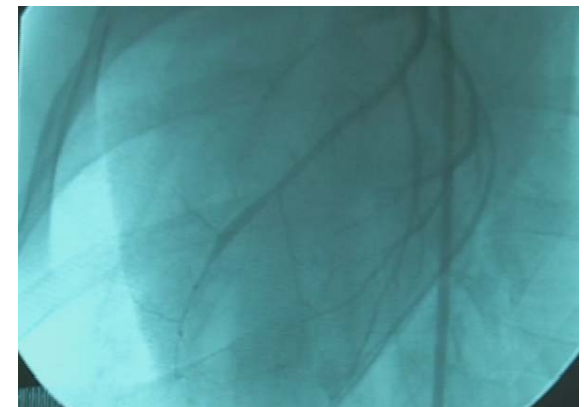
Occlusion of the LAD



Intravenous administration of
porcine APOSEC
40 minutes after occlusion

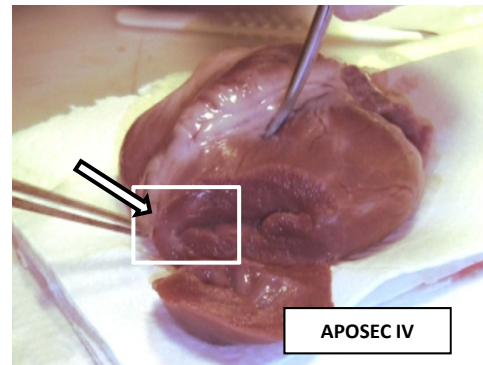
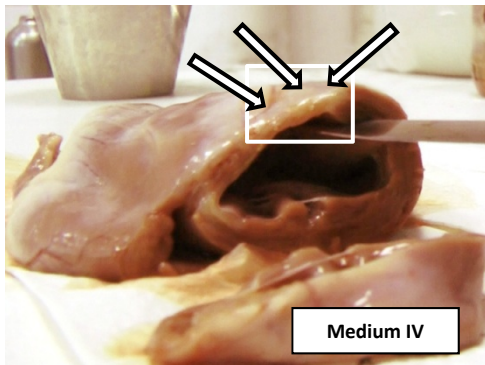
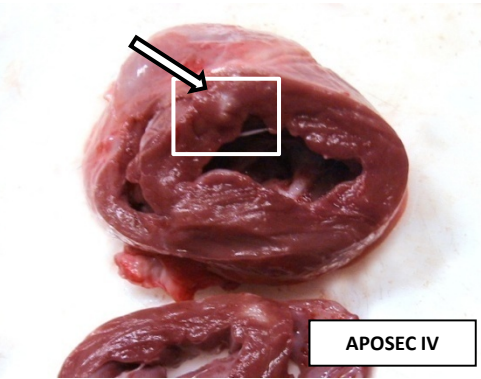
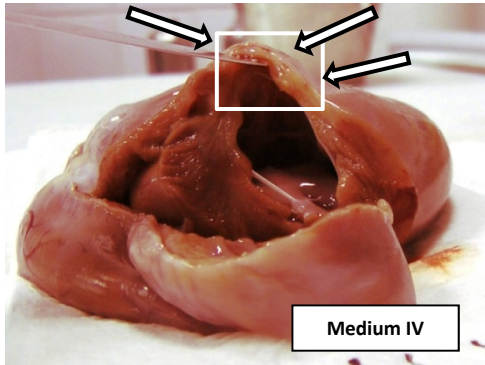


According to
AHA & ESC
Guidelines

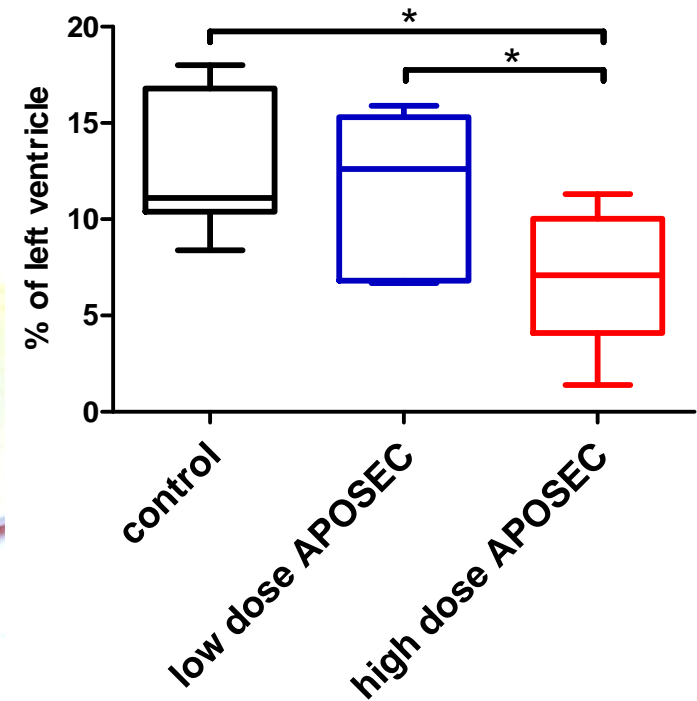


Reperfusion after 90 minutes

APOSEC Reperfused AMI Large Animal Model



Infarction Size after 30 days



What is APOSEC – Lessons learned from secretome analysis

Good evidence for treating AMI with stem cell secretome („conditioned medium“)



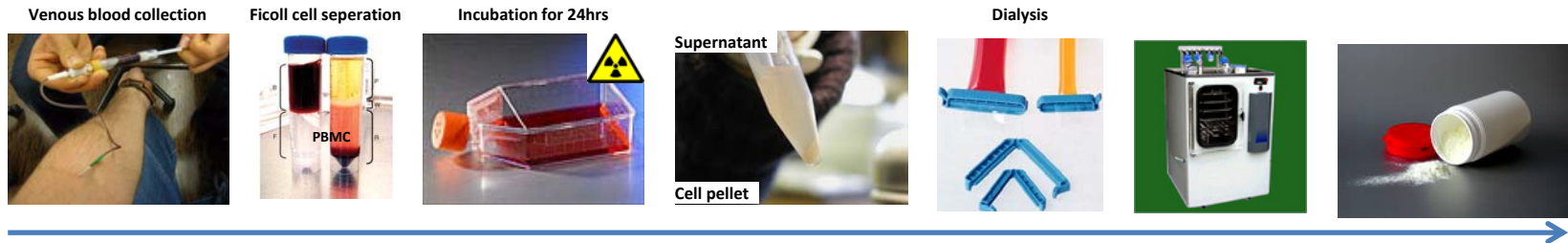
Paracrine action accounts for marked protection of ischemic heart by Akt-modified mesenchymal stem cells

Nat Med. 2005 Apr;11(4):367-8.

Secretome of conditioned stem cells and peripheral blood cells contains comparable levels of cytokines/chemokines

Eur Heart J. 2008 Dec;29(23):2851-8.

APOSEC – Secretome of irradiated peripheral monuclear cells



APOSEC attenuates myocardial injury during AMI



Basic Res Cardiol. 2011 Nov;106(6):1283-97.

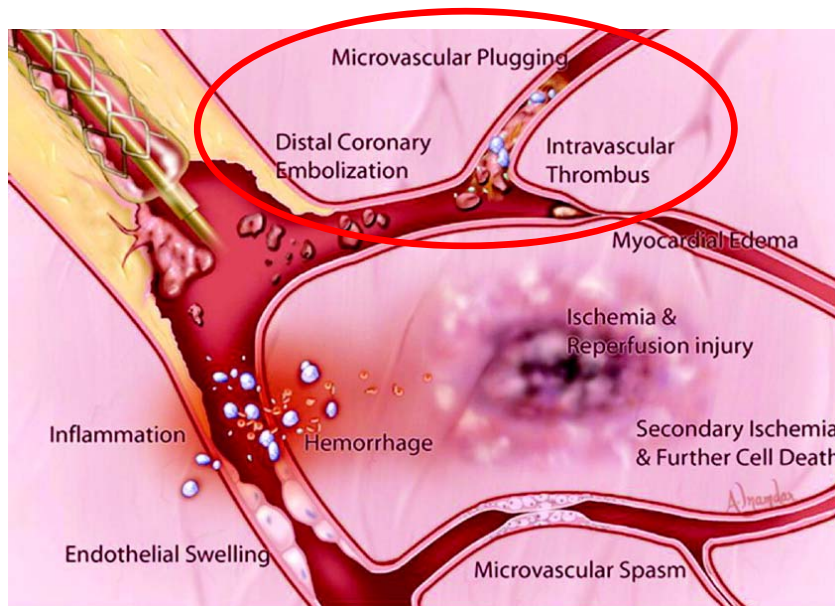
Basic Res Cardiol. 2011 Jun;106(4):645-55.

Eur J Clin Invest. 2009 Jun;39(6):445-56.

No-reflow – Role of microvascular obstruction (MVO)

Despite infarct vessel patency ... disordered microvascular function and inadequate myocardial tissue perfusion are often present

Circulation. May 1992;85(5):1699-1705.



Circulation 2008;117:3152-3156.

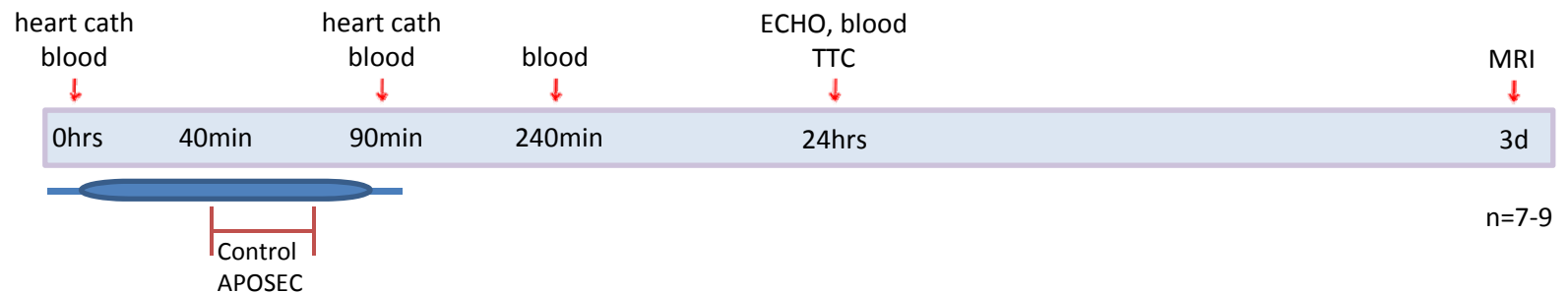


Microvasculature of a porcine heart
provided by M Gyöngyösi

Aim of the study – Experimental setting

Impact of APOSEC on MVO

Influence of APOSEC on microvasculature in a porcine AMI model



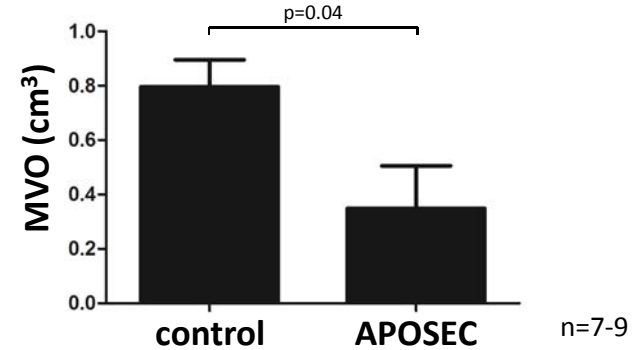
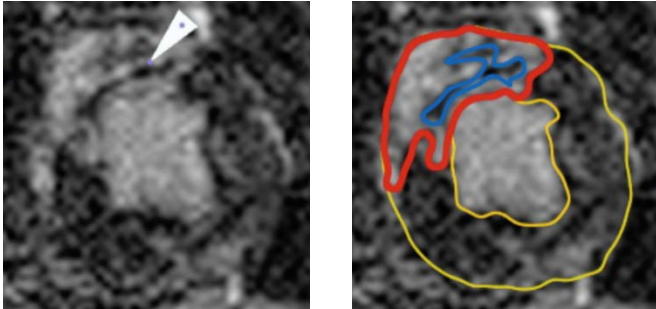
Finding the mode of action: Effects on platelets and vasodilation *in vitro*

in vitro experiments

- (I) aggregometer FACS ELISA western blot
- (II) coronary ring assays ELISA western blot

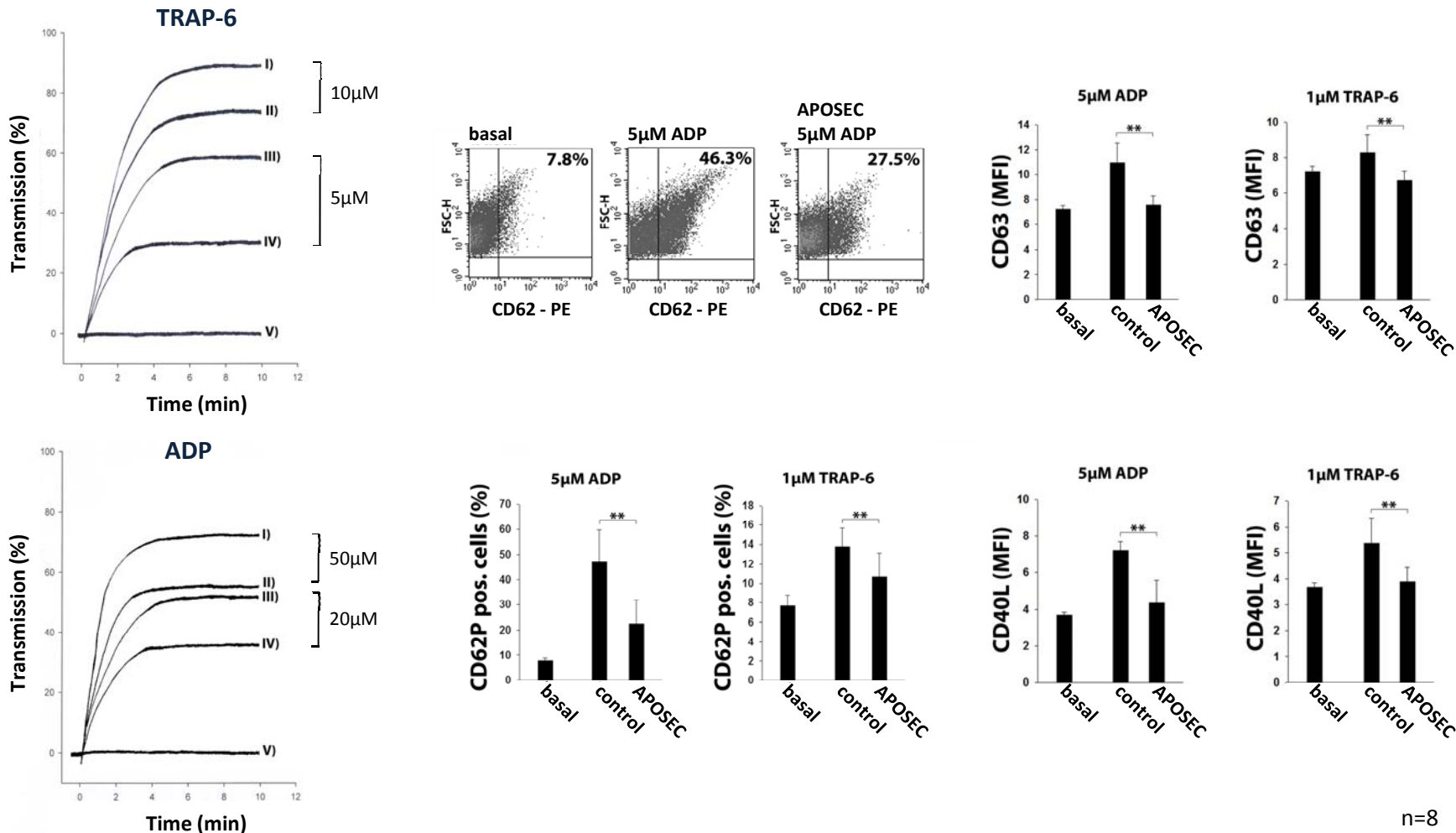
Results I – APOSEC reduces MVO during AMI

MVO = hypoenhanced areas in late-enhanced MRI images

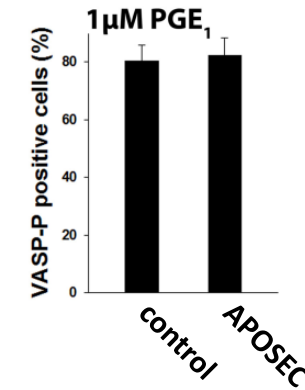
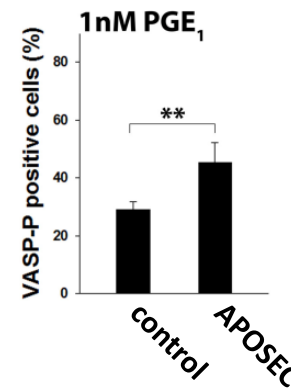
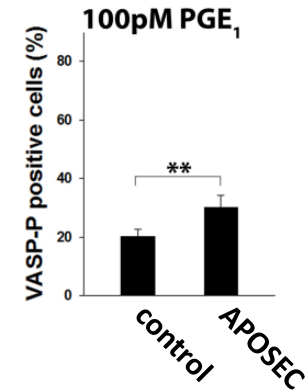
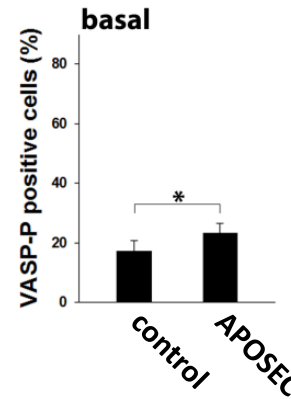
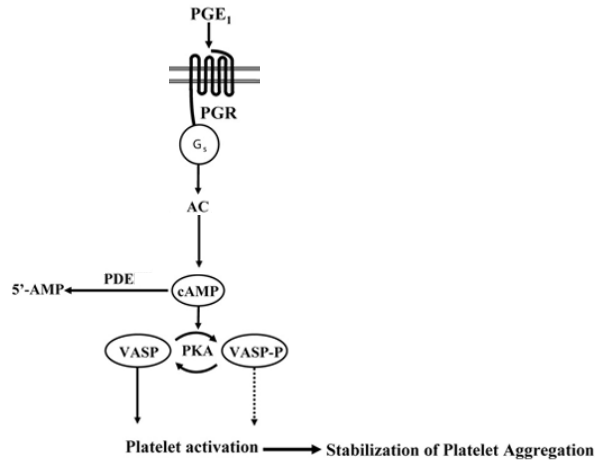


triplet		VT	
control	APOSEC	control	APOSEC
0.7 ±8.5	0.2 ±0.2	5.7 ±3.4	2.4 ±1.9
1.8 ±3.3	3.4 ±2.0	3.2 ±1.9	3.4 ±2.4

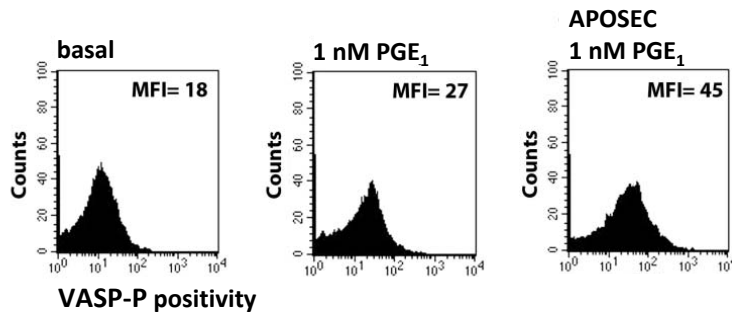
Results II – APOSEC mediates anti-aggregatory effects *in vitro*



Results III – mode of action – VASP phosphorylation

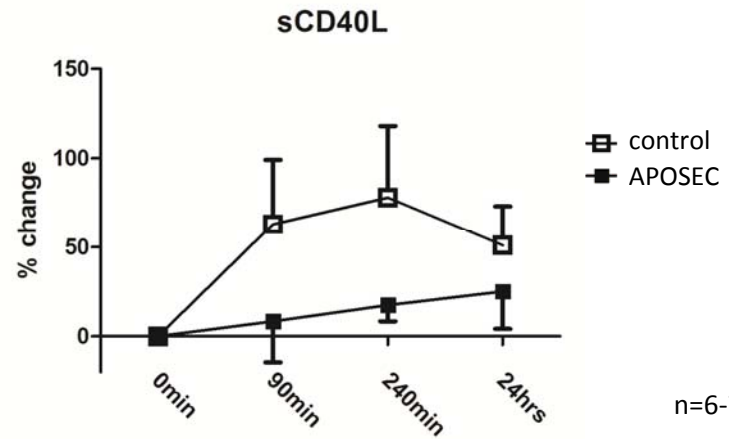
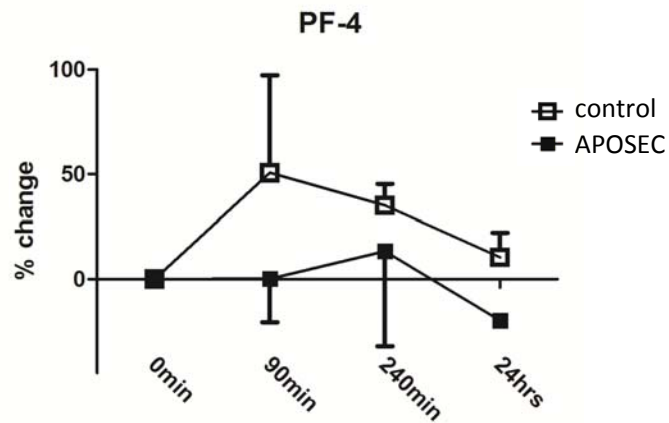
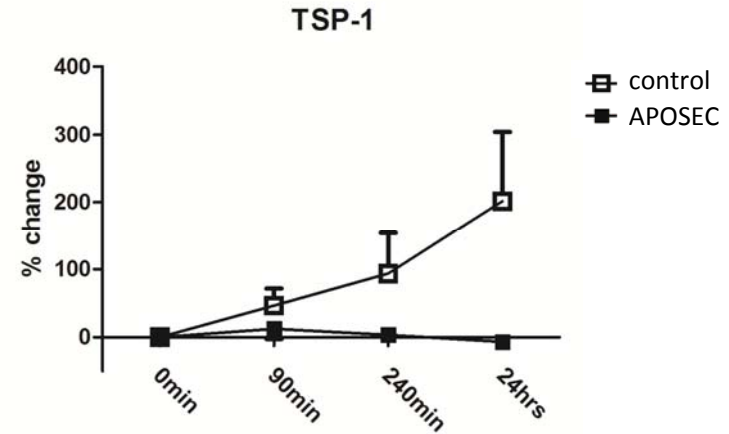
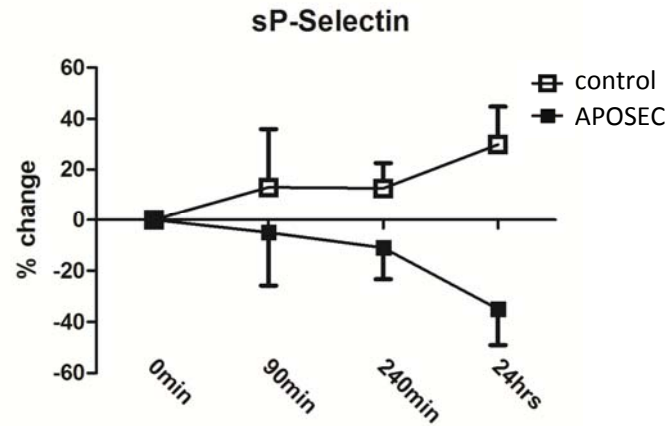


Thromb Haemost. 2011 Aug 1;106(2):253-62.



n=8

Results IV – platelet inhibition *in vivo*

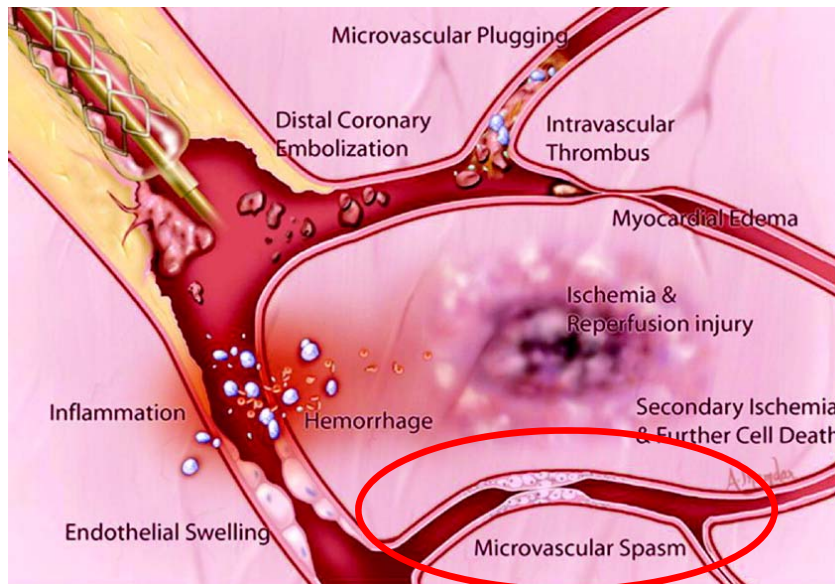


n=6-7

No-reflow – Role of microvascular obstruction (MVO)

Despite infarct vessel patency ... disordered microvascular function and inadequate myocardial tissue perfusion are often present

Circulation. May 1992;85(5):1699-1705.

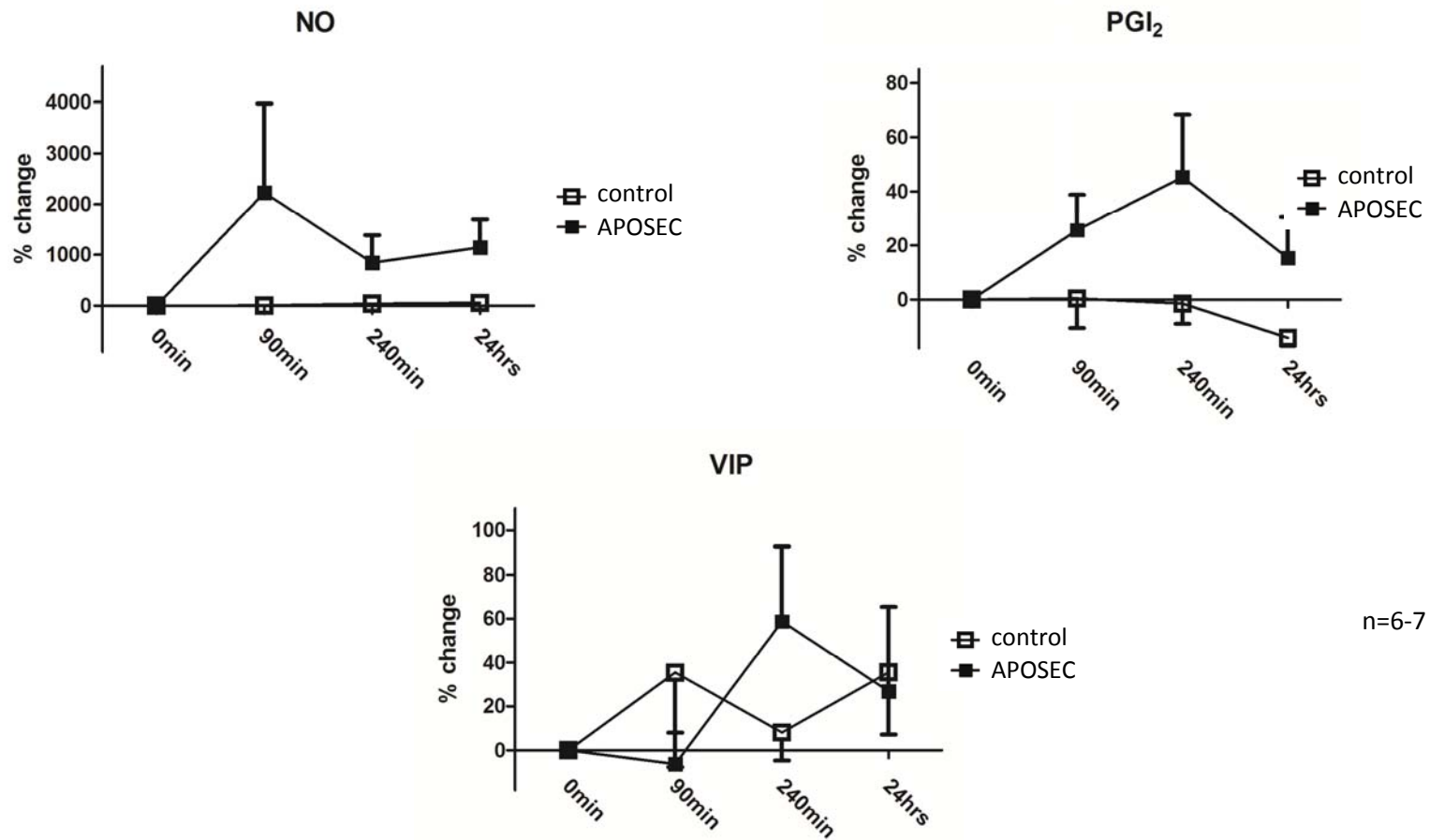


Circulation 2008;117:3152-3156.

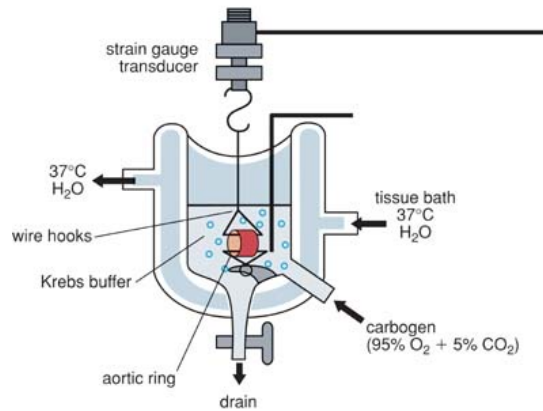


Microvasculature of a porcine heart
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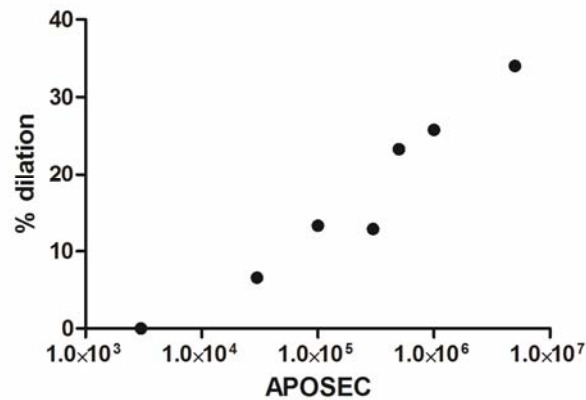
Results V – APOSEC mediates vasodilation



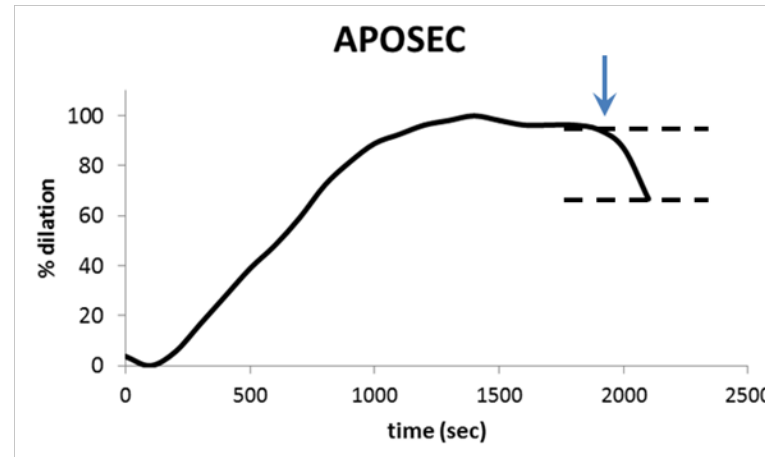
Results VI – APOSEC mediates vasodilation (coronary ring assay)



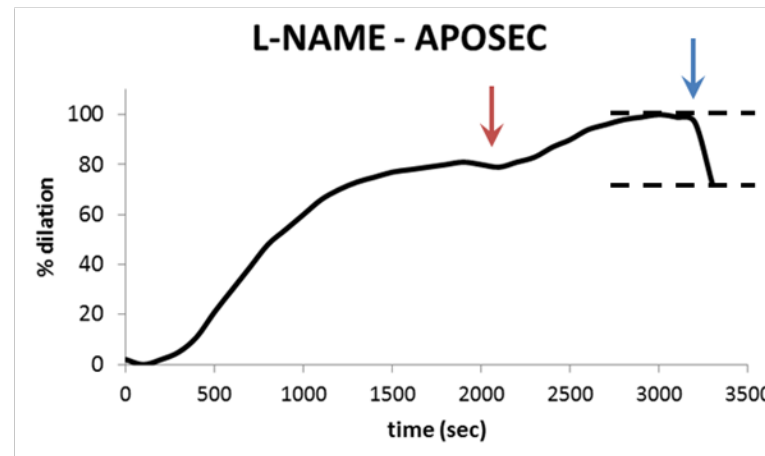
<http://www.currentprotocols.com>



n=6-7



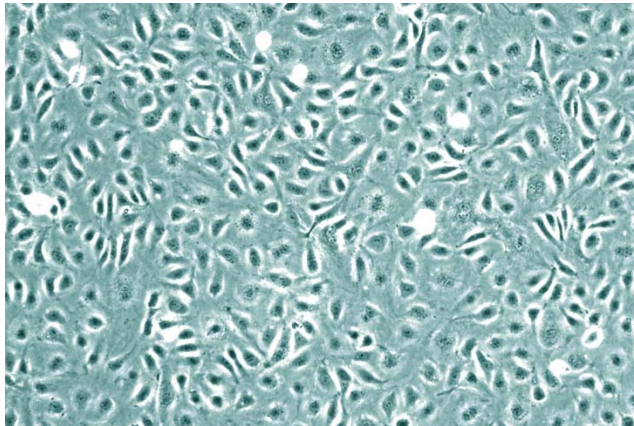
↓ APOSEC (20×10^6)



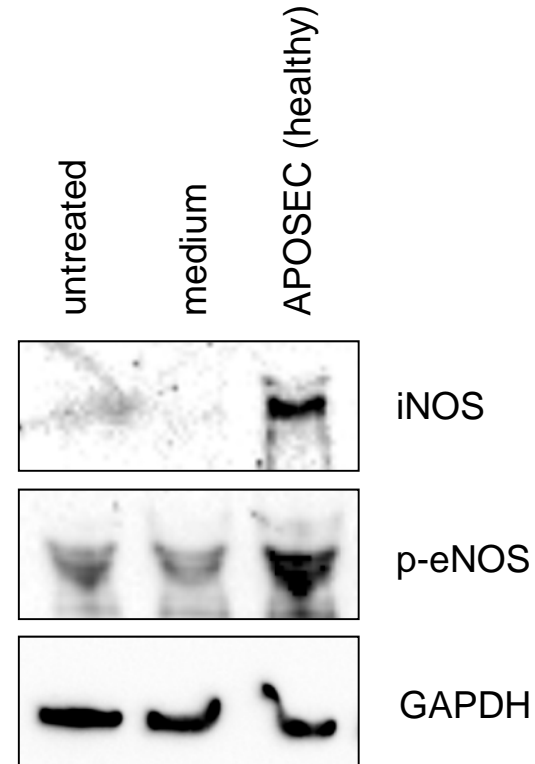
↓ APOSEC (20×10^6)

↓ L-NAME (100 μ M)

Results VII – APOSEC mediates vasodilation (HUVEC culture)



<http://www.sciencellonline.com>



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Department of Surgery

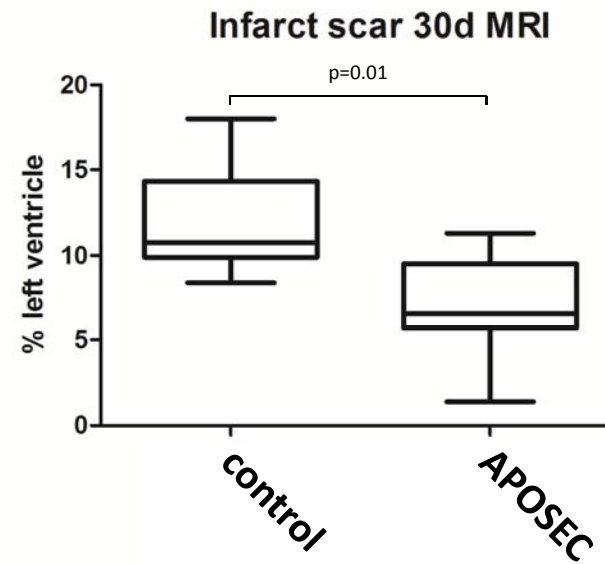
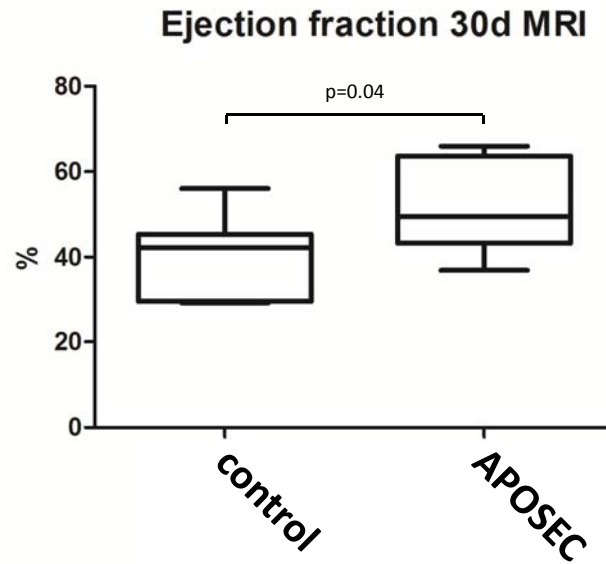
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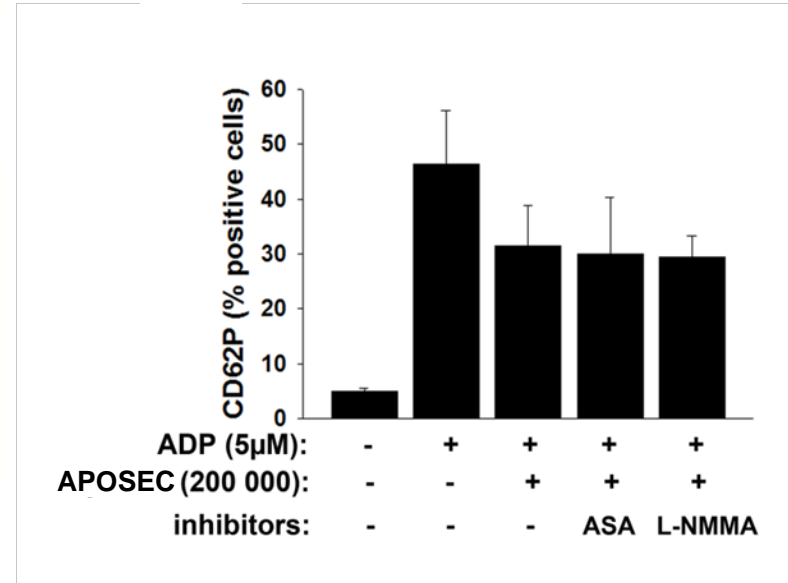
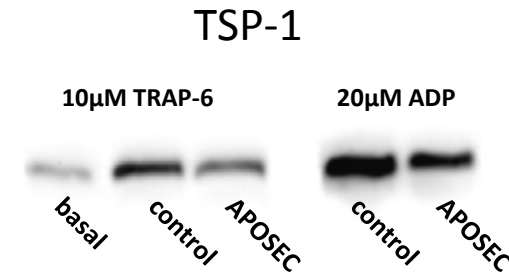
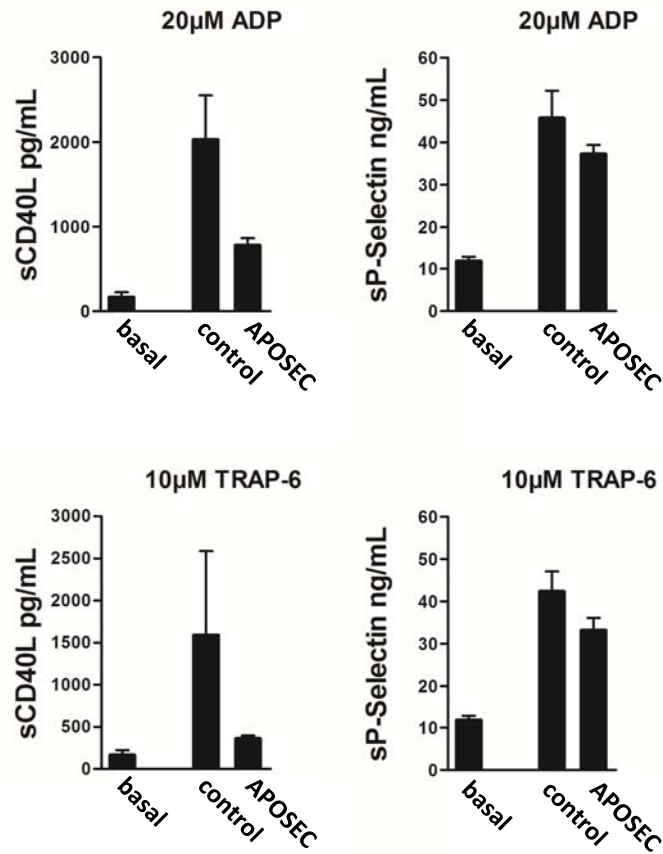
András Jakab
Ervin Berényi
Zsolt Petrási

Results IX – Treatment of APOSEC leads to increased functional parameters in the long time



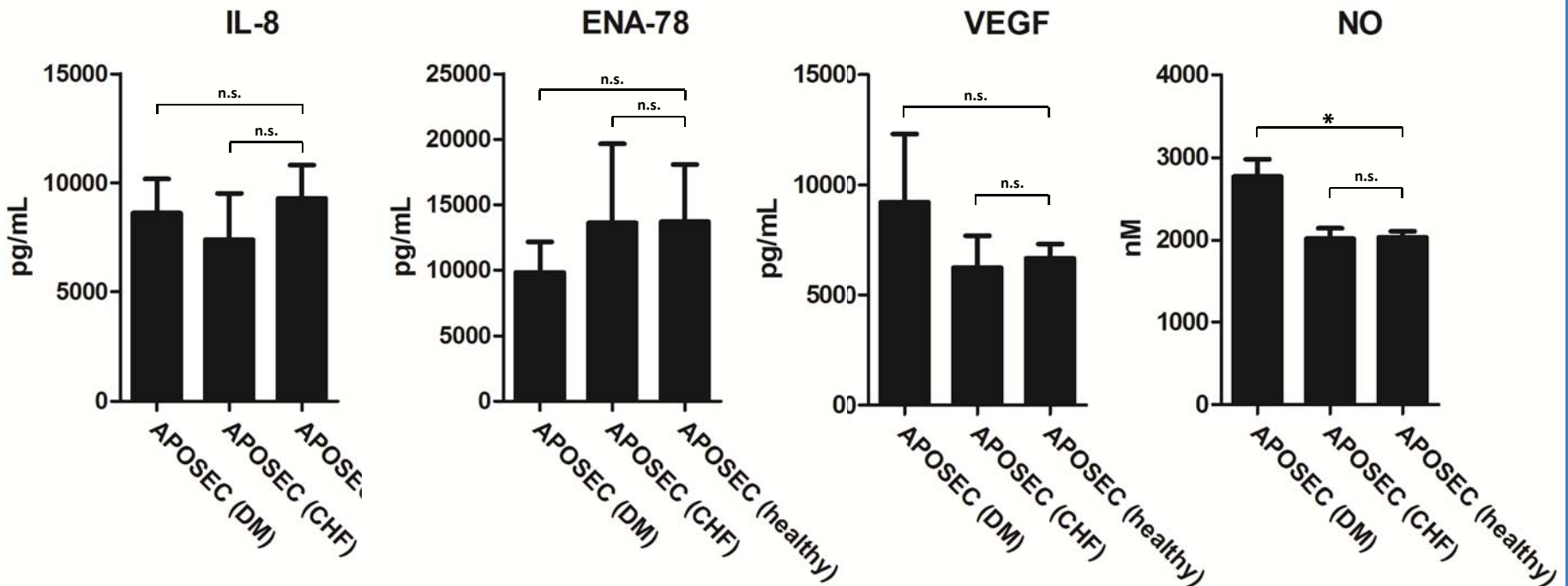
n=7-9

Results III – APOSEC mediates anti-aggregatory effects *in vitro* COX and NO inhibition



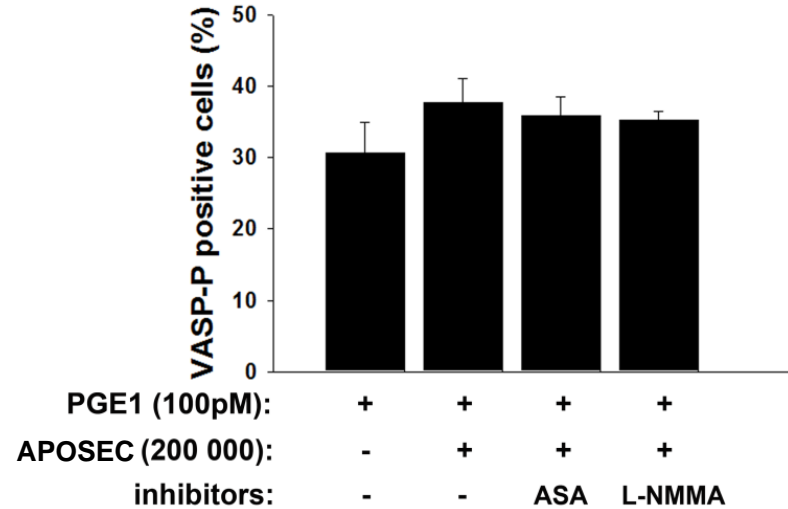
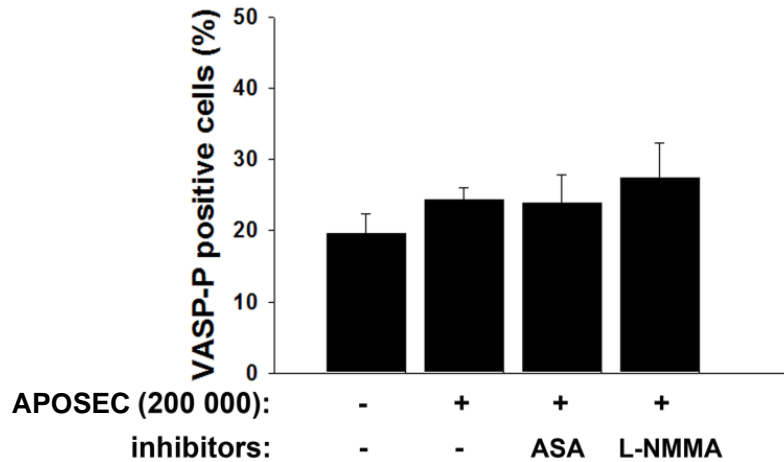
n=3

Excursus – Is the effect of APOSEC limited to „healthy“ donors?



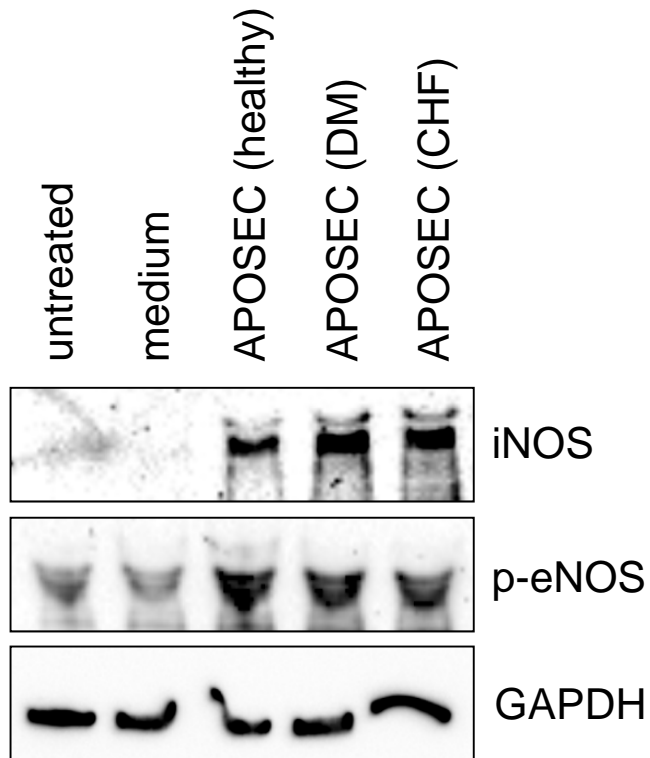
n=6-7

Results V – mode of action – VASP phosphorylation



n=3

Excursus – Is the effect of APOSEC limited to „healthy“ donors?



data on platelet function...