

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

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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

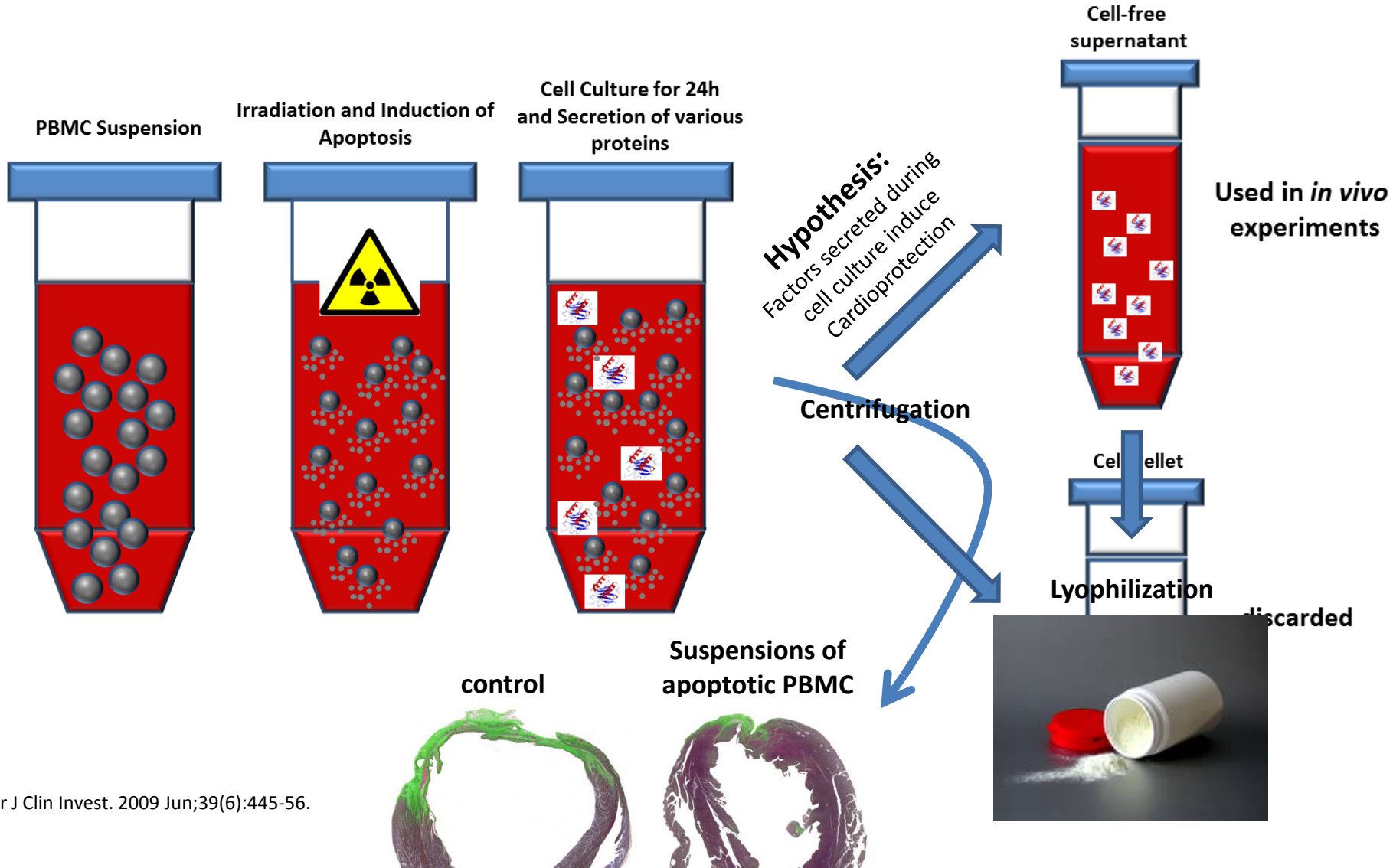
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EP10194916.2

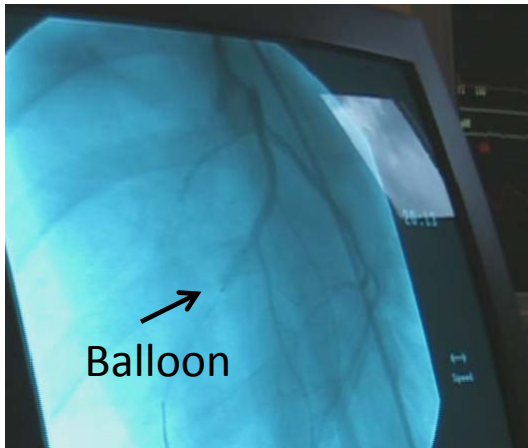
Ankersmit HJ: APOSCIENCE AG, shareholder , Vienna based Start Up



APOSEC Reperfused AMI Large Animal Model



Pigs (~30kg)



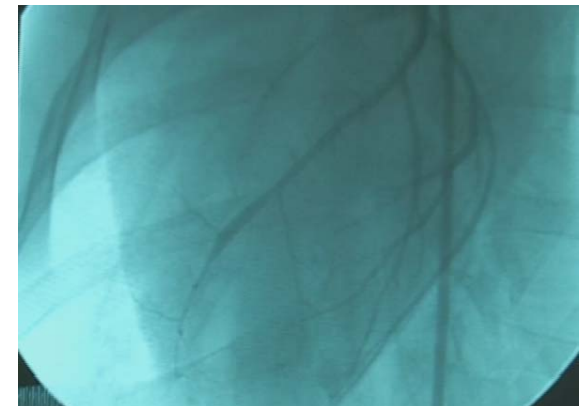
Occlusion of the LAD



Intravenous administration of
porcine APOSEC
40 minutes after occlusion

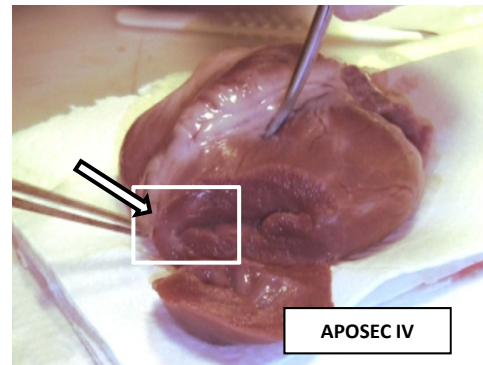
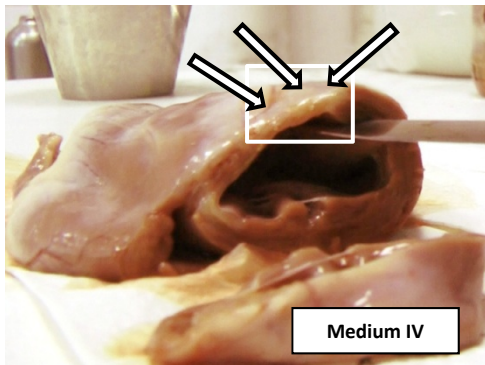
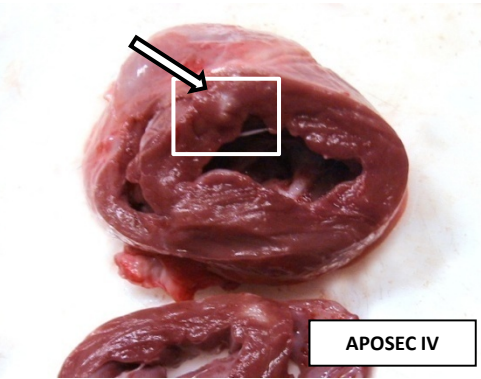
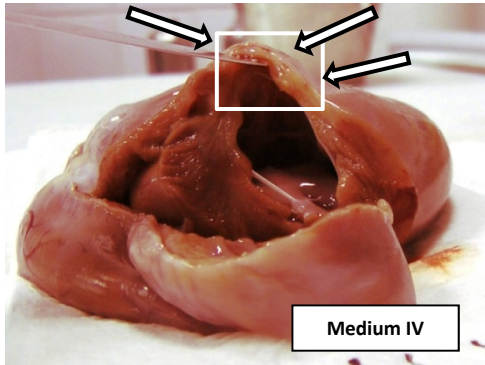


According to
AHA & ESC
Guidelines

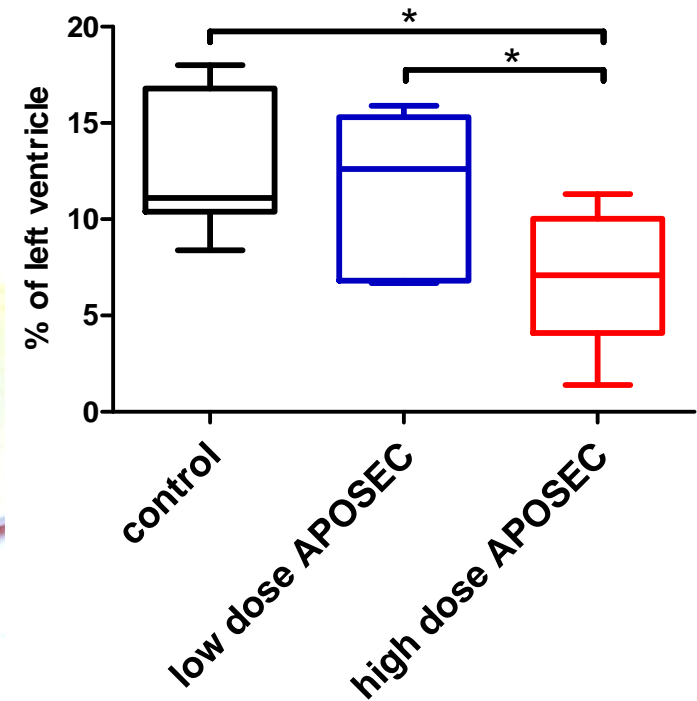


Reperfusion after 90 minutes

APOSEC Reperfused AMI Large Animal Model



Infarction Size after 30 days



Myocarditis, secretome and immunosuppression

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.

Immunosuppression might be beneficial in the treatment of myocarditis



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

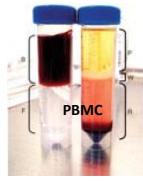
Secretome of stem cells and peripheral blood cells is similar

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

Venous blood collection



Ficoll cell separation



Incubation for 24hrs

Supernatant



Cell pellet

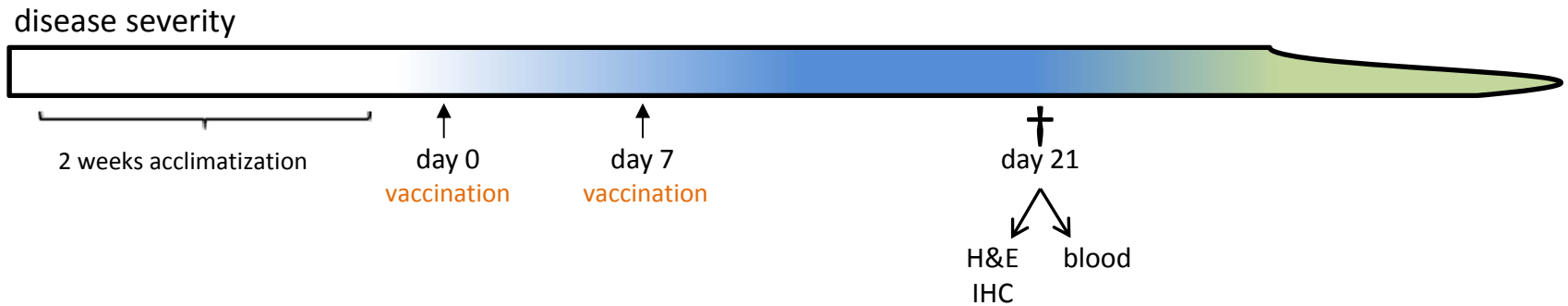
Dialysis



Aim of the study – Experimental setting

Impact of MNC secretome on EAM

Influence of APOSEC on the development of experimental autoimmune myocarditis



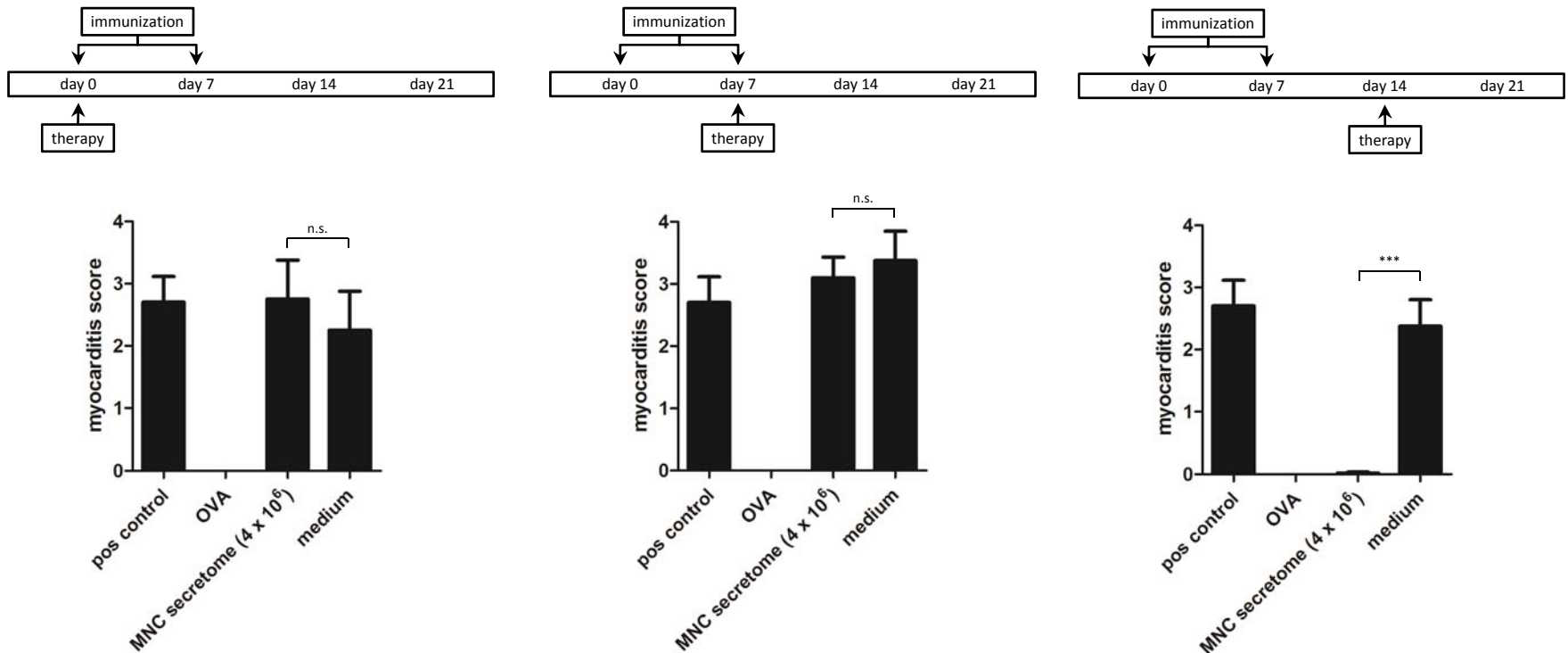
Finding the mode of action: Effects on isolated CD4+ cells *in vitro*

in vitro experiments

proliferation experiments FACS ELISA western blot

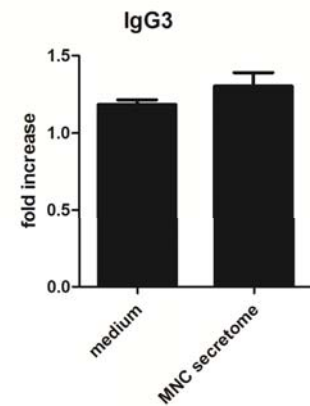
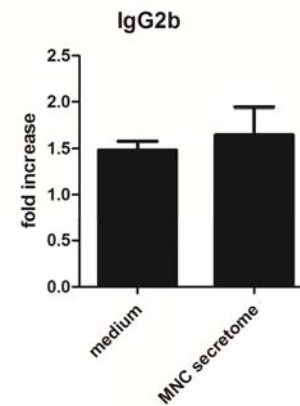
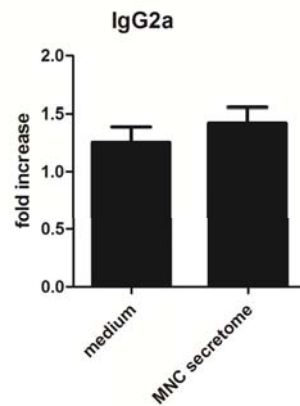
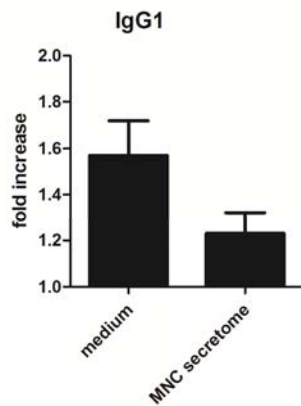
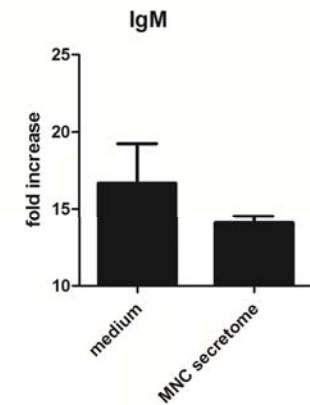
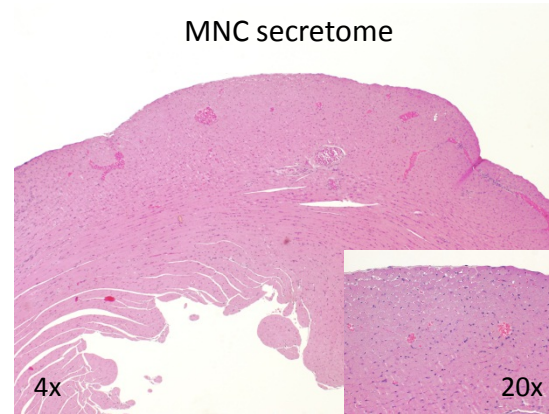
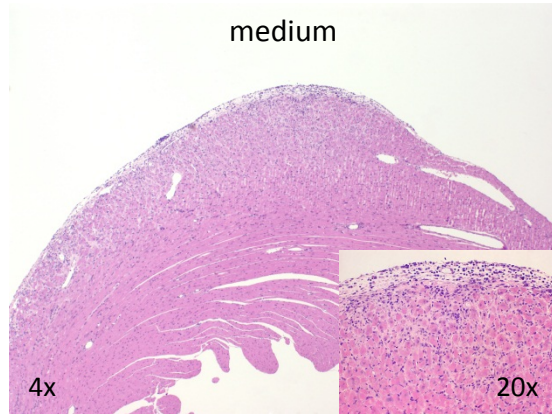


Results I – MNC secretome attenuates myocarditis in the EAM model



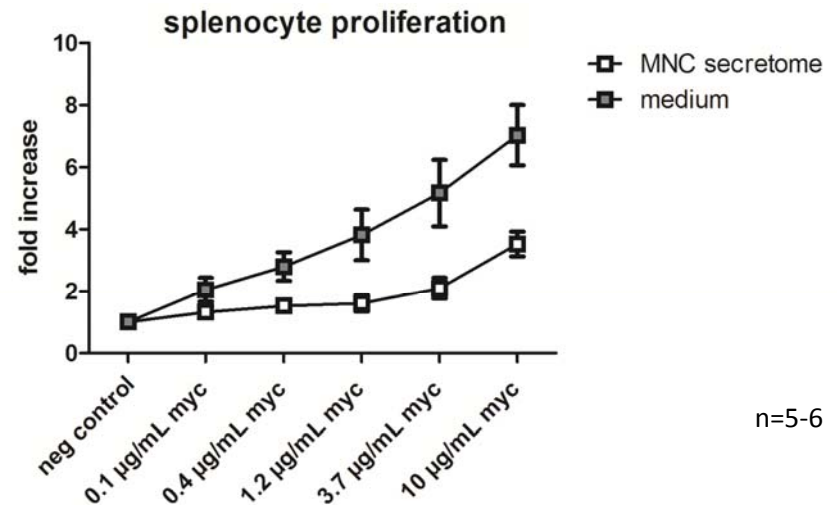
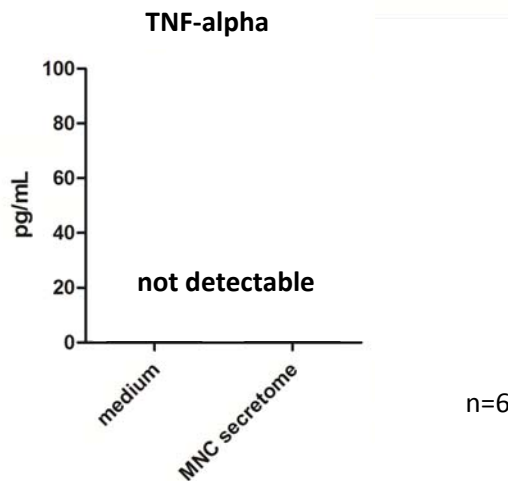
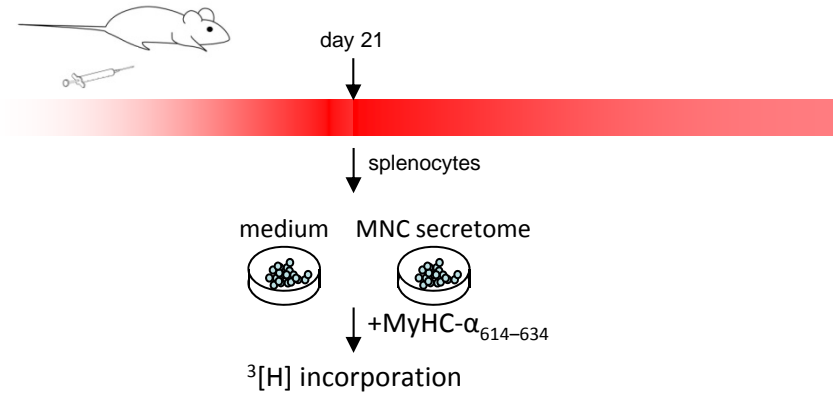
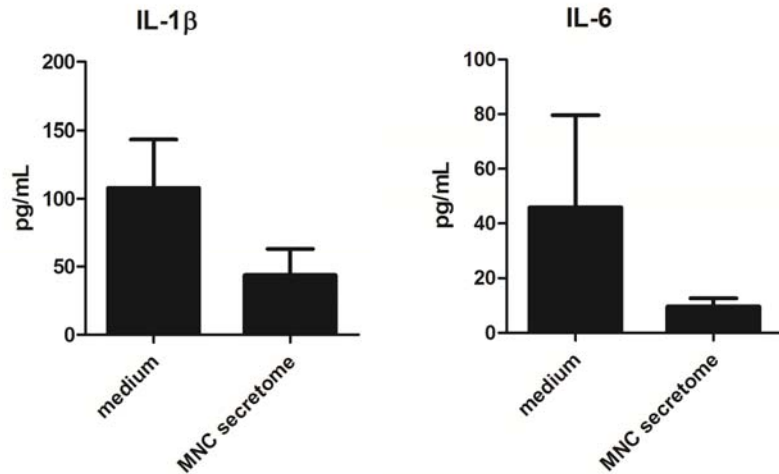
n=5-10

Results II – MNC secretome attenuates myocarditis in the EAM model

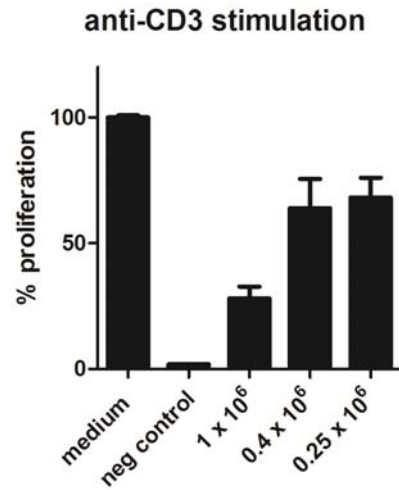
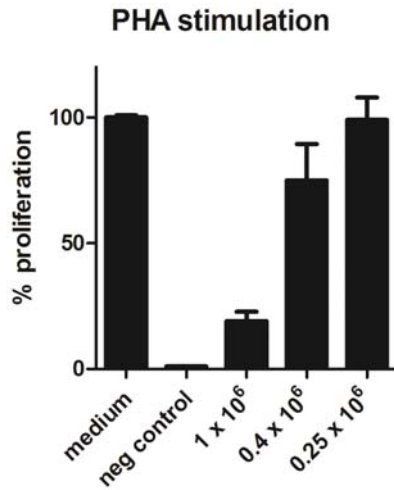


n=6

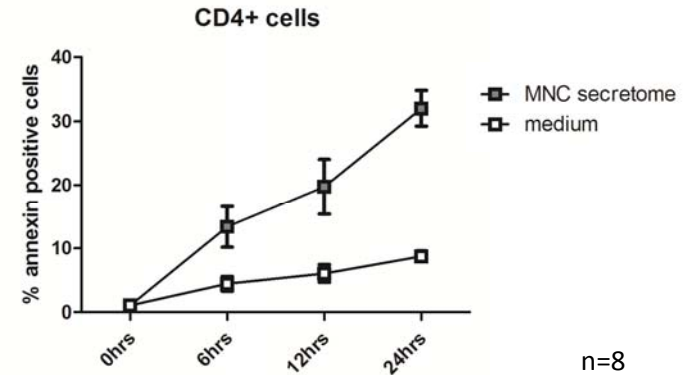
Results III – MNC secretome attenuates myocarditis in the EAM model



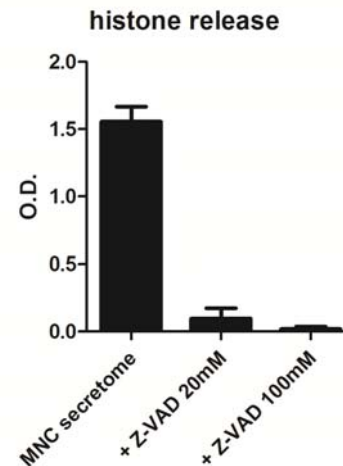
Results IV – MNC secretome mediates anti-proliferative effects *in vitro*



n=5

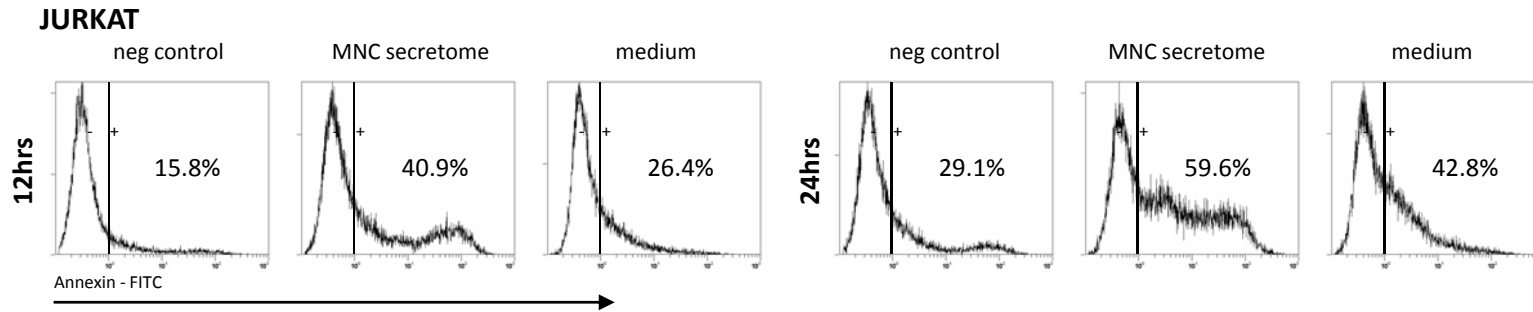


n=8

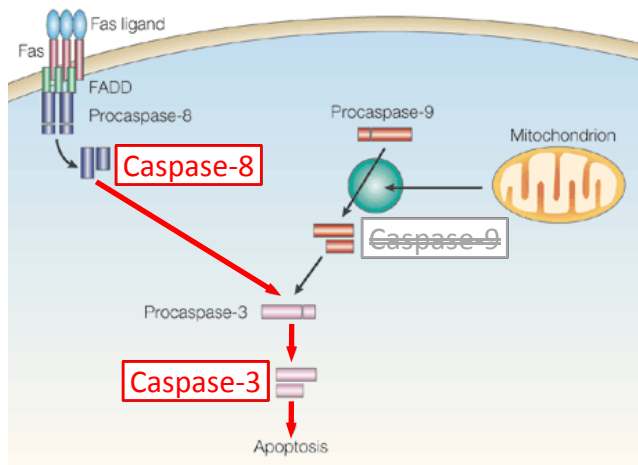


n=2

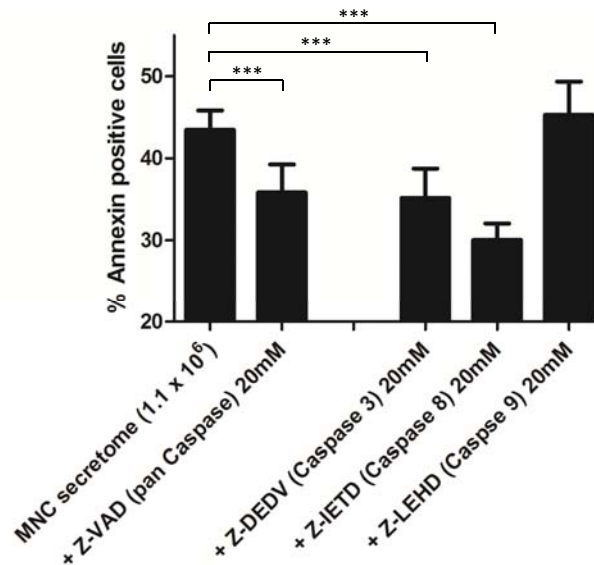
Results V – MNC secretome induces apoptosis via the external pathway



primary CD4+ cells



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



n=8

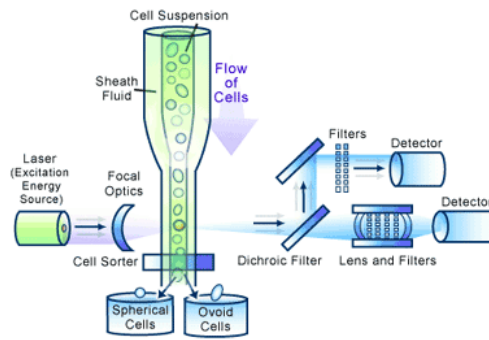
n=4

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

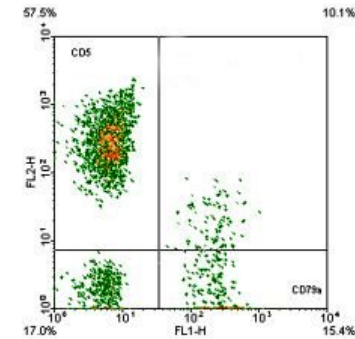
Results VI – CD4/CD8 cell ratio is reduced in MNC secretome treated animals



<http://www.theodora.com>



<http://www.scq.ubc.ca>



<http://www.abcam.com>

12hrs	CD4+ (%)	CD8+ (%)	CD4/CD8 ration	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 ration	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

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