The role of apolipoprotein CI in lipid metabolism and bacterial sepsis

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Chapter 11

List of Abbreviations

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List of Abbreviations

ABCAI	ATP binding cassette transporter AI
AdAPOCI	a recombinant, replication-deficient adenoviral vector expressing human *APOC1*
Ala	alanine
APACHE II	acute physiology and chronic health evaluation II
apo	apolipoprotein
apobec-1	apolipoprotein B mRNA editing enzyme, catalytic polypeptide 1
apoER2	apolipoprotein E receptor 2
ARDS	acute respiratory distress syndrome
Arg	arginine
Asp	asparagnine
ATIII	antithrombin III
BMI	body mass index
BPI	bactericidal/permeability increasing protein
BSA	bovine serum albumin
CAP	community-acquired pneumonia
CARS	compensatory anti-inflammatory response syndrome
CE	cholesteryl ester
CETP	cholesteryl ester transfer protein
CI	confidence interval
CLP	cecal ligation and puncture
CRI	catheter-related infection
CRP	C-reactive protein
CVD	cardiovascular disease
Cys	cysteine
DMEM	Dulbecco's modified eagle medium
E. coli	*Escherichia coli*
ELISA	enzyme linked immunosorbent assay
EGF	endothelial growth factor
FBS	fecal bovine serum
FC	free cholesterol
FFA	free fatty acids
FITC	fluorescein isothiocyanate
FPLC	fast performace liquid chromatography
Glu	glutinine
GPI	glycosylphosphatidylinositol
HAP	hospital-acquired pneumonia
HDL	high-density lipoproteins
His	histidine
HL	hepatic lipase
HR	hazard ratio
HRP	horse radish peroxidase
HSPG	heparan sulphate proteoglycans
ICAM-1	intracellular adhesion molecule-1
ICD-10	international classification of diseases and related health problems, 10th revision
ICU	intensive care unit
IDL	intermediate-density lipoproteins
IFNγ	interferon-γ
IL-1	interleukin-1
IQR	interquartile range
KDO	2-keto-3-deoxyoctonic acid
K. pneumoniae	*Klebsiella pneumoniae*

LALF	*Limulus* anti-LPS factor
LBP	LPS-binding protein
LCAT	lecithin:cholesterol acyltransferase
LDL(r)	low-density lipoprotein (receptor)
Lf	lactoferrin
LPL	lipoprotein lipase
LPS	lipopolysaccharide
LRP	LDL-receptor-related protein
LTA	lipoteichoic acid
Lys	lysine
MALDI-TOF	matrix-assisted laser desorption/ionization time of flight
MBL	mid promannan binding lectin
mCD14	membrane-bound CD14
Mid pro-ANP	mid pro-atrial natriuretic peptide
MIF	macrophage migration inhibitory factor
mLDL	modified LDL
MODS	multiple organ dysfunction syndrome
MTP	microsomal TG transfer protein
NO	nitric oxide
pAdTrack-CMV	cytomegalus virus
PBS	phosphate buffered saline
PL	phospholipids
PLTP	phospholipid transfer protein
Pro	proline
ReLPS	Re595 LPS
rHDL	reconstituted HDL
R-LPS	rough LPS
RP-HPLC	reverse-phase high performance liquid chromatography
SA	serum albumin
SAA	serum amyloid A
SAP	serum amyloid P
sCD14	soluble CD14
SD	standard deviation
SEM	standard error of mean
Ser	serine
SIRS	systemic inflammatory response syndrome
S-LPS	smooth LPS
SMAP-29	sheep myeloid antimicrobial peptide
SMC	smooth muscle cells
S. minnesota	*Salmonella minnesota*
SR (-A / -BI)	scavenger receptor (class A / class B type I)
SR-LPS	semi-rough LPS
TC	total cholesterol
TG	triglycerides
TLR	Toll-like receptor
TNFα	tumor necrosis factor α
TREM-1	triggering receptor expressed on myeloid cells-1
TO	triolein
Tyr	tyrosine
UTI	urinary tract infection
Val	valine
VAP	ventilator-associated pneumonia
VCAM-1	vascular cell adhesion molecule-1
VLDL(r)	very-low-density lipoprotein (receptor)
WT	wild-type

List of Publications

Full papers

1. Berbée JFP, Van der Hoogt CC, Sundararaman D, Havekes LM, Rensen PCN: Severe hypertriglyceridemia in human *APOC1* transgenic mice is caused by apoCI-induced inhibition of lipoprotein lipase. **J Lipid Res 2005,** 46 (2): 297-306.

2. Berbée JFP, Havekes LM, Rensen PCN: Apolipoproteins modulate the inflammatory response to lipopolysaccharide. **J Endotoxin Res 2005,** 11: 97-103.

3. Den Boer MAM, Berbée JFP, Reiss P, Voshol PJ, Kuipers F, Havekes LM, Rensen PCN, Romijn JA: Ritonavir alters tissue-specific fatty acid partitioning in subcutaneous tissue compartments. **Arterioscler Thromb Vasc Biol 2006,** 19 (6): 567-596.

4. Van der Hoogt CC, Berbée JFP, Espirito Santo SMS, Gerritsen G, Krom YD, Van der Zee A, Havekes LM, Willems van Dijk K, Rensen PCN. ApoC-I directly inhibits LPL activity independent of the VLDL receptor and apoC-III in mice. **Biochim Biophys Acta 2006,** 1761 (2): 213-220.

5. Mooijaart SP, Berbée JFP, Van Heemst D, Havekes LM, De Craen T, Slagboom E, Rensen PCN, Westendorp RGJ: ApoE plasma levels and risk of cardiovascular mortality in old age. **PLoS Med 2006,** 3 (6): e176.

6. Westerterp M, De Haan W, Berbée JFP, Havekes LM, Rensen PCN: Endogenous apoCI increases hyperlipidemia in apoE-knockout mice by stimulating VLDL production and inhibiting LPL. **J Lipid Res 2006,** 47 (6): 1203-1211.

7. Berbée JFP, Van der Hoogt CC, Kleemann R, Schippers EF, Van Leeuwen HJ, Schifferstein HNJ, Kitchens RL, Van Dissel JT, Bakker-Woudenberg IAJM, Havekes LM, Rensen PCN: Apolipoprotein CI stimulates the inflammatory response to LPS and protects against sepsis. **FASEB J 2006,** 26 (12): 2162-2164.

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10. Mooijaart SP, Van Vliet P, Van Heemst D, Rensen PCN, Berbée JFP, Jolles J, De Craen AJM, Westendorp RGJ: Plasma levels of apolipoprotein E and cognitive function in old age. **Ann NY Acad Sci 2007,** *in press*.

11. Westerterp M, Berbée JFP, Delsing DJM, Jong MC, Gijbels MJJ, Dahlmans VEH, Offerman EH, Romijn JA, Havekes LM, Rensen PCN: Apolipoprotein CI binds free fatty acids and reduces their intracellular esterification. **J Lipid Res 2006,** *in press.*

12. Berbée JFP, Mooijaart SP, De Craen JM, Havekes LM, Van Heemst D, Westendorp RGJ, Rensen PCN: Plasma apoCI independently protects against infection-related mortality in humans. *Submitted for publication.*

13. Berbée JFP*****, Westerterp M*, Pires NMM, Van Mierlo GJD, Kleemann R, Romijn JA, Havekes LM, Rensen PCN: Apolipoprotein CI is crucially involved in lipopolysaccharide-induced atherosclerosis development in apoE-knockout mice. *Submitted for publication.* [*shared first authorship].

14. Berbée JFP, Van der Hoogt CC, De Haas CJ, Van Kessel PK, Dallinga-Thie GM, Romijn JA, Havekes LM, Van Leeuwen HJ, Rensen PCN; Plasma apoCI is associated with increased survival of patients with severe sepsis. *Submitted for publication.*

15. Abildayeva K, Berbée JFP, Blokland A, Kuijpers HJH, Jansen PJ, Hoek, FJ, Meijer O, Lütjohann D, Gautier T, Pillot T, De Vente J, Havekes LM, Ramaekers CS, Kuipers F, Rensen PCN, Mulder M: Human Apolipoprotein CI Expression in Mice Impairs Learning and Memory Functions. *Submitted for publication.*

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1. Rensen P, Berbée J, Van der Hoogt C, Gerritsen G, Van der Zee A, Sundararaman D, Willems van Dijk K, Havekes L: Apolipoprotein CI is a potent inhibitor of lipoprotein lipase *in vitro* and *in vivo*. **Atherosclerosis Suppl 2003,** 4: 229.

2. Rensen PCN, Berbée J, Van Oosten M, Havekes L, Van Berkel T, Kuiper J: Apolipoprotein E attenuates the inflammatory response to lipopolysaccharide: implications for sepsis. **Shock 2004,** 21 [suppl]: 61.

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6. Van der Hoogt CC, Berbée JF, Gerritsen G, Krom YD, Van der Zee A, Havekes LM, Willems van Dijk K, and Rensen PCN: ApoCI impairs the lipolytic conversion of triglyceride-rich lipoproteins in mice. **Arterioscler Thromb Vasc Biol 2004,** 24: E-56.

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8. Den Boer M, Berbée JFP, Rensen PCN, Romijn JA, Reiss P, Van der Valk M, Voshol PJ, Havekes LM. Ritonavir impairs lipoprotein lipase-mediated lipolysis and decreases uptake of fatty acids in adipose tissue. **Antivir Ther 2004,** 9 (6): L13.

9. Berbée JFP, Schippers EF, Van der Hoogt CC, Van Dissel JT, Bakker-Woudenberg IAJM, Havekes LM, Rensen PCN: Apolipoprotein CI augments the inflammatory response to LPS and corelates with improved infection-related survival in mice and humans. **J Endotoxin Res 2004,** 10: 321.

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13. Mooijaart SP, Berbée JFP, Van Heemst D, Havekes LM, De Craen AJM, Rensen PCN, Westendorp RGJ: Plasma apolipoprotein E levels and risk of cardiovascular disease mortality in old age. **Atherosclerosis 2006,** 7 (3): 37.

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Curriculum Vitae

Jimmy Fransiscus Paulus Berbée werd geboren op 17 september 1977 te Leiden. Na het behalen van het VWO diploma aan het Teylingen College te Noordwijkerhout in juni 1996, studeerde hij Biofarmaceutische Wetenschappen aan de Universiteit van Leiden. Het propedeutisch examen werd in augustus 1998 behaald. Van september 1999 tot en met september 2000 werd in het kader van het doctoraal examen voor de hoofdvakstage onderzoek verricht binnen de vakgroep Biofarmacie onder leiding van Dr. C.C.M Appeldoorn en Prof. Dr. E.A.L. Biessen met als onderwerp “Development and evaluation of a targeting device that uses a synthetic apolipoprotein E peptide to target to the atherosclerotic plaque”. Daarnaast werd van oktober 2000 tot en met mei 2001 een onderzoeksstage verricht onder leiding van Dr. G. Mannens and Dr. R. Gilissen bij de afdeling Niet-Klinische Farmacokinetiek van Janssen Research Foundation te Beerse, België, met als onderwerp “The use of WGA cells, a subclone of HepG2 cells, to study the induction of CYP1A and CYP3A4 enzymes at mRNA, protein and metabolism level”. Het doctoraal examen werd op 10 juni 2001 gehaald.

Van augustus 2001 tot september 2005 was hij als assistent in opleiding (A.I.O.) werkzaam bij de afdeling BioMedical Research van TNO-Kwaliteit van Leven en de afdeling Endocrinologie en Metabole Ziekten van het Leids Universitair Medisch Centrum te Leiden. Tijdens deze periode werd het in dit proefschrift beschreven onderzoek uitgevoerd onder leiding van Dr. P.C.N. Rensen en Prof. Dr. Ir. L.M. Havekes. Dit onderzoek maakte deel uit van een door NWO RIDE gesubsidieerd project (014-90-001). Hij won de DAS-fellowship 2004 van het 7^{e} Symposium van de Dutch Atherosclerosis Society en de New Investigator Award 2004 van het 5^{e} Annual Conference on Arteriosclerosis, Thrombosis and Vascular Biology.

Sinds september 2005 is hij aangesteld als postdoc bij de afdeling Endocrinologie en Metabole Ziekten van het Leids Universitair Medisch Centrum op een door de Hartstichting gefinancierd project (NHS 2005B226).