MEDIZINISCHE UNIVERSITÄT WIEN

Christian Doppler Laboratory for Cardiac and Thoracic Diagnosis & Regeneration

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

Secretome from mononuclear cells confers immunosuppression in a murine autoimmune myocarditis model

K HOETZENECKER

DIVISION OF THORACIC SURGERY

CHRISTIAN DOPPLER LABORATORY

for the Diagnosis & Regeneration of Cardiac and Thoracic Diseases

MEDICAL UNIVERSITY OF VIENNA

www.meduniwien.ac.at/applied-immunology

Vienna, 05 Dec 2012

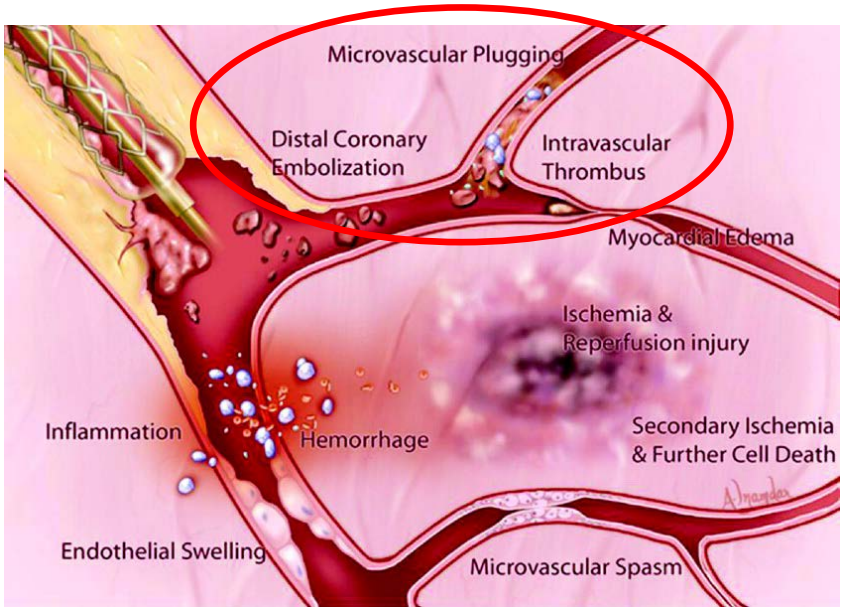
Seminar room 8G, AKH

Austria

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

What is APOSEC – Lessons learned from secretome analysis

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

nature medicine

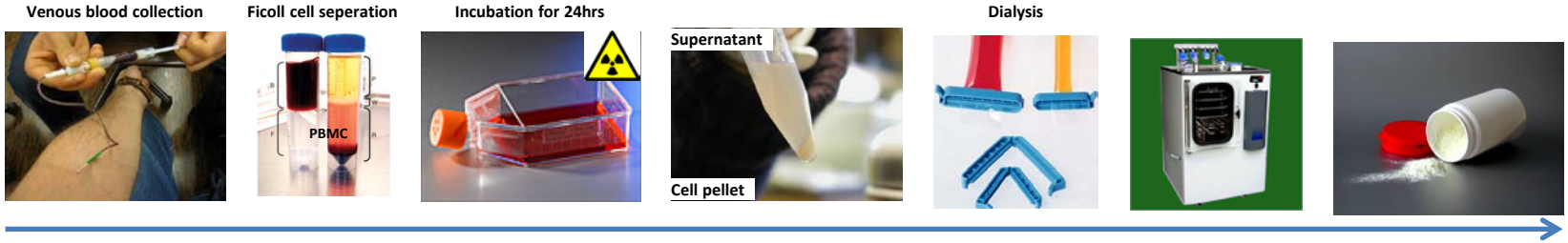
Paracrine action accounts for marked protection of ischemic heart by Akt-modified mesenchymal stem cells

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

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

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

3. APOSEC – Secretome of irradiated peripheral mononuclear cells



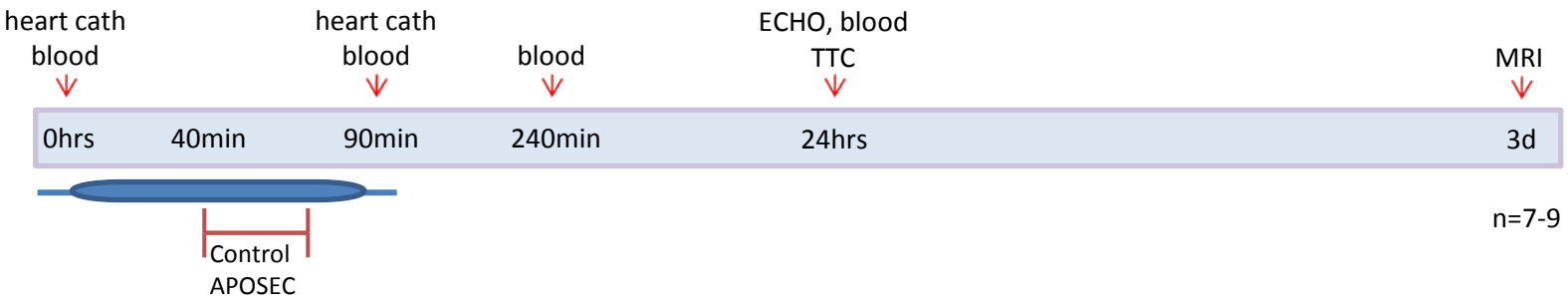
4. APOSEC attentuates myocardial injury during AMI

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.

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*

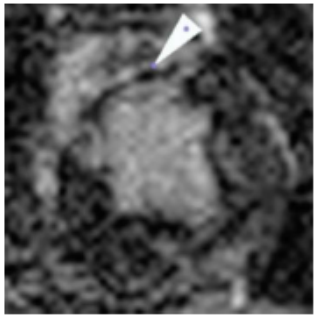
in vitro experiments

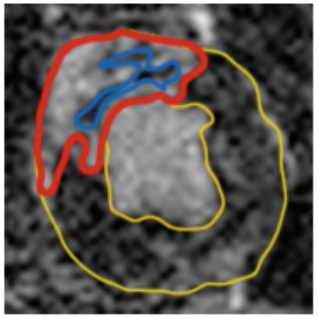
(I) aggregometer | FACS | ELISA | western blot

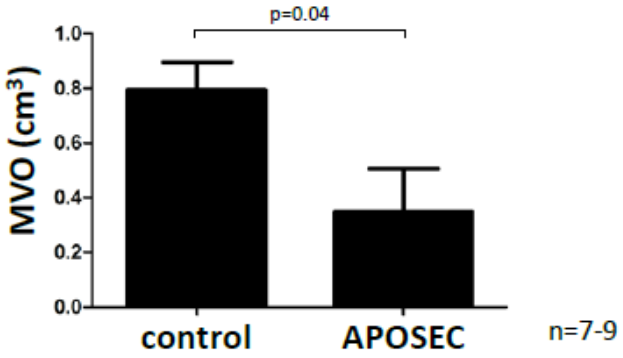
(II) coronary ring assays | ELISA | western blot

Results I – APOSEC reduces MVO during AMI

MVO = hypoenhanced areas in late-enhanced MRI images



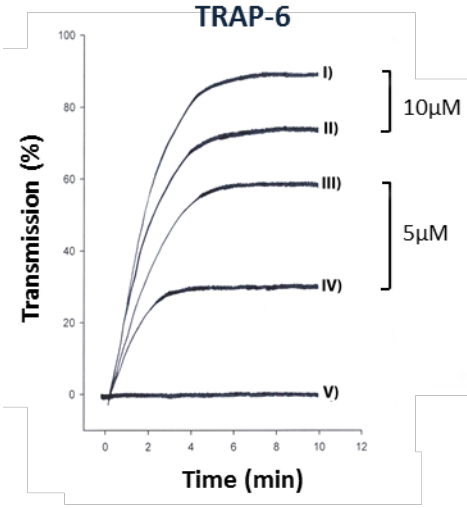


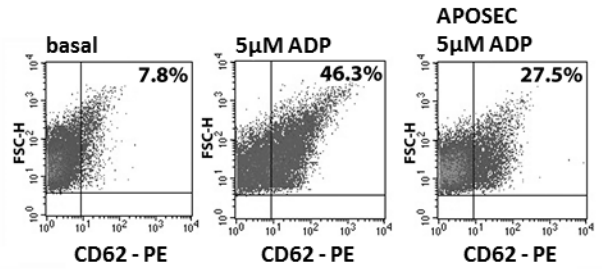


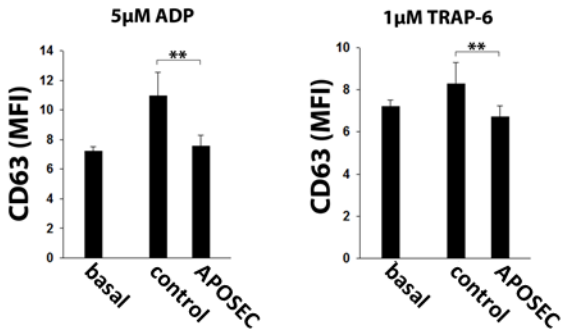
n=7-9

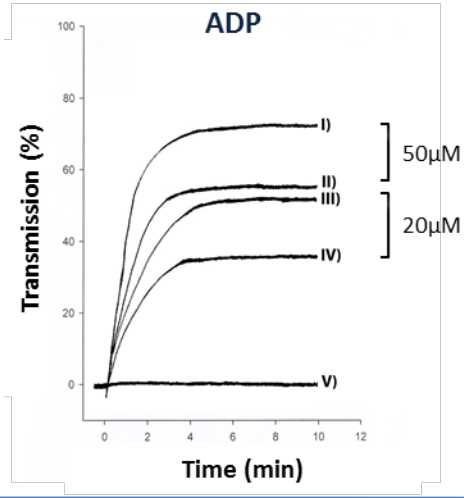
triplets		VT	
control	APOSEC	control	APOSEC
0.7 ±8.5	0.2 ±0.2	5.7 ±3.4	2.4 ±1.9
.8 ±3.3	3.4 ±2.0	3.2 ±1.9	3.4 ±2.4

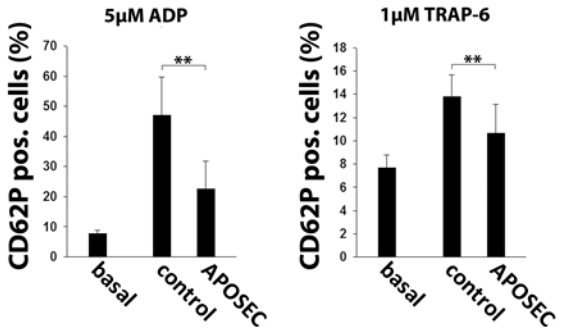
Results II – APOSEC mediates anti-aggregatory effects *in vitro*

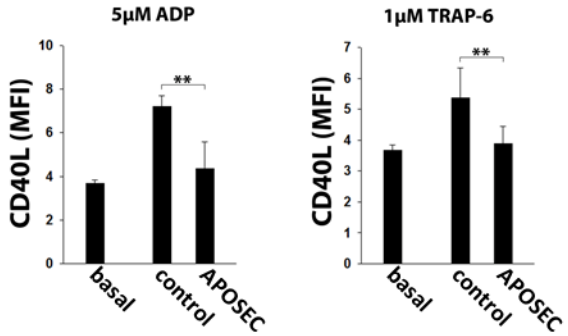






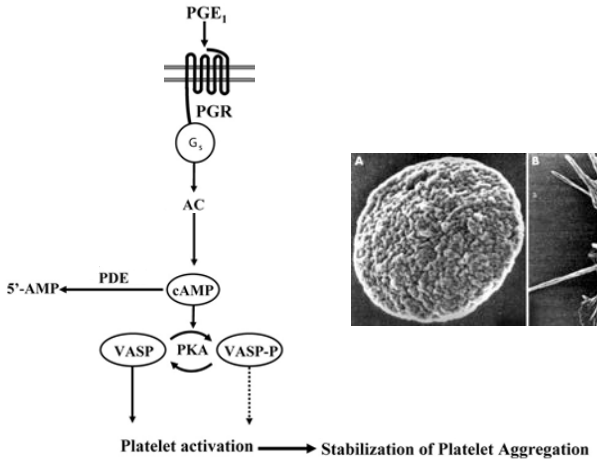


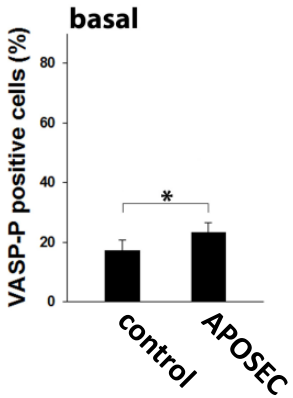


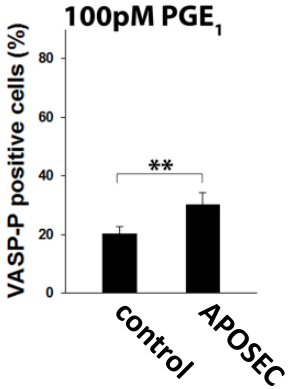


n=8

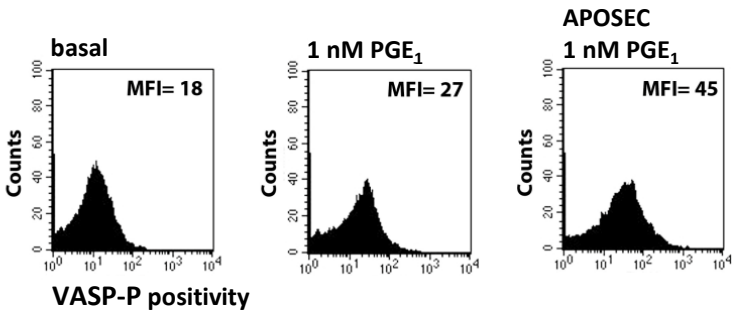
Results III – mode of action – VASP phosphorylation

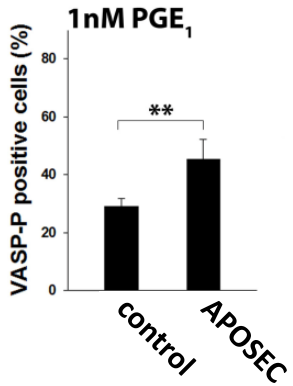


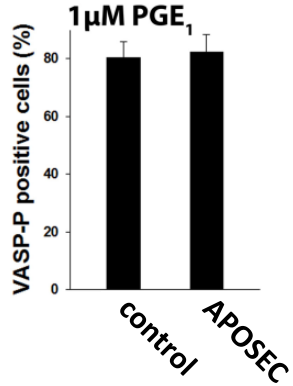




Thromb Haemost. 2011 Aug 1;106(2):253-62.
J Heart 2003;89:1273-1278

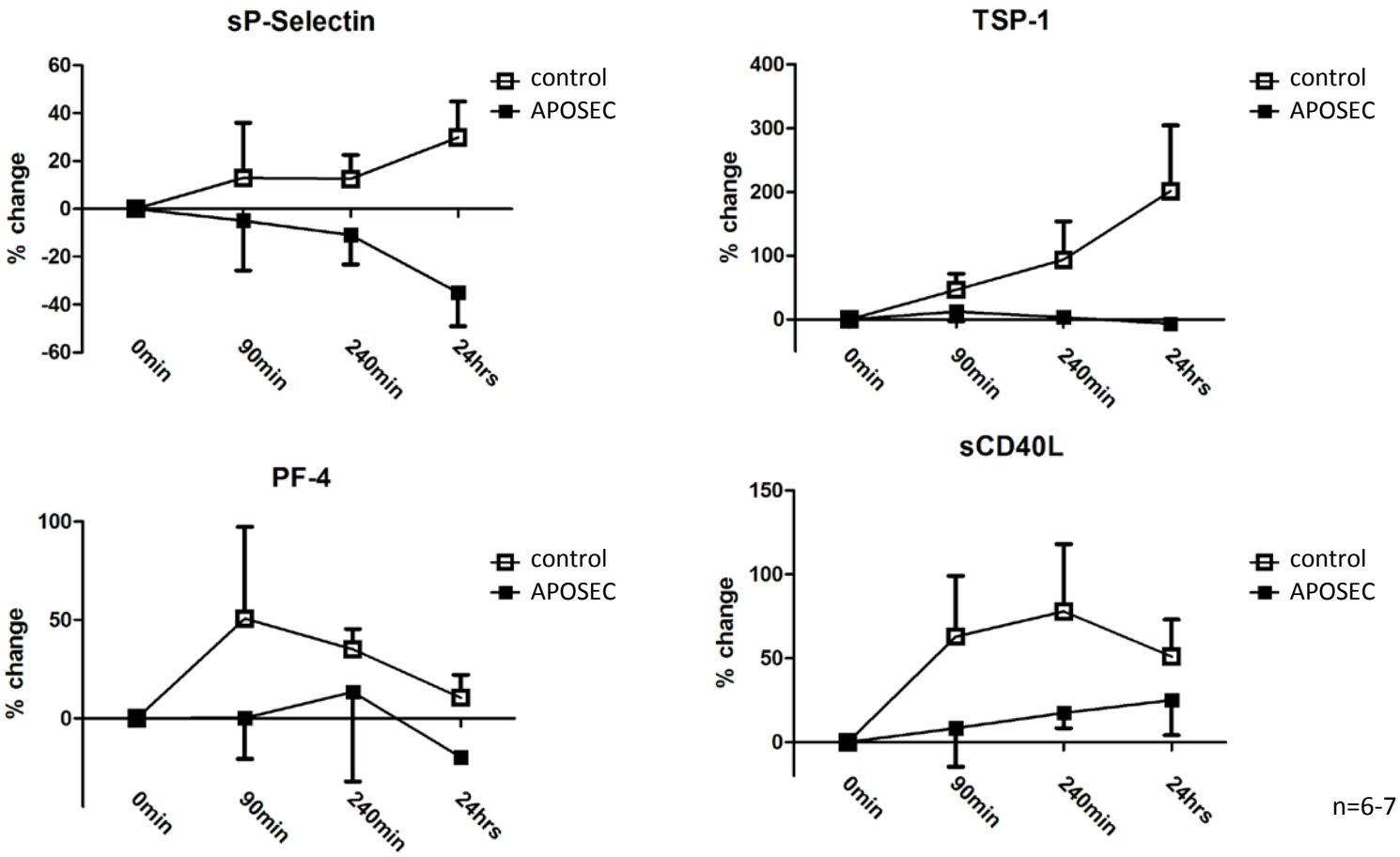






n=8

Results IV – platelet inhibition *in vivo*



n=6-7

No-reflow – Role of microvascular obstruction (MVO)

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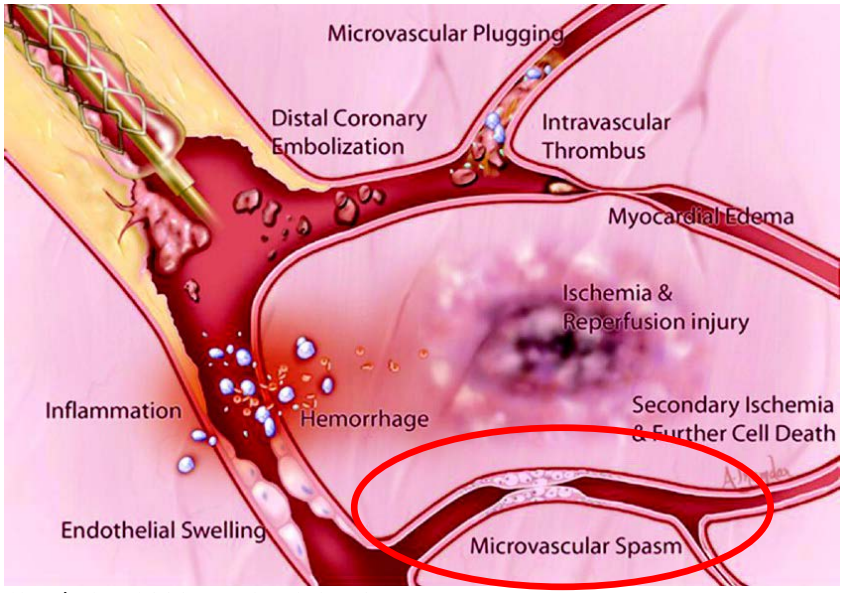

Circulation 2008;117:3152-3156.

Microvasculature of a porcine heart
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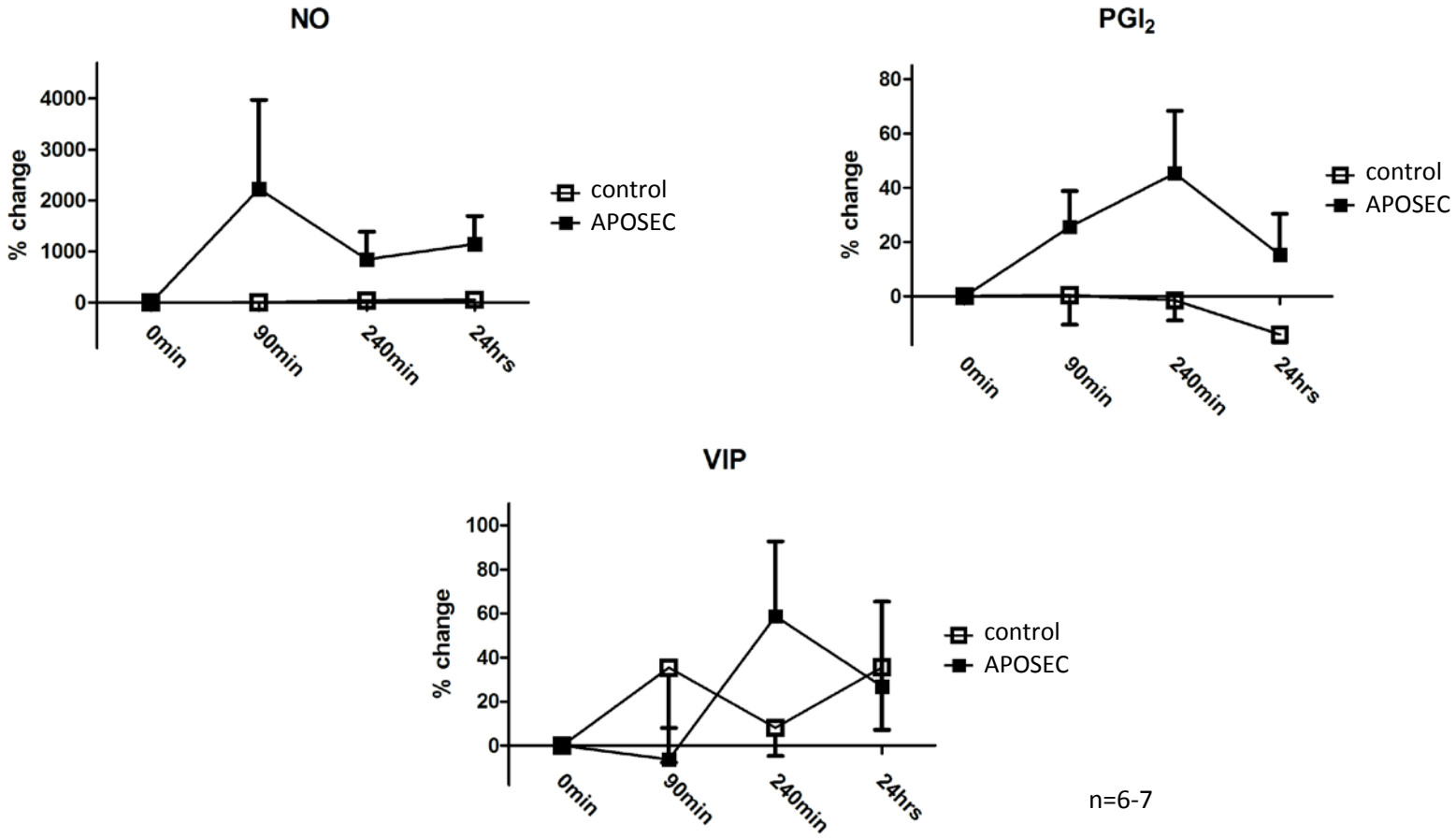
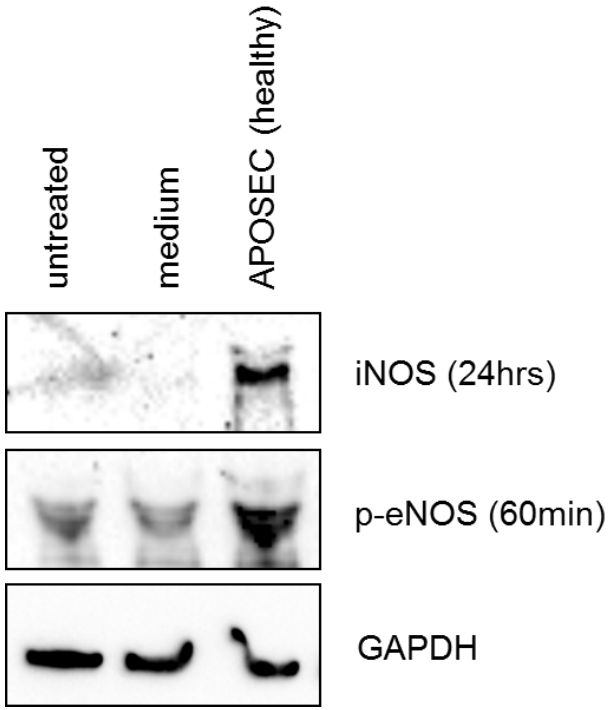
Results V – APOSEC mediates vasodilation



n=6-7

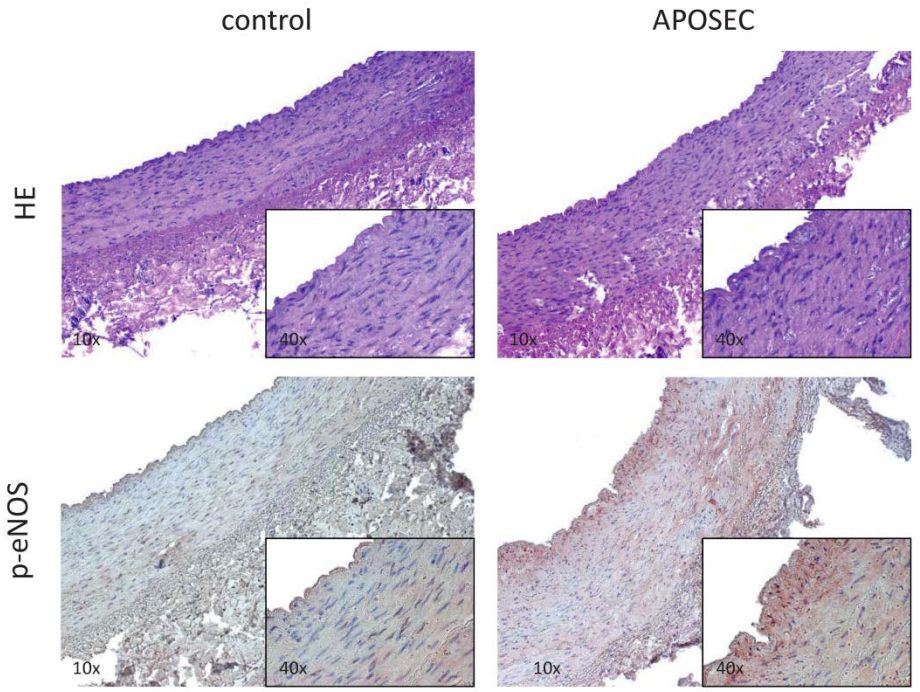
Results VI – APOSEC mediates vasodilation (indirect effects)

HUVEC culture



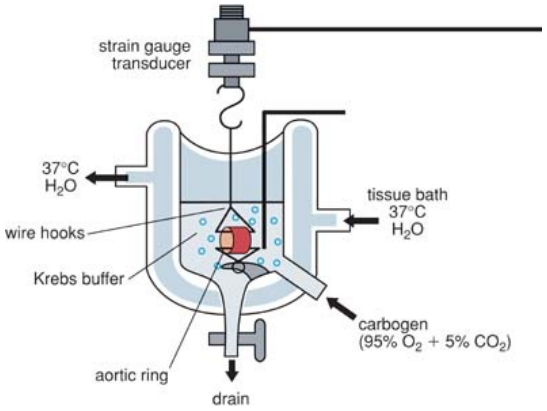
n=3

Isolated coronary rings

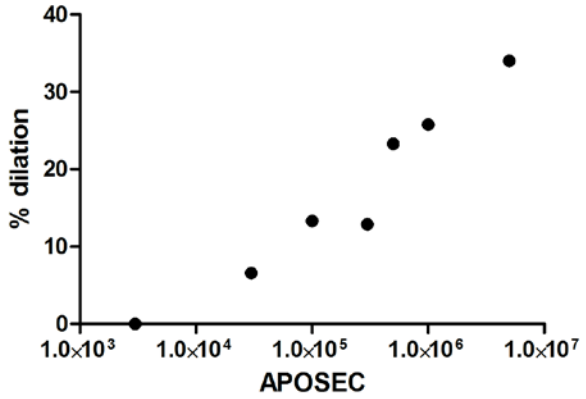


n=3

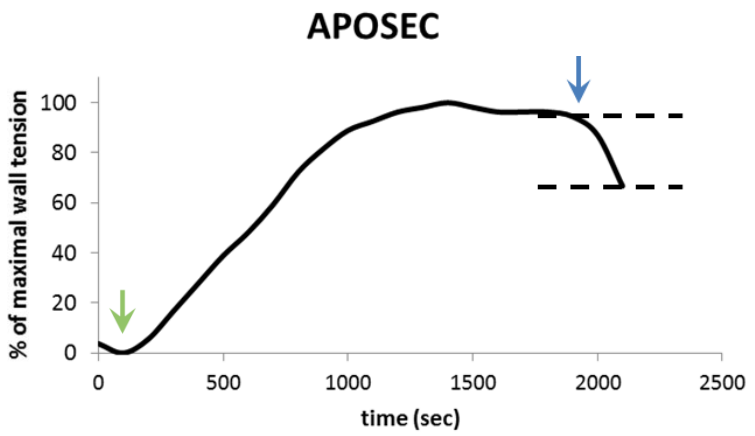
Results VII – APOSEC mediates vasodilation (direct effects, NOS independent)

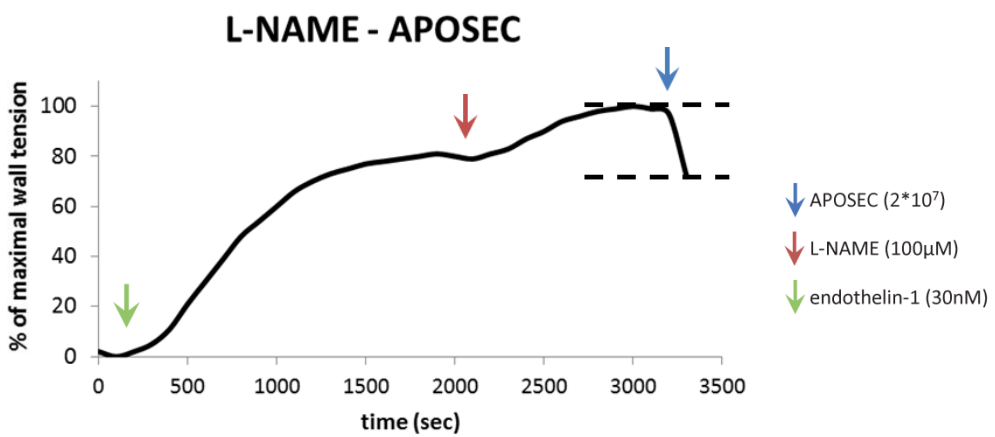


http://www.currentprotocols.com

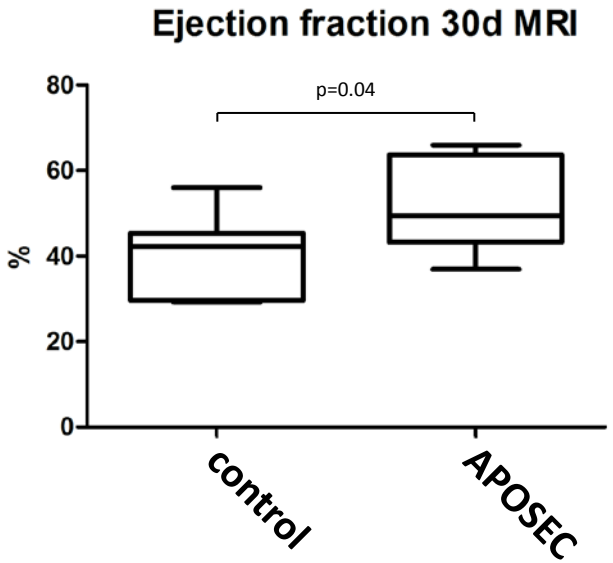


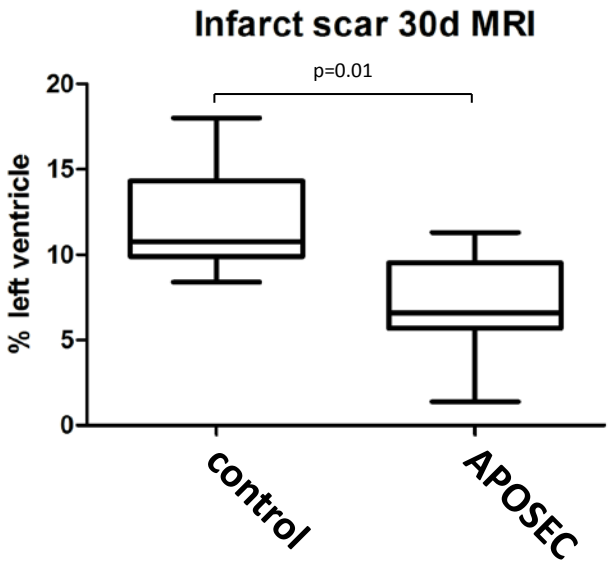
n=6-7





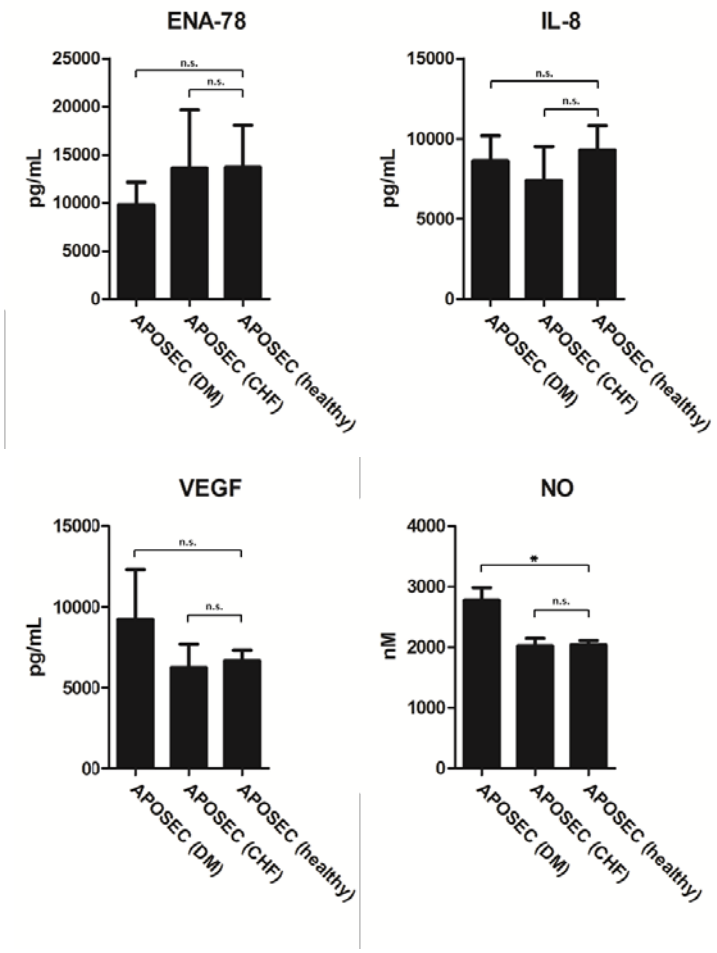
Results VIII – Treatment of APOSEC leads to increased functional parameters in the long time



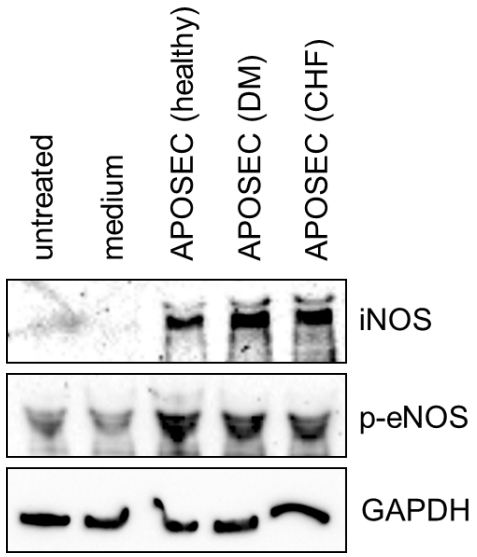


n=7-9

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



n=6-7



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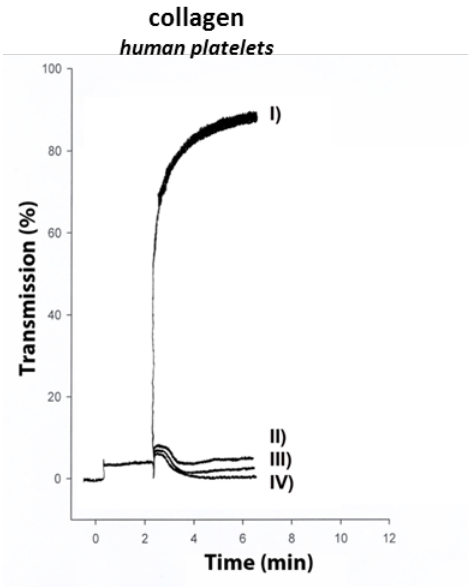

n=3

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Vienna, 05 Dec 2012

Seminar room 8G, AKH

Austria

Myocarditis, secretome and immunosuppression

1. Stem cell secretome possess immunosuppressive features

THE LANCET
Volume 376 · Number 9734 · Pages 1-68 · July 3-9, 2010 www.thelancet.com

Lancet. 2008 May 10;371(9624):1579-86.

2. Immunosuppression might be beneficial in the treatment of myocarditis

European Heart Journal
Journal of the European Society of Cardiology

Eur Heart J. 2009 Aug;30(16):1995-2002.

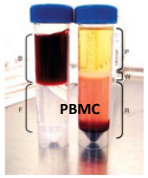
3. Secretome of stem cells and peripheral blood cells are comparable

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

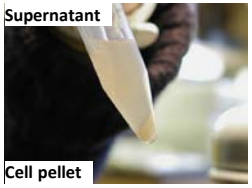
4. Production process of MNC secretome

Venous blood collection

Ficoll cell seperation



Incubation for 24hrs

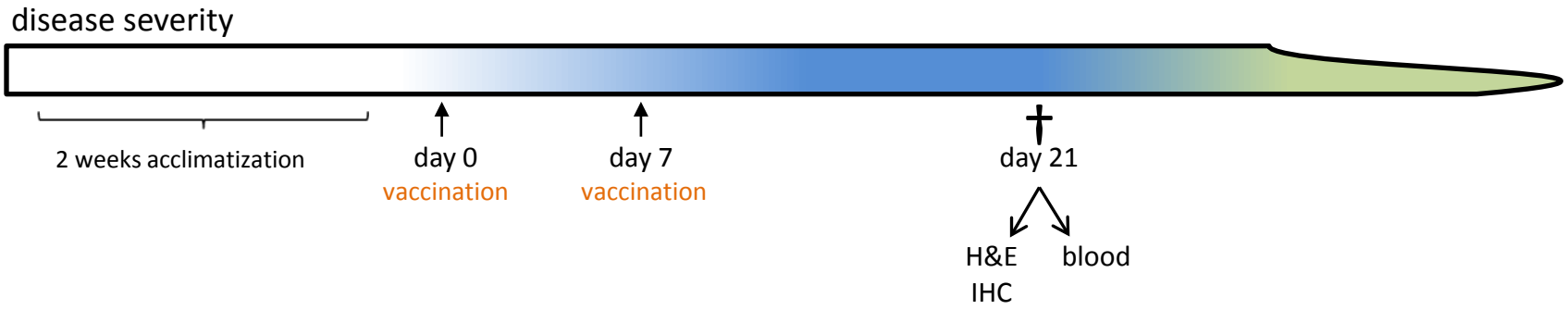


Dialysis

Aim of the study – Experimental setting

Impact of MNC secretome on EAM

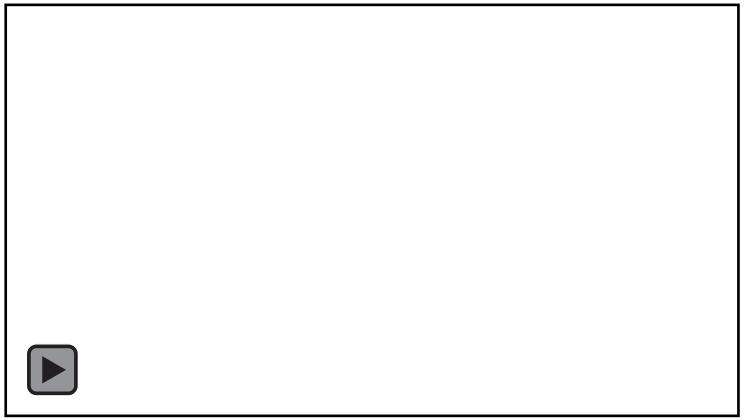
Influence of MNC secretome on the development of experimental autoimmune myocaridits



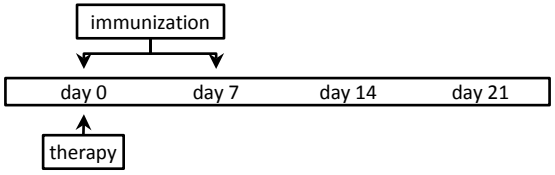
Finding the mode of action: Effects on isolated CD4+ cells *in vitro*

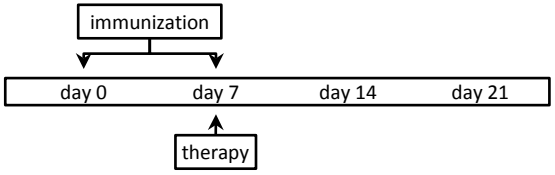
in vitro experiments

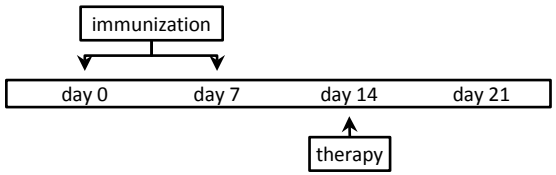
proliferation experiments	FACS	ELISA	viability assay	cytokine arrays	DC assays

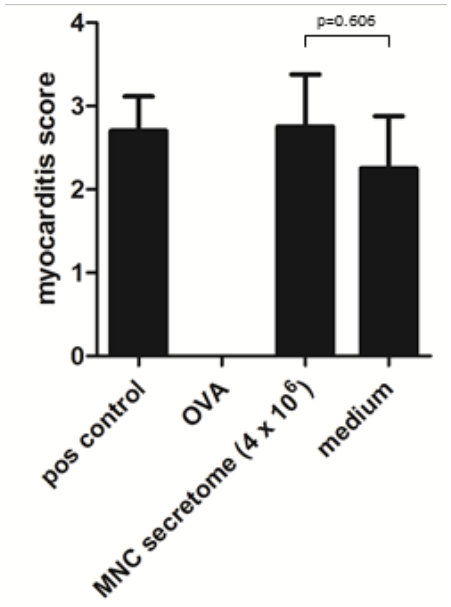


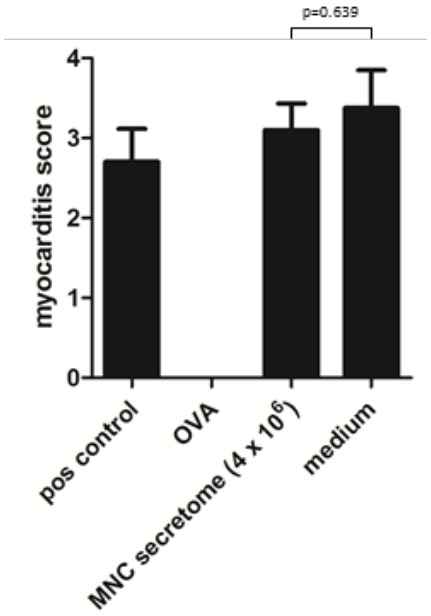
Results I – MNC secretome attenuates myocarditis in the EAM model

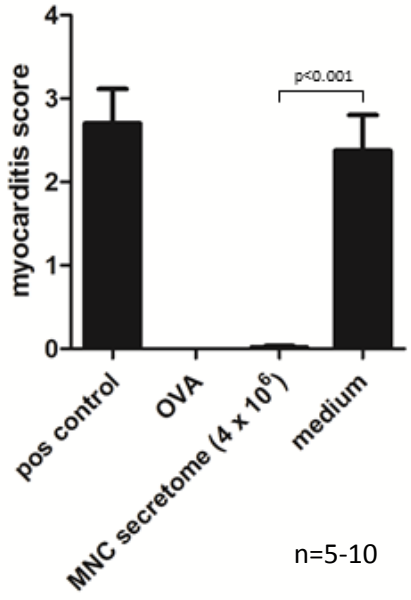






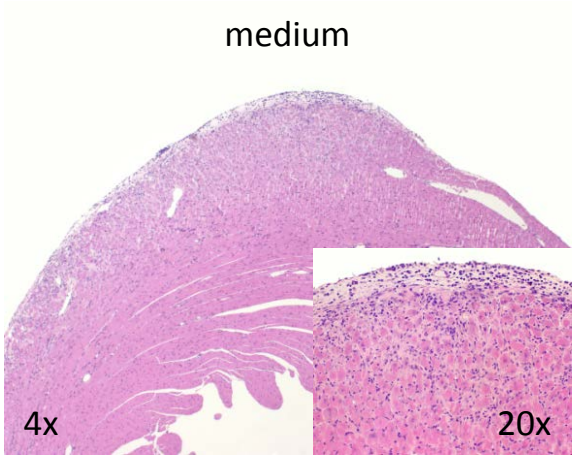


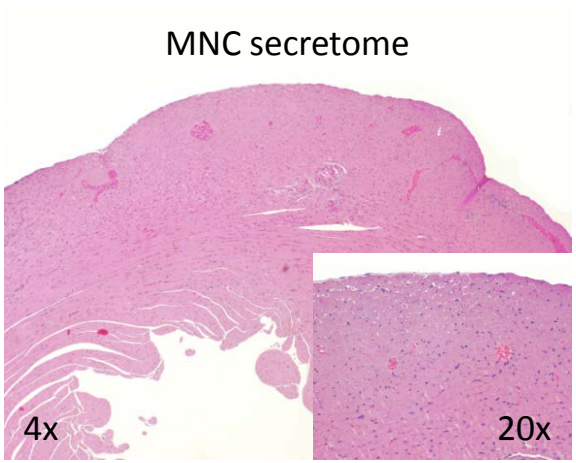


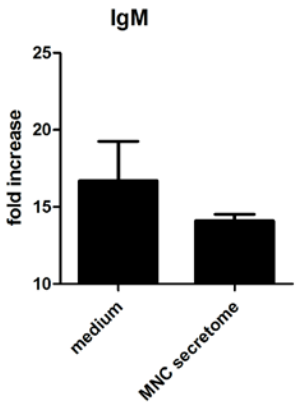


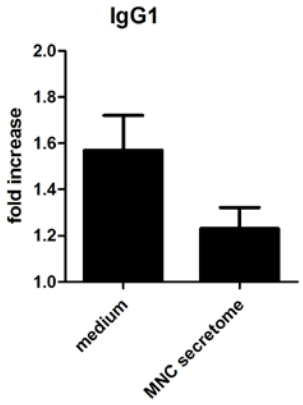
n=5-10

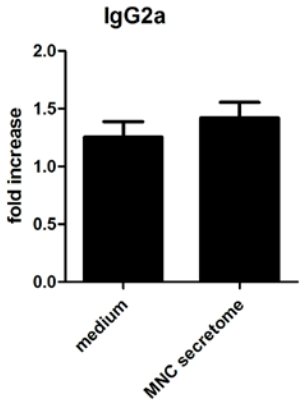
Results II – MNC secretome attenuates myocarditis in the EAM model

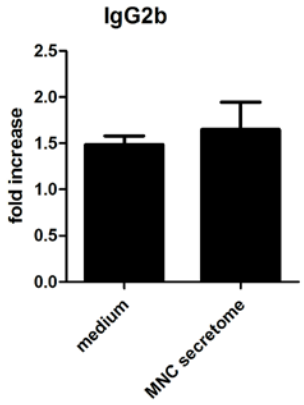


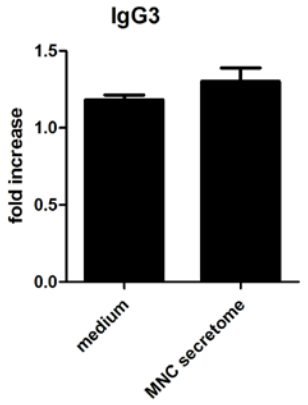






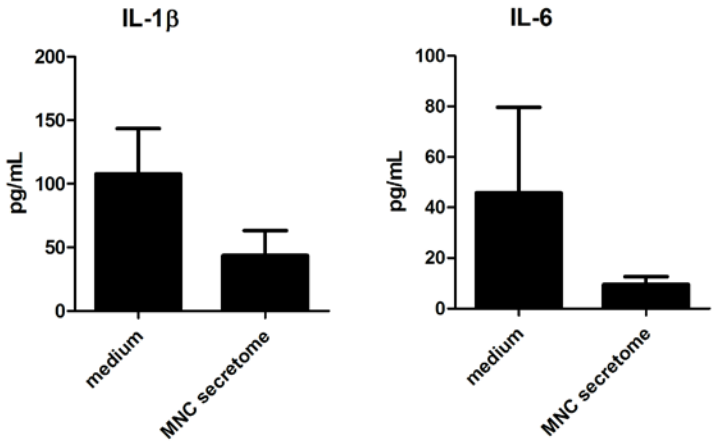


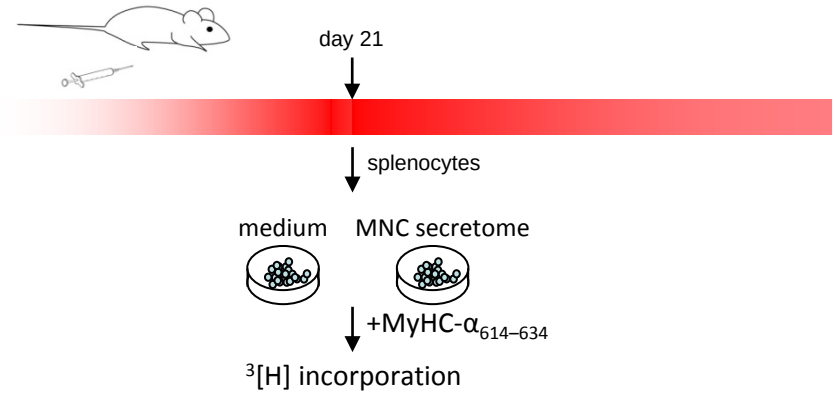


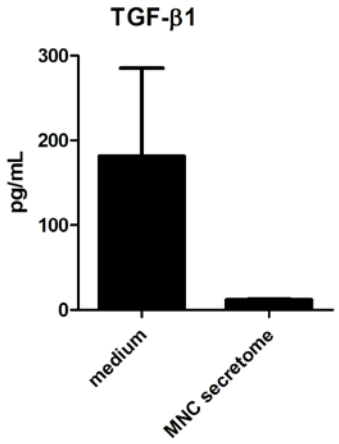


n=6

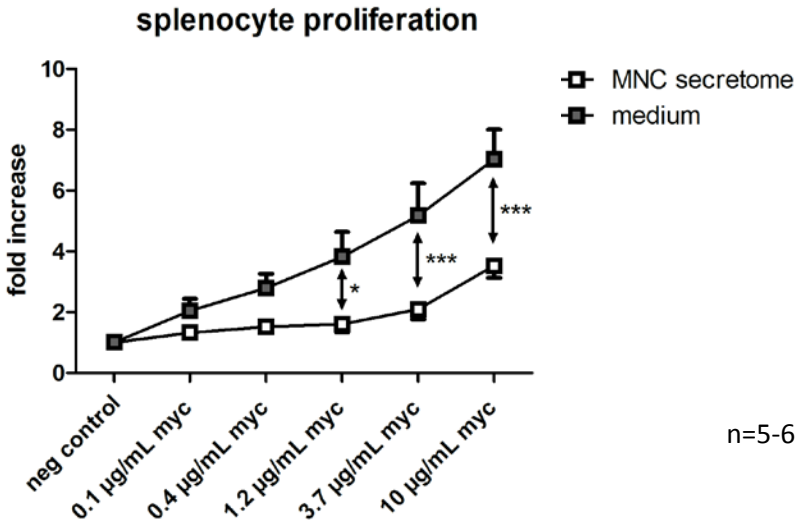
Results III – MNC secretome attenuates myocarditis in the EAM model





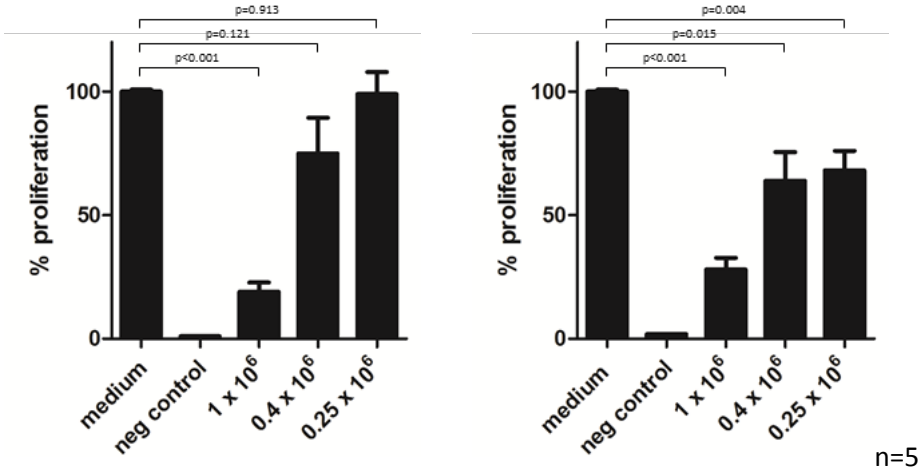


n=6

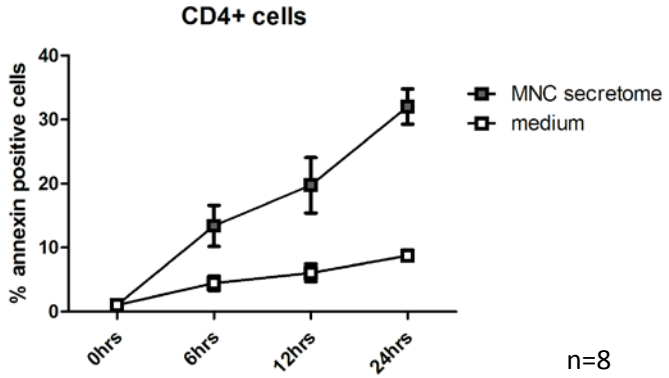


n=5-6

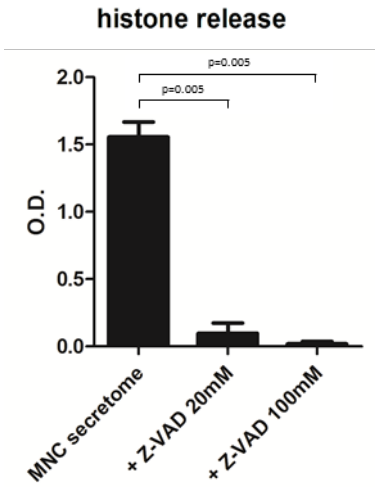
Results IV – MNC secretome mediates anti-proliferative effects *in vitro*



n=5



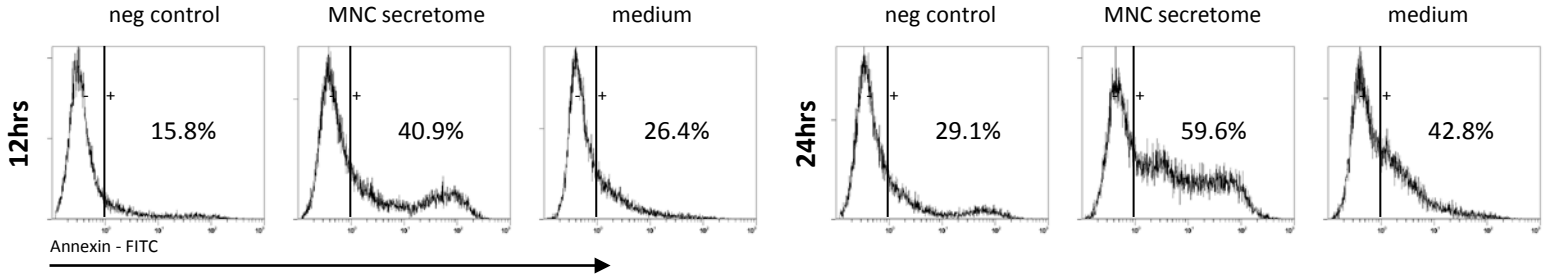
n=8



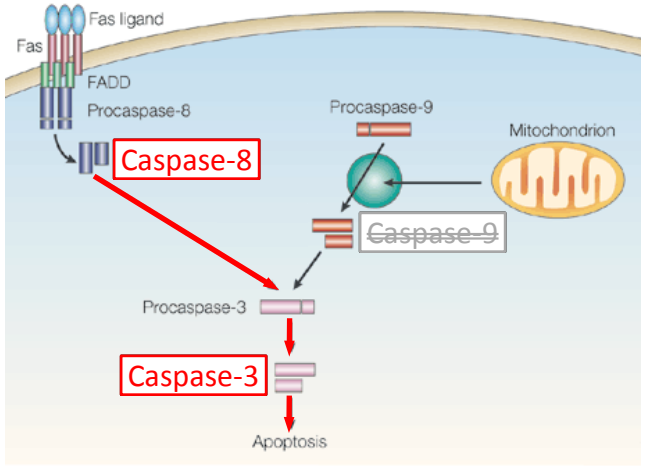
n=2

Results V – MNC secretome induces apoptosis via the external pathway

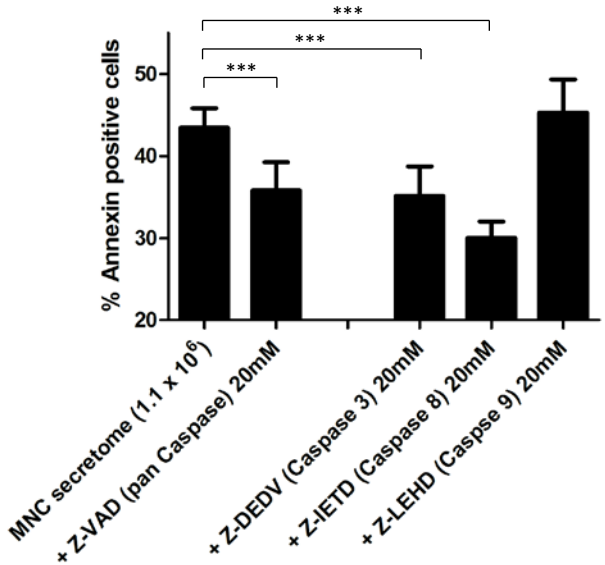
JURKAT



primary CD4+ cells



Nat Rev Mol Cell Biol. 2001 Jul;2(7):550-6.

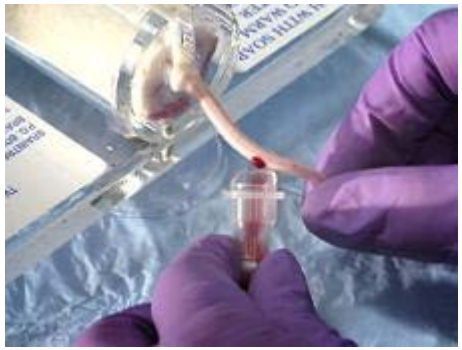


n=8

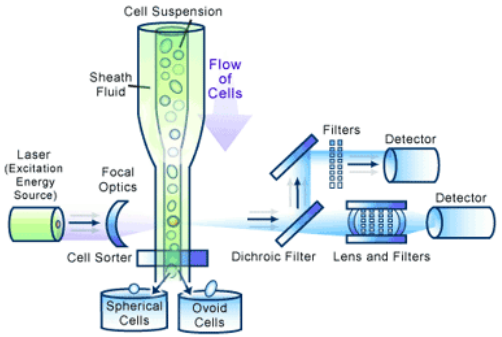
n=4

	MNC secretome
TNF-α (pg/mL)	6.6±2.1
sCD40L (pg/mL)	288.1±101.4
sFAS (pg/mL)	25.4±18.2
sFASL (pg/mL)	n.d.

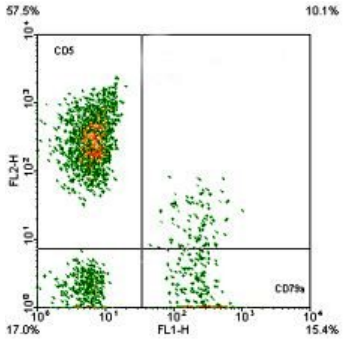
Results VI – CD4/CD8 cell ratio is reduced in MNC secretome treated animals



http://www.theodora.com



http://www.scq.ubc.ca



http://www.abcam.com

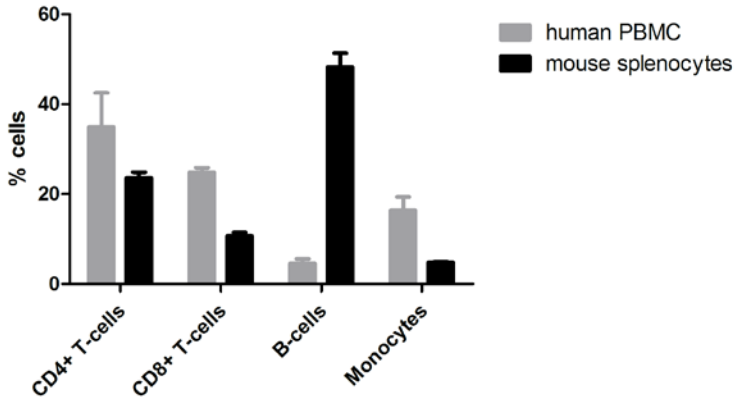
12hrs	CD4+ (%)	CD8+ (%)	CD4/CD8 ratio	CD4+/7-AAD pos
medium	19.9±1.3	10.8±1.9	2.1±0.3	8.1±0.7
MNC secretome	13.3±1.0	9.3±2.0	1.7±0.4	8.8±2.8

36hrs	CD4+ (%)	CD8+ (%)	CD4/CD8 ratio	CD4+/7-AAD pos
medium	23.9±1.6	7.4±1.1	2.9±0.2	5.4±0.5
MNC secretome	19.1±2.4	9. ±30.5	2.0±0.1	10.6±1.1

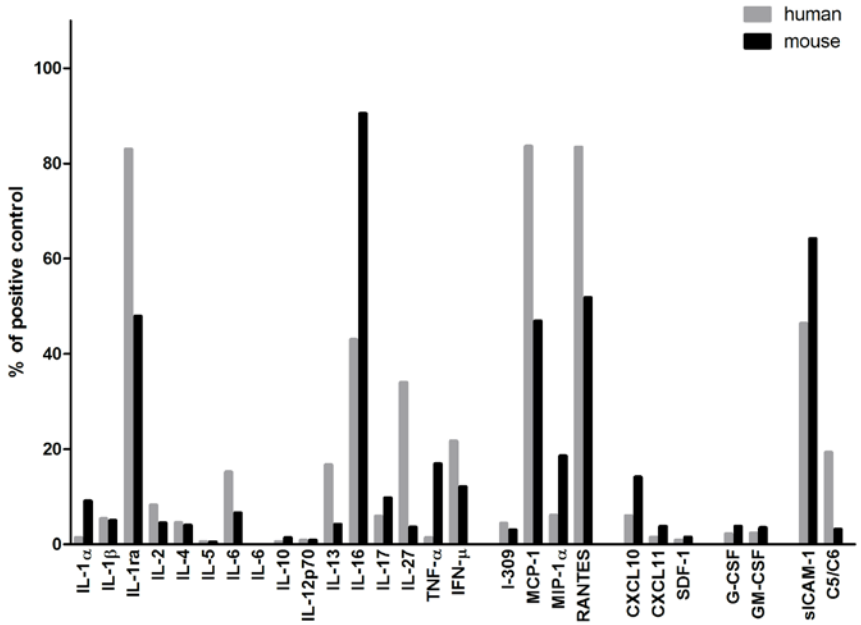
n=4-5

Results VII – Is MNC secretome from human PBMC and murine splenocytes comparable?

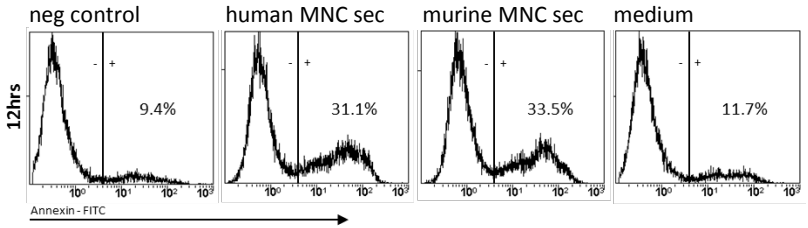
Distribution of cell types



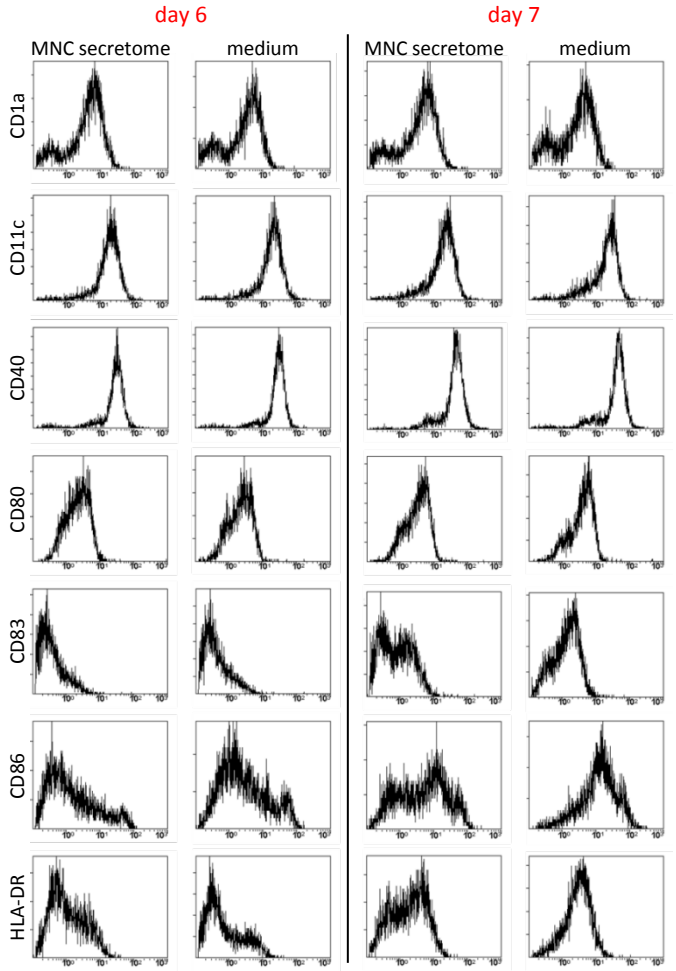
Cytokine arrays



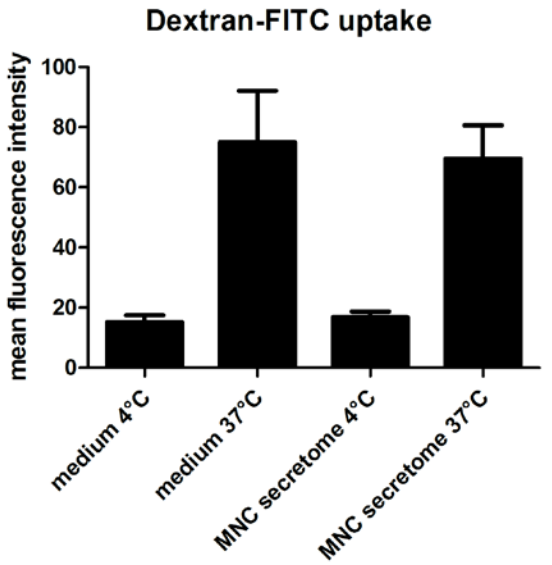
Apoptosis induction



Results VIII – Is dendritic cell function influenced by MNC secretome?



n=2



n=4

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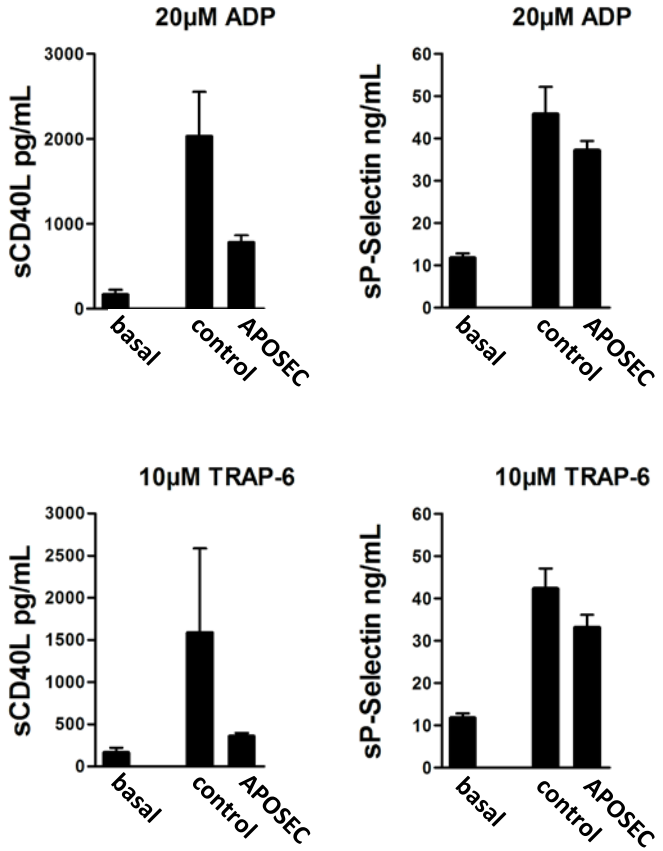
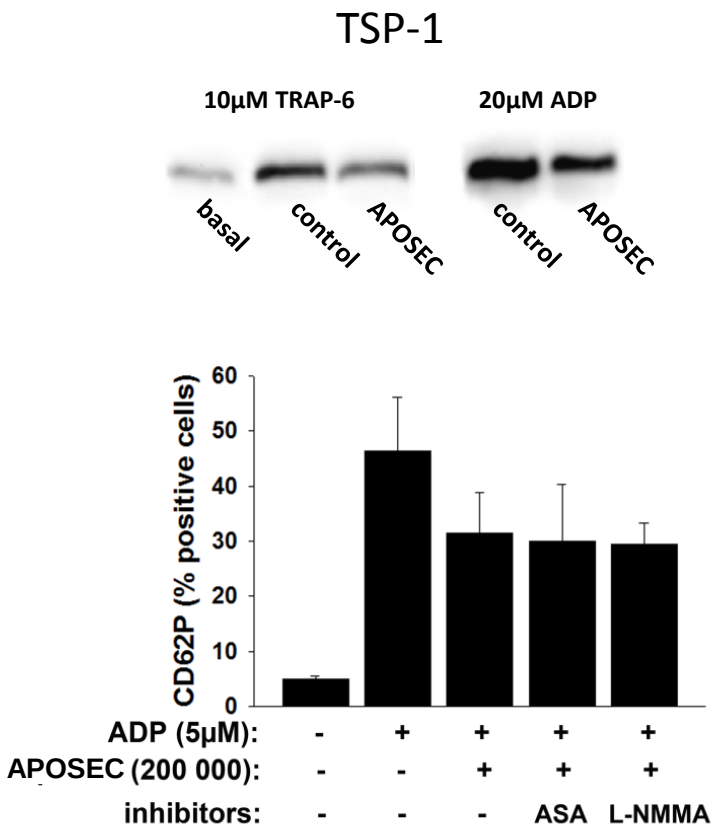
Vienna, 05 Dec 2012
Seminar room 8G, AKH
Austria

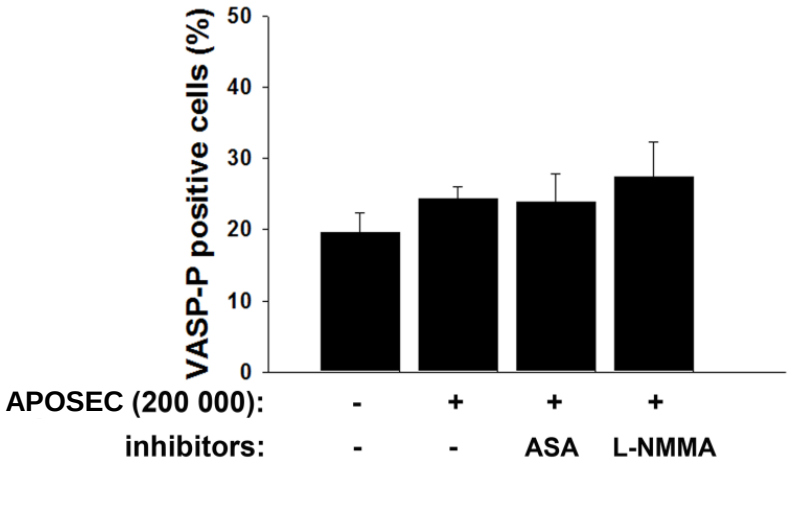
Results – APOSEC mediates anti-aggregatory effects *in vitro* COX and NO inhibition

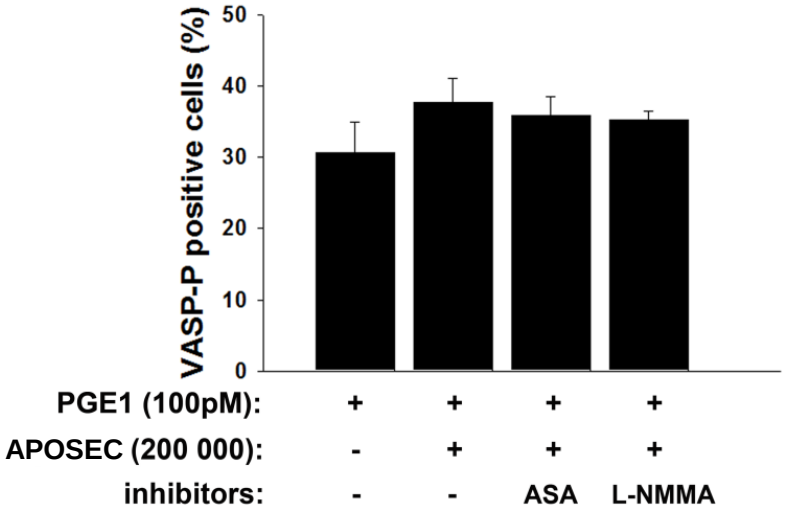




n=3

Results – mode of action – VASP phosphorylation





n=3

Results – Factors of APOSEC determined by membrane arrays

Cytokines	VIABLE SN	APO SN	Fold increase
Eotaxin-2	0,08	0,01	0,07
IGF-1	0,07	0,06	0,90
Leptin	0,06	0,06	1,02
PDGF-BB	0,92	0,67	0,73
Eotaxin-3	not detect.	not detect.	not detect.
IL-10	not detect.	not detect.	not detect.
LIGHT	not detect.	not detect.	not detect.
RANTES	0,97	1,74	1,80
FGF-6	0,07	0,06	0,81
IL-13	not detect.	not detect.	not detect.
MCP-1	0,23	0,23	0,99
SCF	not detect.	not detect.	not detect.
FGF-7	not detect.	0,06	APO SN only
IL-15	not detect.	not detect.	not detect.
MCP-2	0,15	0,07	0,48
SDF-1	not detect.	not detect.	not detect.
Flt-3 Ligand	not detect.	not detect.	not detect.
IL-16	0,15	0,75	4,99
MCP-3	0,07	0,09	1,19
TARC	0,13	not detect.	VIABLE SN only
Angiogenin	0,67	0,92	1,37
Fractalkine	not detect.	not detect.	not detect.
IL-1α	0,09	0,02	0,27
MCP-4	not detect.	not detect.	not detect.
TGF-β1	0,11	0,05	0,48
BDNF	0,42	0,44	1,05
PSA-free	0,04	0,05	1,08
CA125	0,03	0,05	1,45
CRP	0,09	0,13	1,44
Erythropoietin R	not detect.	not detect.	not detect.
S-100b	not detect.	not detect.	not detect.
CA15-3	0,04	0,06	1,42
DAN	0,04	0,04	1,07
FSH	0,13	0,12	0,92
Shh N	0,07	0,09	1,25
CA19-9	0,06	0,07	1,22
Decorin	0,14	0,19	1,37
HB-EGF	0,07	0,07	0,90
Thyroglobulin	not detect.	not detect.	not detect.
4-1BB	0,05	0,05	0,95
Carbonic Anhydrase IX	not detect.	not detect.	not detect.
DKK-1	not detect.	0,04	APO SN only
hCGa, intact	not detect.	not detect.	not detect.
Ubiquitin+1	0,04	0,05	1,20
BCMA	not detect.	not detect.	not detect.
CEACAM-1	0,08	0,05	0,55

Cytokines	VIABLE SN	APO SN	Fold increase
CTACK	0,02	0,04	1,79
ICAM-1	0,25	0,47	1,86
I-TAC	not detect.	not detect.	not detect.
TECK	not detect.	not detect.	not detect.
Dtk	not detect.	not detect.	not detect.
ICAM-3	not detect.	not detect.	not detect.
Lymphotactin	0,05	0,07	1,41
TIMP-1	0,30	0,44	1,46
EGF-R	0,08	0,03	0,45
IGFBP-3	0,13	0,15	1,16
MIF	0,19	0,43	2,24
TIMP-2	0,26	0,45	1,72
ENA-78	0,21	0,56	2,66
IGFBP-6	0,14	0,35	2,43
MIP-1α	0,05	0,13	2,45
Thrombopoietin	0,02	0,06	2,43
Fas/TNFRSF6	0,18	0,33	1,85
IGF-1 SR	0,03	0,05	1,89
MIP-1β	0,16	0,16	0,97
TRAIL R3	0,15	0,36	2,40
Acrp30	1,22	2,19	1,80
FGF-4	0,21	0,34	1,61
IL-1 R4/ST2	0,05	0,04	0,87
MIP-3β	not detect.	not detect.	not detect.
TRAIL R4	not detect.	not detect.	not detect.
AgRP	0,07	0,09	1,39
DKK-4	0,04	0,05	1,23
IL-13R1	0,10	0,12	1,17
Angiopoietin-1	0,12	0,20	1,63
CCL21	0,15	0,30	2,03
DPPIV	0,14	0,32	2,32
IL-17B	not detect.	not detect.	not detect.
Angiostatin	0,08	0,10	1,19
CD23	0,10	0,11	1,05
E-Cadherin	not detect.	not detect.	not detect.
IL-17C	0,06	0,09	1,43
ANGPTL4	not detect.	not detect.	not detect.
CD40 Ligand	0,03	0,06	1,87
EDA-A2	not detect.	not detect.	not detect.
IL-17F	0,03	0,05	1,51
Bate2 M	0,17	0,33	1,88
CEA	0,15	0,16	1,02
EG-VEGF	0,11	0,19	1,81
IL-17R	0,06	0,08	1,31
EpCAM	not detect.	not detect.	not detect.
Procalcitonin	not detect.	not detect.	not detect.

GCP-2	not detect.	not detect.	not detect.
IL-1β	0,17	0,06	0,36
M-CSF	0,11	0,11	1,00
TGF-β 3	not detect.	0,08	APO SN only
BLC	not detect.	not detect.	not detect.
GDNF	not detect.	not detect.	not detect.
IL-1ra	0,27	0,43	1,62
MDC	0,16	0,29	1,83
TNF-α	0,10	0,05	0,53
BMP-4	0,16	0,20	1,28
GM-CSF	not detect.	not detect.	not detect.
IL-2	not detect.	not detect.	not detect.
MIG	not detect.	not detect.	not detect.
TNF-β	0,14	0,13	0,92
BMP-6	0,14	not detect.	VIABLE SN only
I-309	0,27	0,25	0,91
IL-3	0,24	0,24	0,99
MIP-1δ	0,15	0,11	0,71
CK β 8-1	0,15	0,16	1,09
IFN-γ	not detect.	not detect.	not detect.
IL-4	not detect.	not detect.	not detect.
MIP-3α	0,25	0,16	0,64
CNTF	not detect.	not detect.	not detect.
IGFBP-1	not detect.	not detect.	not detect.
IL-5	not detect.	not detect.	not detect.
NAP-2	0,48	0,77	1,61
EGF	0,74	1,00	1,34
IGFBP-2	0,10	0,10	1,08
IL-6	0,34	0,05	0,15
NT-3	0,16	0,18	1,13
Eotaxin	not detect.	not detect.	not detect.
IGFBP-4	0,10	0,20	2,05
IL-7	not detect.	not detect.	not detect.
PARC	not detect.	not detect.	not detect.
Endoglin	not detect.	not detect.	not detect.
IL-21R	not detect.	not detect.	not detect.
PDGF AA	0,34	0,40	1,18
VE-Cadherin	not detect.	not detect.	not detect.
ErbB3	0,08	0,07	0,92
IL-5 R alpha	0,04	0,07	1,74
PDGF-AB	0,18	0,20	1,06
VEGF R2	0,06	not detect.	VIABLE SN only
E-Selectin	0,09	0,12	1,25
IL-9	0,11	0,11	0,99
PDGF-R alpha	not detect.	not detect.	not detect.
VEGF R3	0,18	0,20	1,06

FGF-9	0,18	0,22	1,24
IL-1 RI	0,06	0,19	2,99
MSP-α	0,27	0,45	1,67
uPAR	0,27	0,41	1,48
Angiopoietin-2	0,15	0,30	1,98
GCSF	not detect.	not detect.	not detect.
IL-11	not detect.	not detect.	not detect.
NT-4	0,08	0,09	1,08
VEGF	0,08	0,25	3,34
Amphiregulin	0,10	0,13	1,40
GITR-Ligand	0,08	0,12	1,58
IL-12 p40	0,22	0,55	2,49
Osteoprotegerin	0,06	0,10	1,82
VEGF-D	0,08	0,23	2,86
Axl	0,13	0,13	0,96
GITR	0,13	0,16	1,22
IL-12 p70	0,08	0,11	1,42
Oncostatin M	0,11	0,19	1,78
bFGF	0,03	0,06	1,95
GRO	0,65	1,06	1,63
IL-17	not detect.	not detect.	not detect.
PlGF	0,15	0,24	1,61
b-NGF	0,03	0,05	1,61
GRO-α	0,25	0,33	1,36
IL-2 R alpha	0,09	0,22	2,54
sgp130	0,15	0,29	1,94
BTC	0,11	0,13	1,23
HCC-4	0,07	0,11	1,47
IL-6 R	0,34	0,85	2,47
sTNF RII	0,35	0,77	2,20
CCL-28	not detect.	not detect.	not detect.
HGF	0,18	0,16	0,89
IL-8	0,43	1,48	3,41
sTNF-RI	0,12	0,12	0,99
Futin	0,12	0,13	1,10
LYVE-1	0,15	0,17	1,09
Osteopontin	0,10	0,07	0,71
Trappin-2	0,05	0,09	1,87
Galectin-7	not detect.	not detect.	not detect.
Marapsin	0,07	0,06	0,84
PAI-I	0,19	0,30	1,60
TREM-1	0,05	0,06	1,29
GDF-15	0,13	0,13	1,03
MICA	0,07	0,07	0,97
Platelet Factor 4	0,11	0,14	1,23
TSH	0,05	0,06	1,40

Fas Ligand	0,13	0,07	0,57
IP-10	0,14	0,16	1,16
PDGF-R beta	not detect.	not detect.	not detect.
ICAM-2	0,28	0,46	1,66
LAP	0,24	0,33	1,38
PECAM-1	0,11	0,10	0,96
Activin A	not detect.	not detect.	not detect.
IGF-II	0,17	0,22	1,29
Leptin R	0,05	0,07	1,37
Prolactin	0,09	0,07	0,86
ALCAM	0,17	0,22	1,30
IL-1 R II	0,06	0,05	0,77
LIF	0,14	0,15	1,09
SCF R	0,27	0,28	1,04
B7-1(CD80)	0,14	0,08	0,58
IL-10 R beta	not detect.	not detect.	not detect.
L-Selectin	0,21	0,23	1,07
SDF-1beta	not detect.	not detect.	not detect.
BMP-5	0,24	0,17	0,73
IL-13 R alpha 2	0,17	0,25	1,46
M-CSF R	0,20	0,40	1,99
Siglec-5	0,63	0,87	1,37
BMP-7	not detect.	not detect.	not detect.
IL-18 BP alpha	0,14	0,09	0,65
MMP-1	0,20	0,28	1,39
TGF-alpha	0,12	0,10	0,85
Cardiotrophin-1	not detect.	not detect.	not detect.
IL-18 R beta	0,17	0,16	0,93
MMP-13	0,11	0,13	1,13
TGF beta 2	0,19	0,21	1,13
CD14	0,36	0,57	1,55
MMP-3	0,08	0,20	2,58
MMP-9	0,10	0,20	1,93
Tie-1	not detect.	not detect.	not detect.
CXCL- 16	0,31	0,45	1,48
IL-2 R beta	0,11	0,18	1,73
MPIF-1	not detect.	not detect.	not detect.
Tie-2	0,06	0,08	1,31
DR6 (TNFRSF21)	0,12	0,15	1,18
IL-2 R gamma	0,12	0,13	1,13
NGF R	not detect.	not detect.	not detect.
TIMP-4	0,22	0,28	1,30
beta IG-H3	0,09	0,08	0,82
Cripto-1	not detect.	not detect.	not detect.
ErbB2	not detect.	not detect.	not detect.

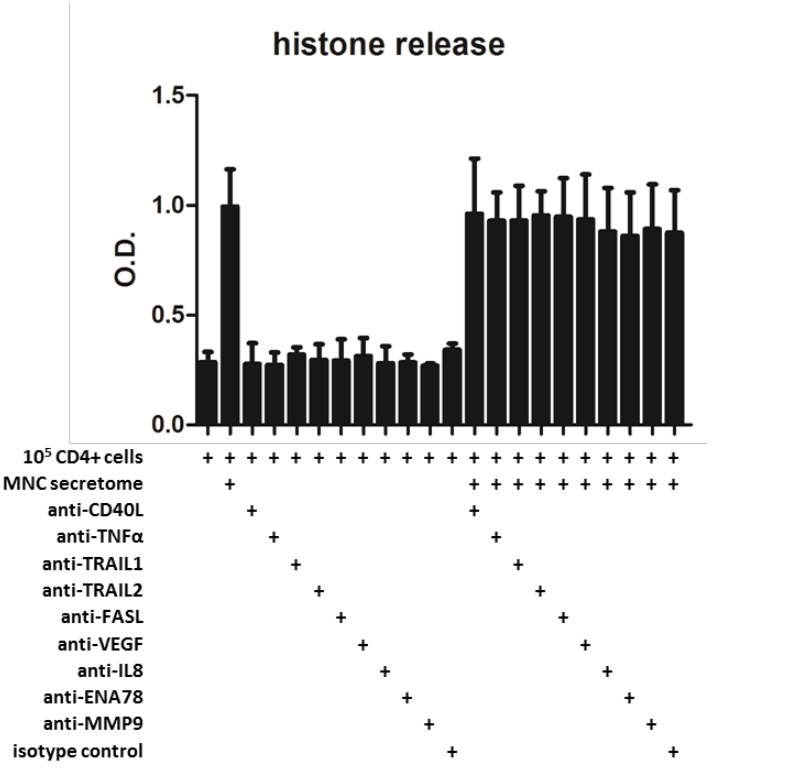
Growth Hormon	0,05	0,04	0,78
MICB	0,09	0,08	0,92
PSA-total	0,07	0,08	1,15
TSLP	not detect.	not detect.	not detect.
Adiposin	0,29	0,43	1,49
IL-10 R alpha	0,09	0,15	1,64
MMP-2	0,08	0,12	1,47
RAGE	0,05	0,10	2,07
VCAM-1	0,05	0,07	1,35
BCAM	0,09	0,12	1,39
IL-22	0,07	0,09	1,35
MMP-7	0,12	0,13	1,10
RANK	0,09	0,07	0,88
VEGF-C	0,15	0,14	0,91
CD30	0,12	0,16	1,27
IL-28A	0,19	0,21	1,12
MMP-8	0,19	0,30	1,54
Resistin	0,08	0,08	0,97
XEDAR	0,07	0,10	1,39
CD40	0,06	0,05	0,89
IL29	0,17	0,21	1,27
MMP-10	0,05	0,08	1,51
SAA	0,14	0,16	1,18
Fer RIIB/C	0,06	0,07	1,01
IL-31	0,05	0,08	1,64
NCAM-1	0,19	0,21	1,10
Siglec-9	0,06	0,05	0,84
Ferritin	0,12	0,20	1,66
Insulin	0,10	0,07	0,65
Nidogen-1	0,26	0,30	1,16
TACE	0,06	0,10	1,58
FLRG	not detect.	not detect.	not detect.
Luteinizing Hormone	0,10	0,11	1,15
NrCAM	0,08	0,11	1,30
TIM-1	0,04	0,04	0,85
Follistatin	0,14	0,15	1,04
LIMPII	0,03	0,04	1,20
NRGI-beta 1	0,13	0,12	0,92
TRAIL R2	0,13	0,10	0,80
ACE-2	not detect.	not detect.	not detect.
Cathepsin S	0,08	0,12	1,52
DKK-3	0,06	0,06	1,09
HVEM	0,10	0,16	1,58
Alpha-Fetoprotein	not detect.	not detect.	not detect.
CCL14a	0,06	0,12	2,13

274 cytokines and growth factors

Results – Apoptosis induction is not mediated by known factors

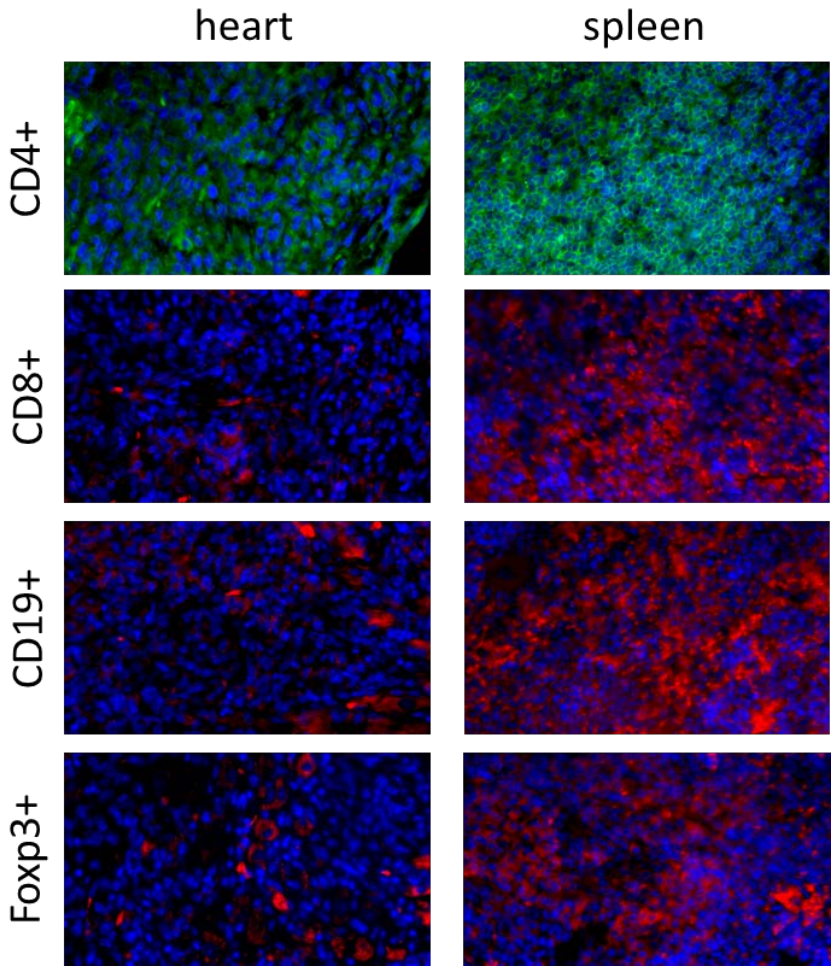
	MNC secretome
TNF-α (pg/mL)	6.6±2.1
sCD40L (pg/mL)	288.1±101.4
sFAS (pg/mL)	25.4±18.2
sFASL (pg/mL)	n.d.

n=4



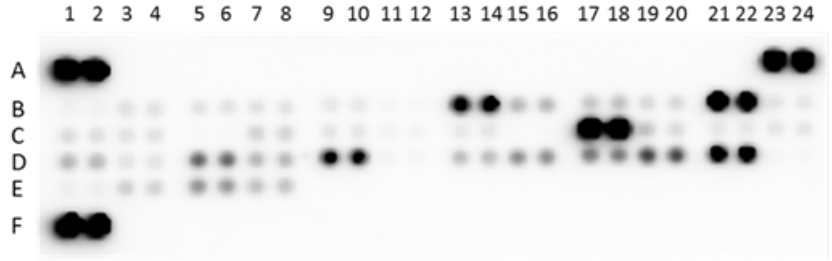
n=4

Results – Myocardial infiltrate



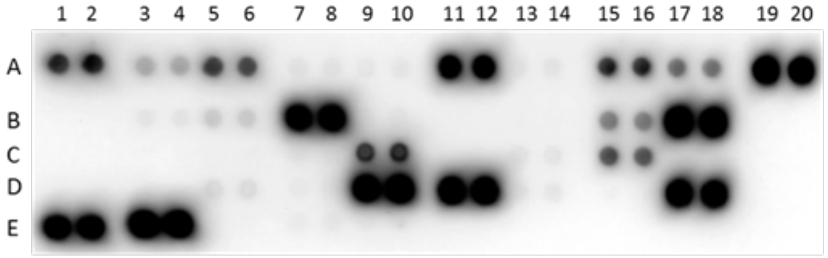
Results – Cytokine arrays

mouse



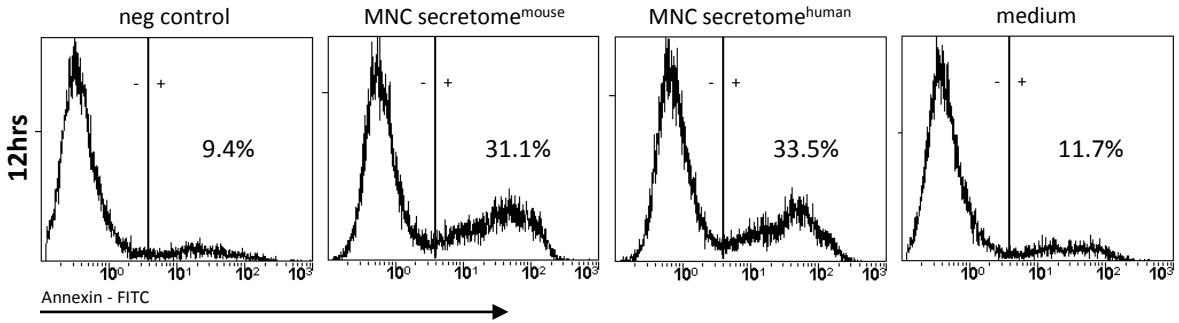
A1,2 p control											A23,24 p control
B1,2 CXCL13	B3,4 C5/C6	B5,6 G-CSF	B7,8 GM-CSF	B9,10 I-309	B11,812 Eotaxin	B13,814 sICAM-1	B15,16 IFN-γ	B17,18 IL-1α	B19,20 IL-1β	B21,22 IL1-ra	B23,24 IL-2
C1,2 IL-3	C3,4 IL-4	C5,6 IL-5	C7,8 IL-6	C9,10 IL-7	C11,12 IL-10	C13,14 IL-13	C15,16 IL-12p70	C17,18 IL-16	C19,20 IL-17	C21,22 IL-23	C23,24 IL-27
D1,2 CXCL10	D3,4 CXCL11	D5,6 CXCL1	D7,8 M-CSF	D9,10 MCP-1	D11,12 CCL12	D13,14 CXCL9	D15,16 MIP-1α	D17,18 MIP-1β	D19,20 CXCL2	D21,22 RANTES	D23,24 SDF-1
E1,2 CCL17	E3,4 TIMP-1	E5,6 TNF-α	E7,8 TREM-1								
F1,2 p control											F23,24 n control

human



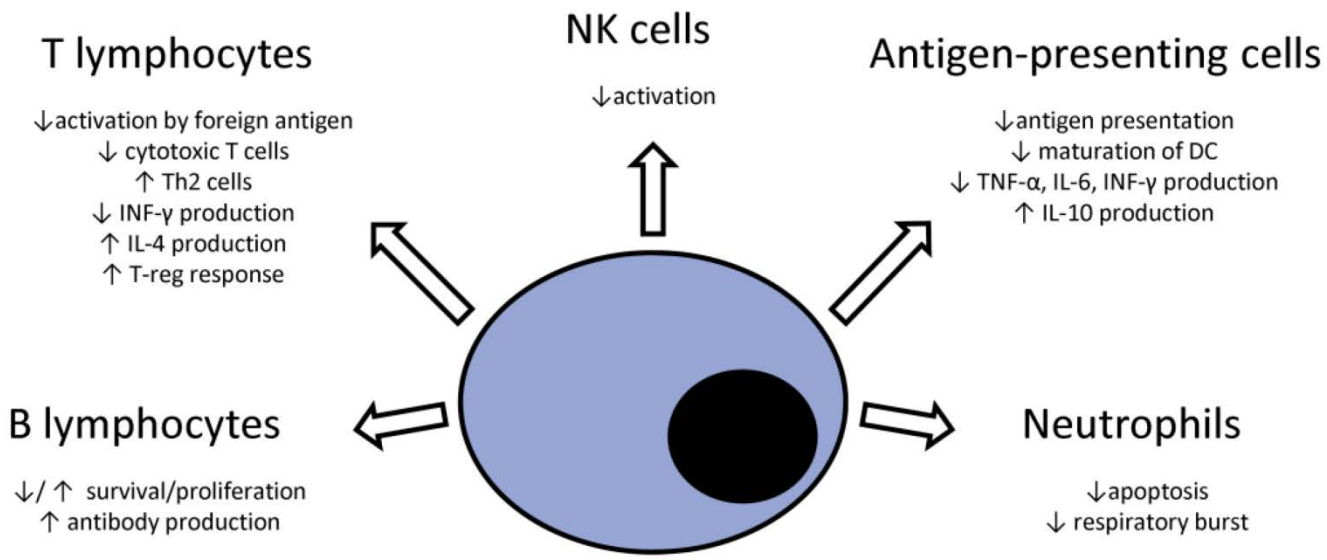
A1,2 p control	A3,4 C5/C6	A5,6 CD40L	A7,8 G-CSF	A9,10 GM-CSF	A11,12 GROα	A13,14 I-309	A15,16 sICAM-1	A17,18 IFN-γ	A19,20 p control
	B3,4 IL-1α	B5,6 IL-1β	B7,8 IL-1ra	B9,10 IL-2	B11,812 IL-4	B13,814 IL-5	B15,16 IL-6	B17,18 IL-8	
	C3,4 IL-10	C5,6 IL-12p70	C7,8 IL-13	C9,10 IL-16	C11,12 IL-17	C13,14 IL-17E	C15,16 IL-23	C17,18 IL-27	
	D3,4 IL-32α	D5,6 CXCL10	D7,8 CXCL11	D9,10 MCP-1	D11,12 MIF	D13,14 MIP-1α	D15,16 MIP-1β	D17,18 PAI-1	
E1,2 p control	E3,4 RANTES	E5,6 SDF-1	E7,8 TNF-α	E9,10 sTRAM-1					E19,20 n control

murine CD4+ lymphoma cell line



n=2

Stem cells and immunomodulation



Weil BR, Manukyan MC, Herrmann JL, Abarbanell AM, Poynter JA, Wang Y, et al. The immunomodulatory properties of mesenchymal stem cells: implications for surgical disease. J Surg Res. 2011;167(1):78-86.