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## Crosstalk between apoptosis and inflammation in atherosclerosis

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**Abbreviations**

36B4	Acidic ribosomal phosphoprotein P0
ACC	Carotid artery
Ad	Adenoviral
AIF	Apoptosis inducing factor
AIM	Apoptosis inhibitor expressed by macrophages
APAF	Apoptotic protease-activating factor
ApoE	Apolipoprotein E
Arg1	Arginase 1
ASMA	$\alpha$ -smooth muscle actin
Bad	Bcl-2-associated agonist of cell death
Bak	Bcl-2 antagonist/killer
Bax	Bcl-2 associated X protein
BCA	Brachiocephalic artery
Bcl-2	B cell lymphoma 2
Bfl-1	Bcl-2-related gene expressed in fetal liver 1
BH	Bcl-2 homology
Bid	BH3 interacting domain death agonist
Bik	Bcl-2 interacting killer
Bim	Bcl-2 like interacting mediator of cell death
Blk	Bik-like killer protein
BM	Bone marrow
Bmf	Bcl-2 modifying factor
BMT	Bone marrow transplantation
BMDM	Bone marrow derived macrophages
CCR	CC chemokine receptor
CD	Cluster of differentiation
CMV	Cytomegalovirus
Ct	Threshold cycle
CXCR	CXC chemokine receptor
DC	Dendritic cell
DD	Death domain
DFF	DNA fragmentation factor
DISC	Death inducing signaling complex
DMEM	Dulbecco's Modified Eagle Medium
DR	Death receptor
DT(R)	Diphtheria toxin (receptor)
EC	Endothelial cell
EDTA	Ethylene diamine tetra-acetic acid
ELISA	Enzyme-linked immunosorbent assay
eNOS	Endothelial nitric oxide synthase
ESAM	Endothelial cell-selective adhesion molecule

## *Abbreviations*

Fabp	Fatty acid binding protein
FACS	Fluorescence activated cell sorting
FADD	Fas-associated death domain
FAK	Focal adhesion kinase
FAS	Fatty acid synthase
FCS	Fetal calf serum
FGF	Fibroblast growth factor
FRNK	FAK related non kinase
GC	Group specific component
GM-CSF	Granulocyte-macrophage colony stimulating factor
GTC	Guanidine thiocyanate
HE	Hematoxylin and eosin
HGF	Hepatocyt growth factor
HPRT	Hypoxanthine-guanine phosphoribosyltransferase
Hrk	Harakiri, Bcl-2 interacting protein
HSP	Heat shock protein
ICAM	Intracellular adhesion molecule
IFN	Interferon
Ig	Immunoglobulin
IGF-1	Insulin-like growth factor
IL	Interleukin
IL1-RA	Interleukin 1 receptor antagonist
IMDM	Iscoe's Modified Dulbecco's Medium
iNOS	Inducible nitric oxide synthase
LDL(r)	Low density lipoprotein (receptor)
LO	Lipoxygenase
LOX-1	Lectin-like oxidized low density lipoprotein receptor
LPS	Lipopolysaccharide
MARCO	Macrophage receptor with a collagenous structure
Mcl-1	Myeloid cell leukemia 1
MCP-1	Monocyte chemoattractant protein 1
M-CSF	Macrophage colony stimulating factor
Mfge8	Milk fat globule epidermal growth factor 8
MHC	Major Histocompatibility complex
MIF	Macrophage migration inhibitory factor
MLN	Mediastinal lymph node
MMP	Matrix metalloproteinases
Moma-2	Monocyte/macrophage antibody 2
Mup	Major urinary protein
NF-κB	Nuclear factor κB
NK	Natural killer
NO	Nitric oxide
Npy	Neuropeptide γ

n.s.	Non significant
Ox-LDL	Oxidized LDL
PAF	Platelet activating factor
PBS	Phosphate buffered saline
PCR	Polymerase chain reaction
PDGF	Platelet derived growth factor
PECAM	Platelet/endothelial-cell adhesion molecule
PGE2	Prostaglandin E2
Plagl1	Pleiomorphic adenoma gene-like-1
PTCA	Percutaneous transluminal coronary angioplasty
Puma	P53-up-regulated modulator of apoptosis
RAG	Recombination activating gene
ROS	Reactive oxygen species
RT-PCR	Reverse transcriptase PCR
SCD1	Stearoyl-coenzyme A desaturase 1
SDF-1	Stromal cell derived factor 1
SEM	Standard error of the mean
SRA	Scavenger receptor 1
SREBP	Sterol regulatory element-binding protein
SR-PSOX	Scavenger receptor that binds phosphatidylserine and oxidized lipoprotein
TC	Total cholesterol
TG	Triglyceride
TG2	Transglutaminase 2
TGF $\beta$	Transforming growth factor $\beta$
Th	T helper
TNF(R)	Tumor necrosis factor (receptor)
TRAIL	TNF related apoptosis inducing ligand
TUNEL	Terminal deoxytransferase dUTP nick-end labeling
TWEAK	TNF-like weak inducer of apoptosis
VCAM	Vascular cell adhesion molecule
VEGF	Vascular endothelial growth factor
VLA-4	Very late activation antigen 4
VLDL	Very low-density lipoprotein
vSMC	Vascular smooth muscle cells
WBC	White blood cells
WT	Wild-type
WTD	Western type diet
XAF1	X-linked inhibitor of apoptosis associated factor-1

## Publications

### Full papers

Westra M.M., Van der Lans C.A., 't Hoen P.A., Bot I., Bot M., Van Vlijmen B.J., Van Berkel T.J., Pasterkamp G. and Biessen E.A. Gene Expression Profiling in Atherosclerotic Plaque Vulnerability Identifies Neuropeptide Y as a Marker of Plaque Vulnerability. *Submitted*.

Westra M.M., Bot I., Hoekstra M., Bot M., Van de Water B., Van Vlijmen B.J., Van Berkel T.J. and Biessen E.A. Compromised Focal Adhesion Kinase Function Does Not Alter Atherogenesis in ApoE<sup>-/-</sup> Mice despite Profound Effects on Lipid Metabolism and Inflammatory Status. *Submitted*.

Dysregulated SDF-1 $\alpha$ /CXCR4 Axis during Atherosclerotic Plaque Progression Is Associated With Progressive Plaque Destabilization. Bot I, Daissormont I.T., Zernecke A., de Jager S.C, Westra M.M., Bot M., Herías V.M., van Santbrink P.J., van Berkel T.J., Su L., Weber C. and Biessen E.A. *Submitted*.

Leukocyte Specific CCL3 Deficiency Inhibits Atherosclerotic Lesion Development by Attenuation of Intimal Neutrophil Accumulation. de Jager S.C., Bot I., Kraaijeveld A.O., Bot M., Westra M.M., van Santbrink P.J., van Berkel T.J. and Biessen E.A. *Submitted*.

Westra M.M., Bot I., Bot M., Habets K.L., De Jager S.C., Keulers T.H., Cotter T.G., Van Berkel T.J. and Biessen E.A. Leukocyte Bim Deficiency Induces Anti-Ox-LDL Autoantibody Formation and T Cell and Immunoglobulin Accumulation in Atherosclerotic Lesions of LDLR<sup>-/-</sup> Mice. *Manuscript in preparation*.

Westra M.M., Bot I., Bot M., De Jager S.C.A., Dzhagalov I., He Y.-W., Van Vlijmen B.J., Van Berkel Th.J.C. and Biessen E.A. Increased Foam Cell Formation and Atherosclerotic Plaque Apoptosis and Markedly Decreased Neutrophil Recruitment in LDLR<sup>-/-</sup> Mice Lacking Macrophage Mcl-1. *Manuscript in preparation*.

De Nooijer R., Bot I., Von der Thüsen J.H., Leeuwenburgh M.A., Overkleeft H.S., Kraaijeveld A.O., Dorland R., Van Santbrink P.J., Van Heiningen S.H., Westra M.M., Kovanen P.T., Jukema J.W., Van der Wall E.E., Van Berkel T.J., Shi G.P., Biessen E.A. Leukocyte cathepsin S is a potent regulator of both cell and matrix turnover in advanced atherosclerosis. *Arterioscler Thromb Vasc Biol.* 2009;29(2):188-94.

Published abstracts

Absence of Macrophage Mcl-1 Induces Foam Cell Formation and Atherosclerotic Plaque Apoptosis without Affecting Plaque Development in LDLr<sup>-/-</sup> Mice. Westra M.M., Bot I., Dzhagalov I., He Y.-W., van Berkel T.J., Biessen E.A. *Circulation*. 2008;118(18):II-511.

Chymase Inhibition Reduces the Incidence of Intraplaque Hemorrhage and Induces a Stable Atherosclerotic Plaque Phenotype in ApoE Deficient Mice. Bot I., Westra M.M., van Heiningen S.H., Hilpert H., Lankhuizen I.M., van Berkel T.J., Fingerle J, Biessen E.A. *Circulation*. 2008;118(18):II-410.

Haematopoietic Absence of Sphingosine 1-Phosphate Lyase Decreases Atherosclerotic Lesion Development in LDL-Receptor Deficient Mice. Bot M., Bot I., Westra M.M., De Jager S.C., Van Santbrink P.J., Gijbels M.J., Van Berkel T.J., Van Voldhoven P.P., Nofer J.R., Biessen E.A. *Circulation*. 2008;118(18):II-451.

## **Curriculum vitae**

Marijke Westra werd geboren op 14 juli 1979 te Haskerland. In juni 1997 behaalde zij haar VWO diploma aan scholengemeenschap 'OSG Sevenwolden' in Heerenveen, en in juni 1998 aanvullende VWO certificaten aan het Friesland College in Leeuwarden. In september 1998 werd begonnen met de studie Farmacie aan de Universiteit Utrecht. Het doctoraal examen van deze studie met als afstudeerrichting Farmaceutische Biologie werd in oktober 2004 behaald aan de Rijksuniversiteit Groningen. Tijdens deze opleiding werden twee onderzoeksstages gedaan. De eerste stage vond plaats bij de Basiseenheid Farmaceutische Biologie aan de Rijksuniversiteit Groningen en betrof de ontwikkeling van RANK antagonisten en een trimeerconstructie voor antagonisten en agonisten voor receptoren van de TNF-familie onder begeleiding van Dr. M.M. Mullally en Prof. Dr. W.J. Quax. De tweede stage was getiteld 'Identificatie van genen betrokken bij, en mechanismen van sensitisatie voor TRAIL geïnduceerde apoptose in kanker cellijnen' en werd uitgevoerd bij het Department of Biochemistry, Cell Stress and Apoptosis Research Group aan de National University of Galway in Ierland, onder begeleiding van Dr. E. Szegezdi en Dr. A. Samali. Van januari 2005 tot april 2009 werkte zij als assistent in opleiding bij de afdeling Biofarmacie van het Leiden/Amsterdam Center for Drug Research aan de Universiteit Leiden. Hier werd het onderzoek beschreven in dit proefschrift, gesubsidieerd door NWO/ZonMW (project 912-02-037), uitgevoerd onder begeleiding van Prof. Dr. E.A.L Biessen en Prof. Dr. Th.J.C. van Berkel. Sinds mei 2009 is zij werkzaam als octrooigemachtigde in opleiding bij VEREENIGDE te Amersfoort.





