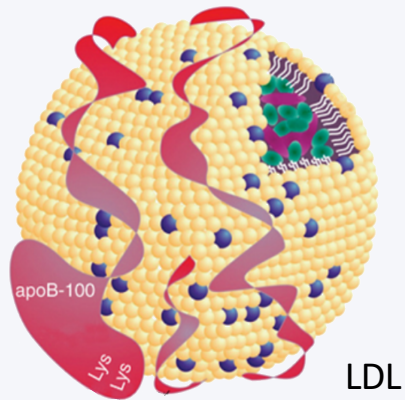




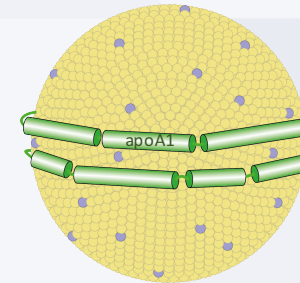
Otago Spotlight Series
Cardiovascular Disease

Lipoproteins in Heart Disease

Professor Sally McCormick
Department of Biochemistry
University of Otago



Blood Fat.



LIPID TESTS

Date:
Lab Number:

16/02/11
1438754

Optimal

Fasting Status
Cholesterol mmol/L
Triglycerides mmol/L
HDL Cholesterol mmol/L
LDL Cholesterol mmol/L
Chol/HDL ratio

Fasting
4.4 < 4.0
0.8 < 1.7
1.58 > 1.0
2.5 < 2.0
2.8 < 4.0

In established CHD and diabetes, use optimal levels published by NZGG as targets. Calculation of cardiovascular risk is recommended, taking into account all known risk factors. For further information see <http://tinyurl.com/nzggGuidelines>

SEEN BY

FILE

NOTES

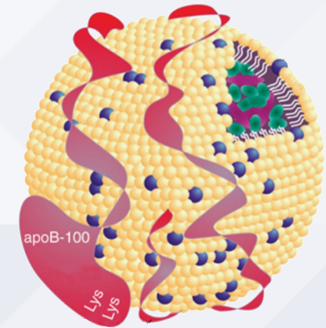
TELL PATIENT

APPOINTMENT

TREATED

REPEAT

SCRIPT



LDL as a Risk Factor for Heart Disease

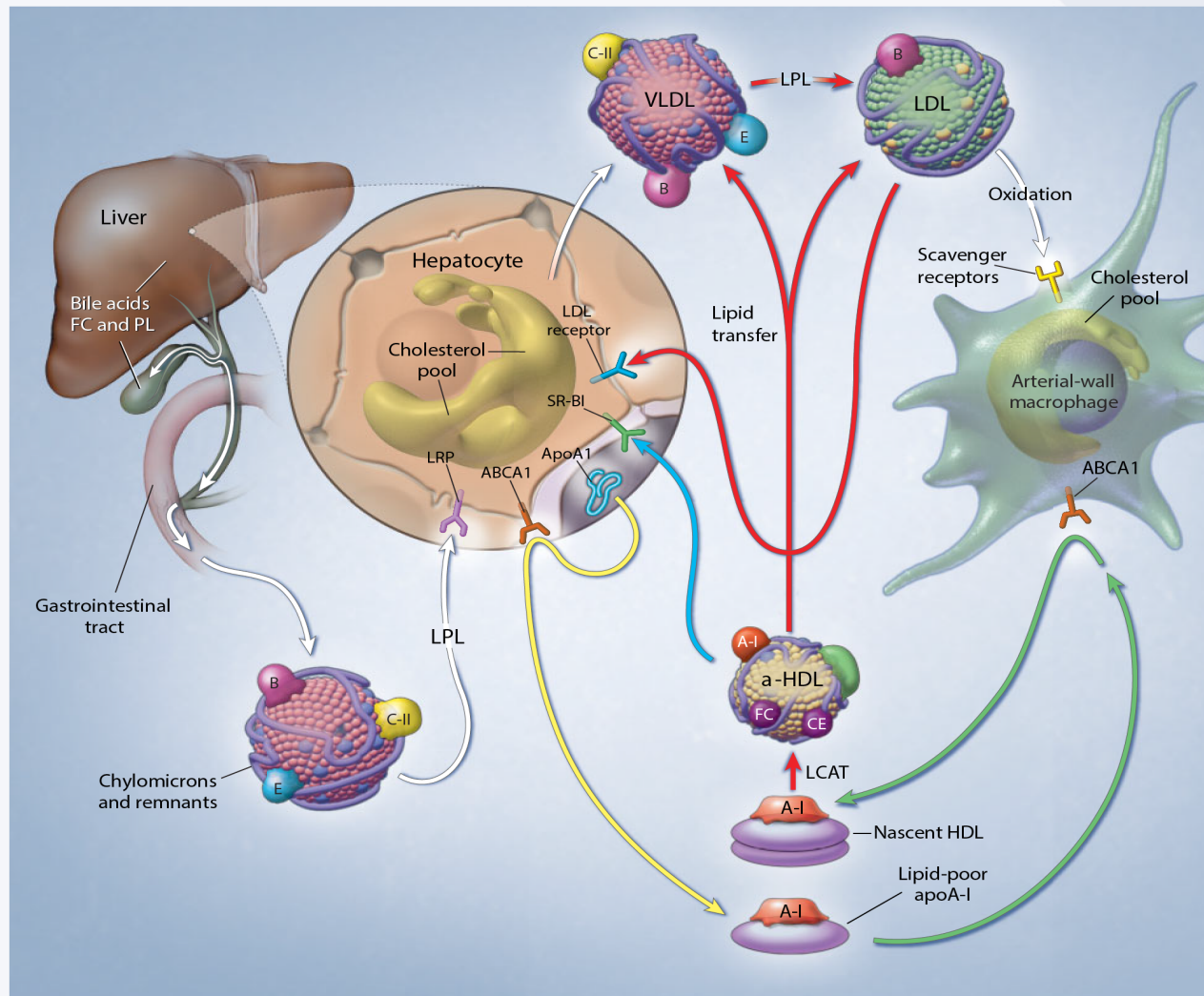
Many large clinical trials show elevated LDL-C to be an independent risk factor

Transgenic animal studies

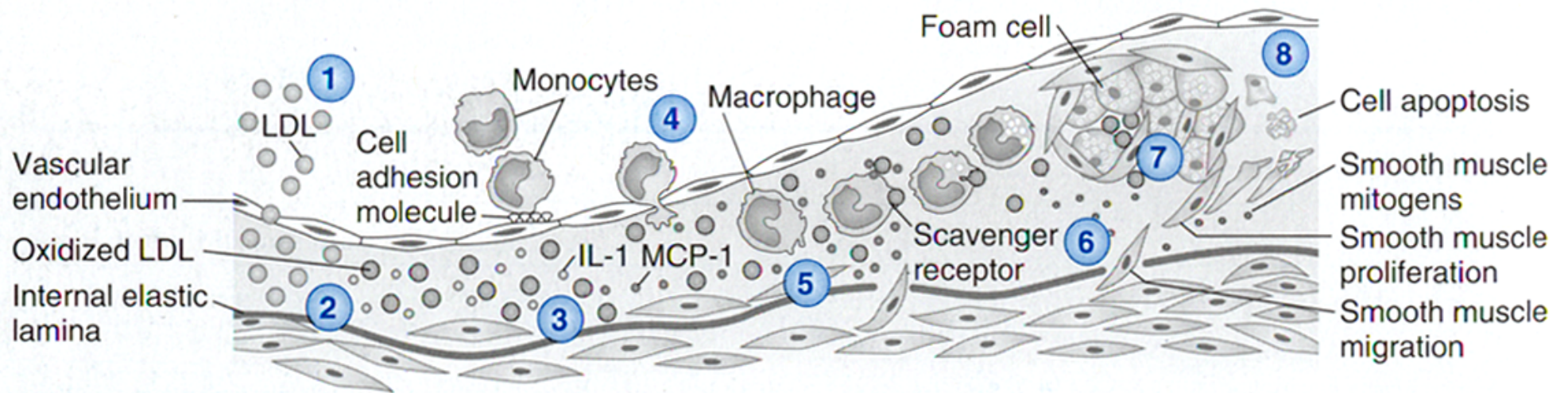
Familial hypercholesterolaemia (FH) individuals develop premature heart disease

Intervention with statins drugs lower the risk

Lipoprotein Metabolism



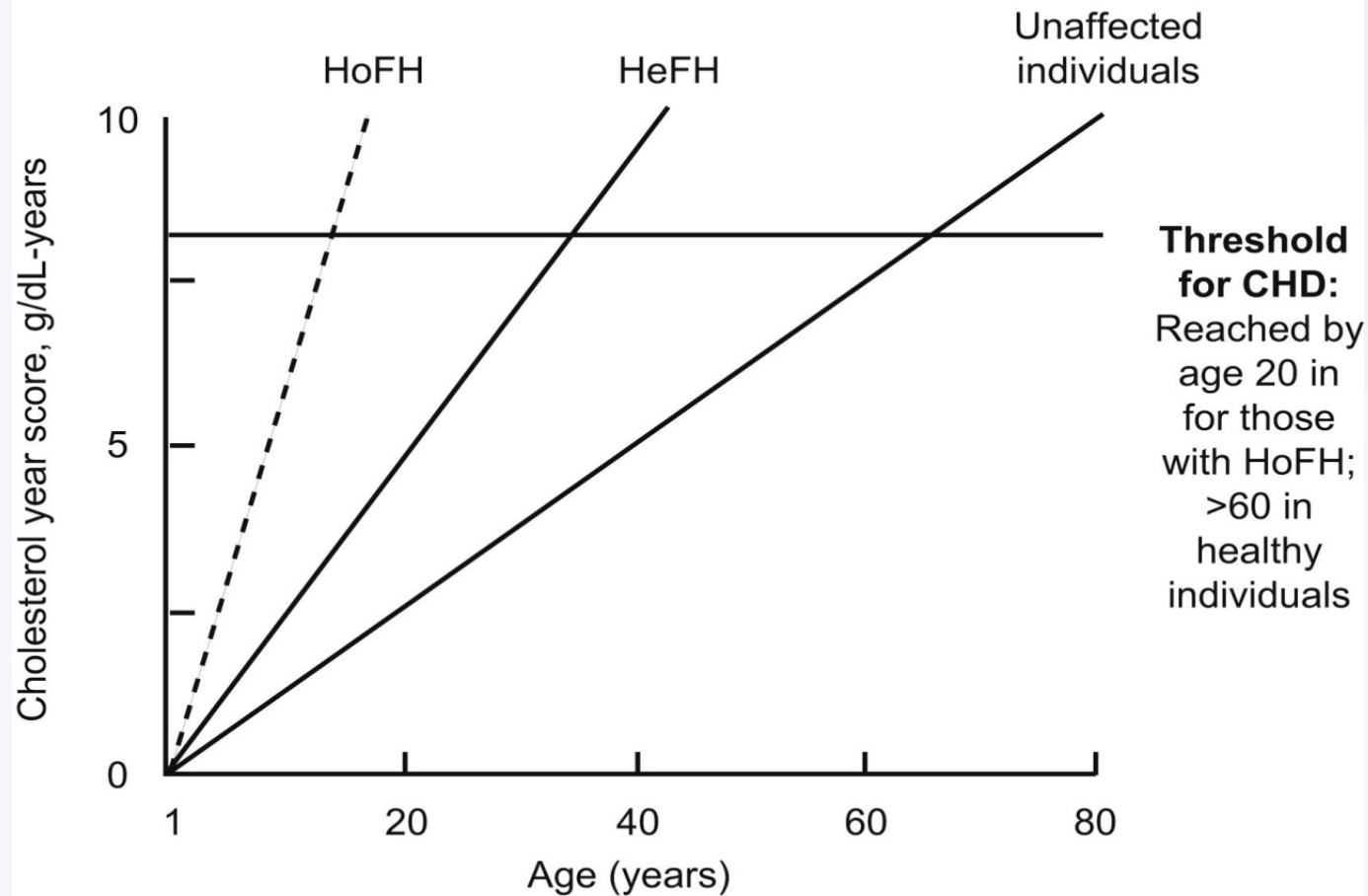
How Heart Disease Develops



Lilly (2010) Pathophysiology of Heart Disease, 5th Ed

Cumulative LDL Exposure in FH

Cumulative exposure (cholesterol yrs) by age:
FH vs. unaffected (healthy) individuals



Adapted from Horton, et al. *J Lipid Res.* 2009;50:S175.



ELSEVIER

Atherosclerosis Supplements 12 (2011) 221–263

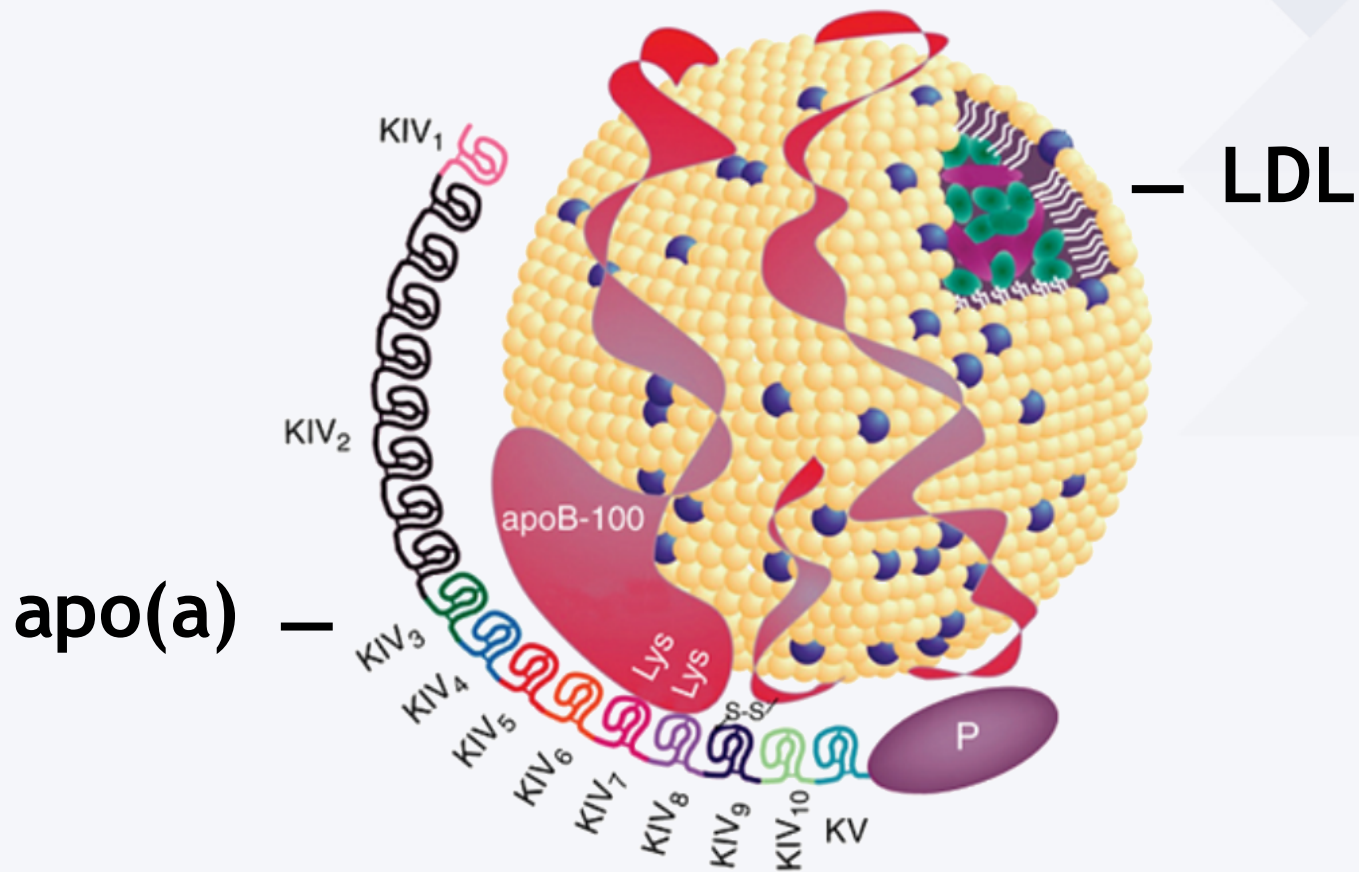
ATHEROSCLEROSIS
SUPPLEMENTS

www.elsevier.com/locate/atherosclerosis

Familial hypercholesterolaemia: A model of care for Australasia

Gerald F. Watts^{a,*}, David R Sullivan^b, Nicola Poplawski^c, Frank van Bockxmeer^d,
Ian Hamilton-Craig^e, Peter M. Clifton^f, Richard O'Brien^g, Warrick Bishop^h, Peter Georgeⁱ,
Phillip J. Barter^j, Timothy Bates^a, John R. Burnett^k, John Coakley^l, Patricia Davidson^m,
Jon Emeryⁿ, Andrew Martin^o, Waleed Farid^p, Lucinda Freeman^q, Elizabeth Geelhoed^r,
Amanda Juniper^{a,s}, Alexa Kidd^t, Karam Kostner^u, Ines Krass^v, Michael Livingston^w,
Suzy Maxwell^s, Peter O'Leary^s, Amal Owaimrin^x, Trevor G. Redgrave^a, Nicola Reid^y,
Lynda Southwell^a, Graeme Suthers^c, Andrew Tonkin^z, Simon Towler^{aa}, Ronald Trent^q,
Familial Hypercholesterolaemia Australasia Network Consensus Group
(Australian Atherosclerosis Society)^l

Lipoprotein(a)



Lp(a) as a risk factor for heart disease

Large clinical studies and meta-analyses show elevated Lp(a) to be an important risk factor

Present in atherosclerotic tissue

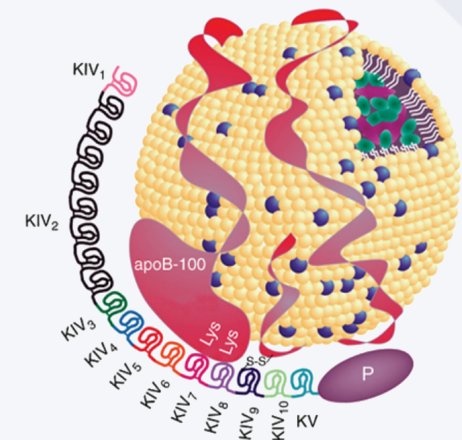
Lp(a) transgenic animals develop atherosclerosis

But:

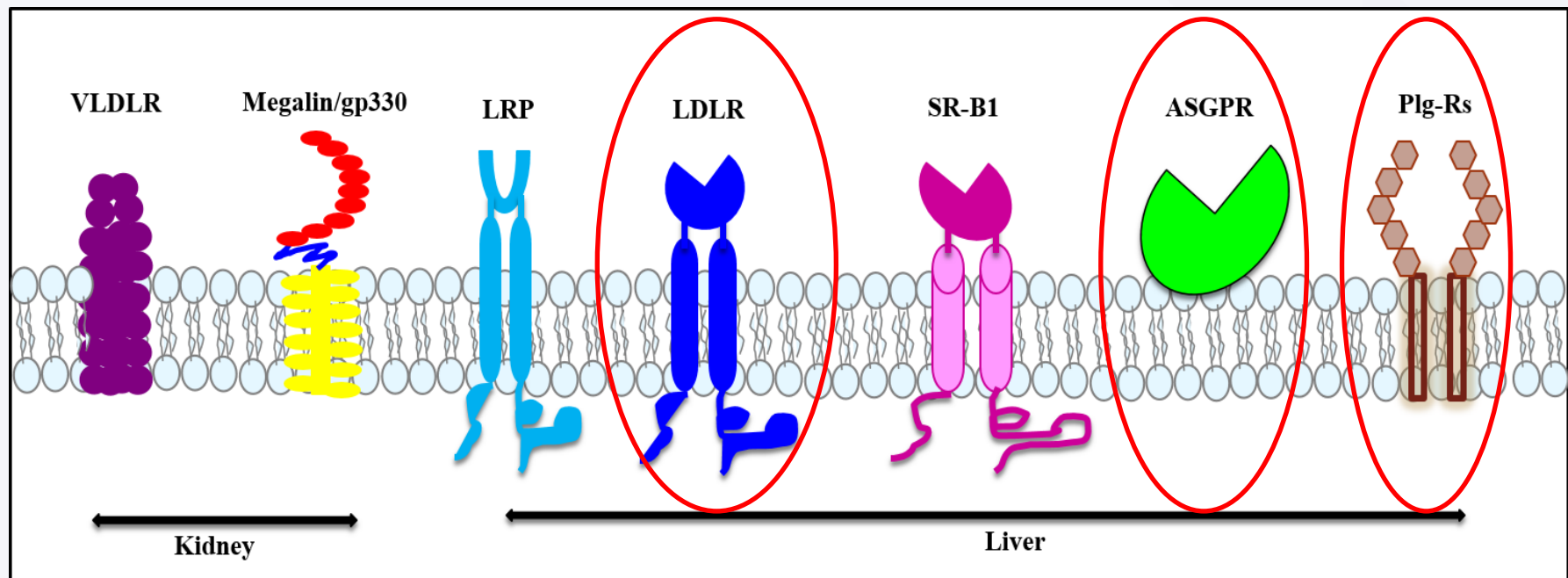
Not routinely measured

Not modified by statins or diet

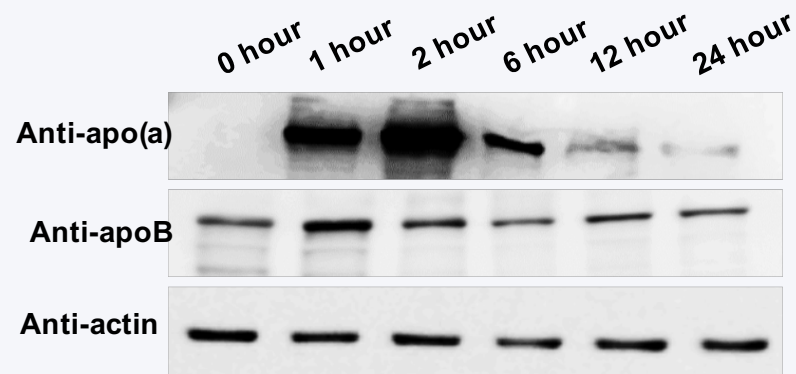
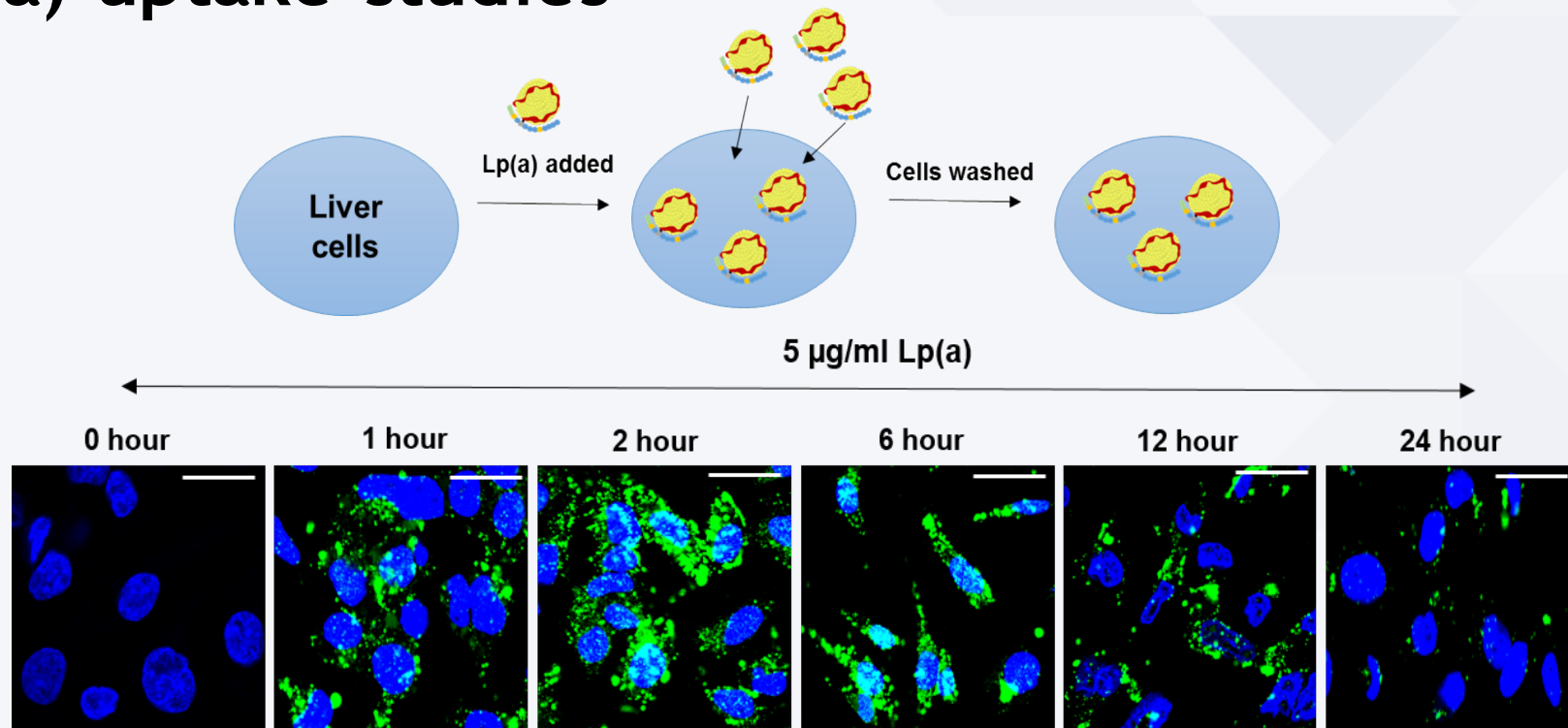
Intervention trials?



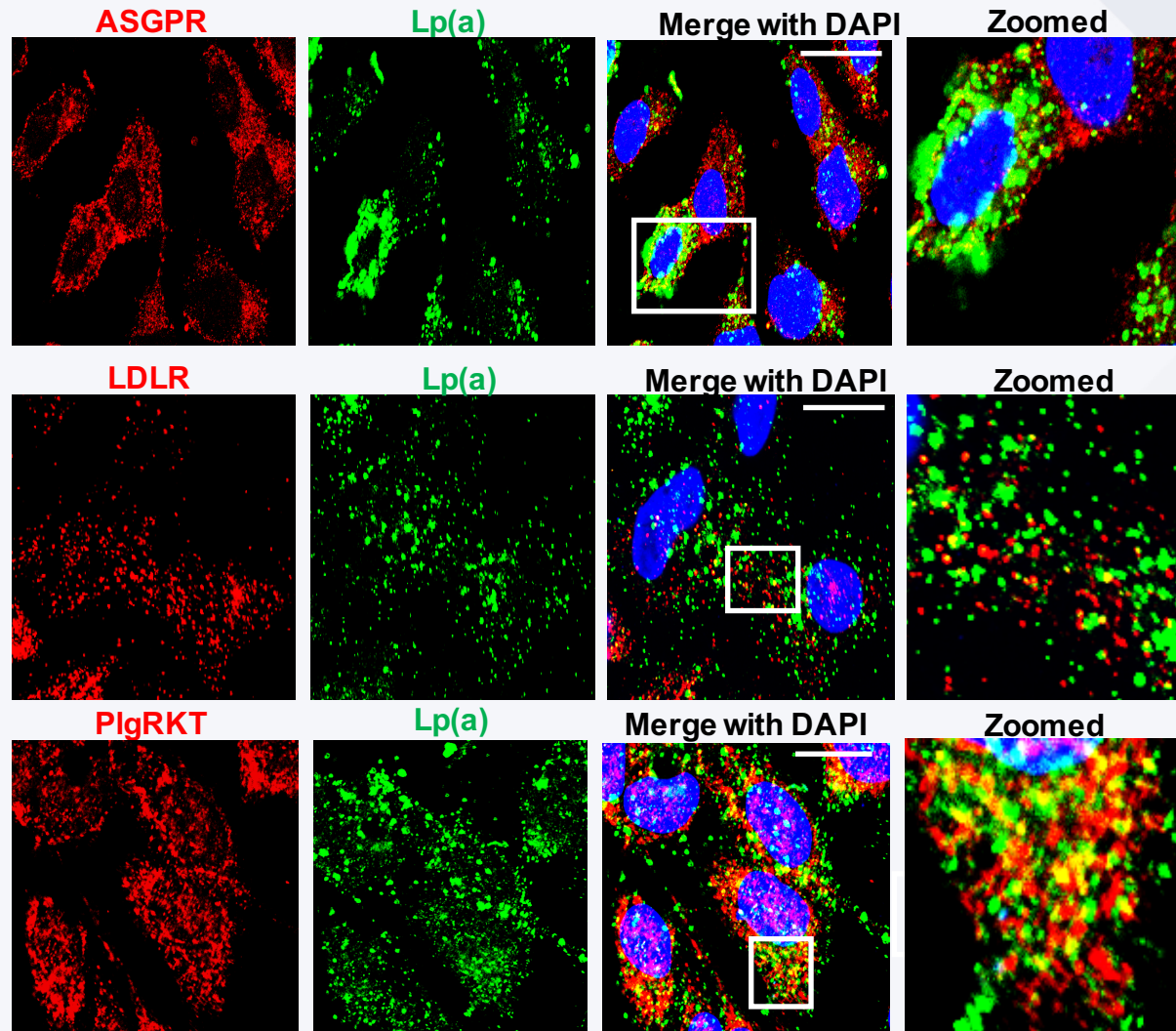
What receptor is responsible for Lp(a) uptake in liver cells?



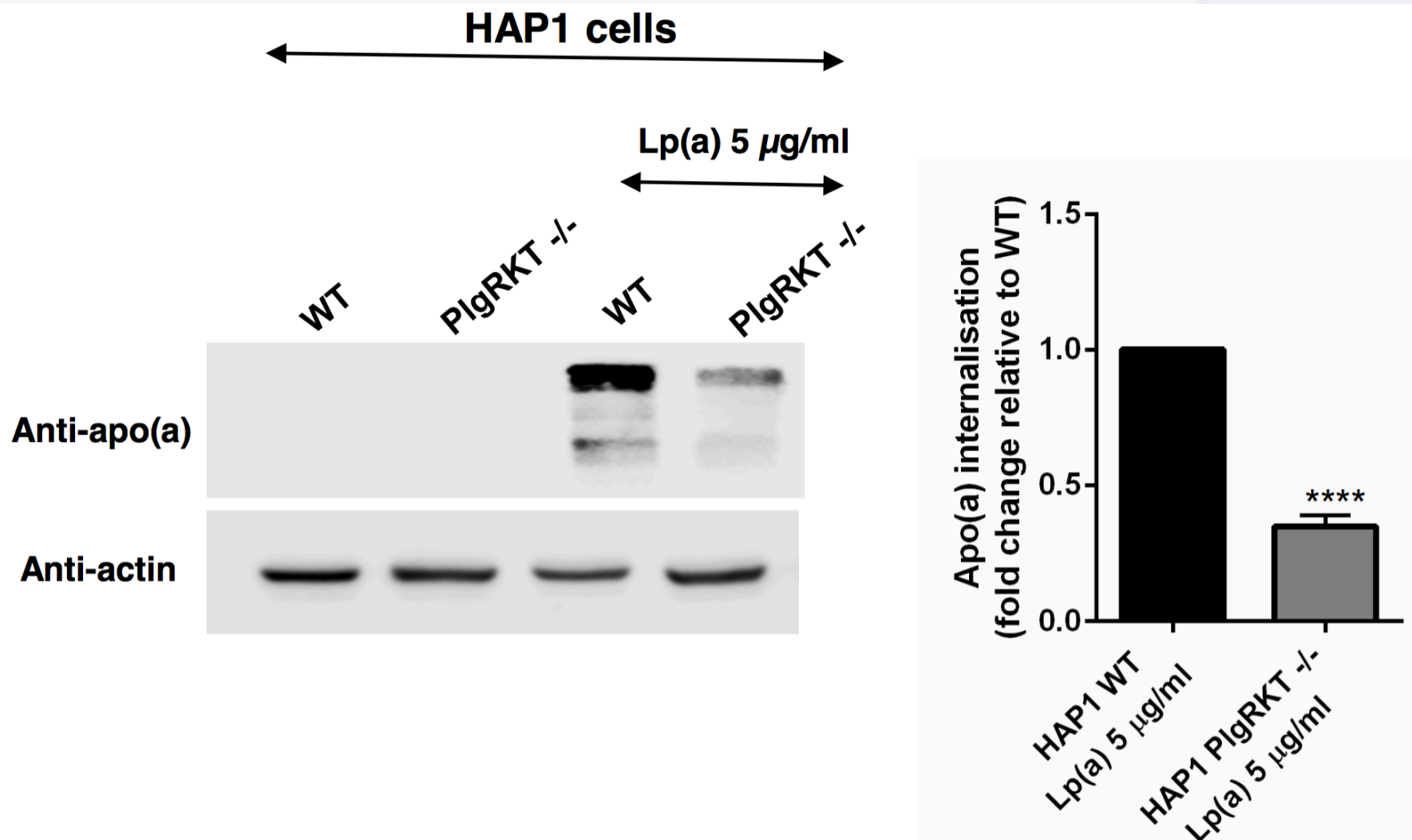
Lp(a) uptake studies



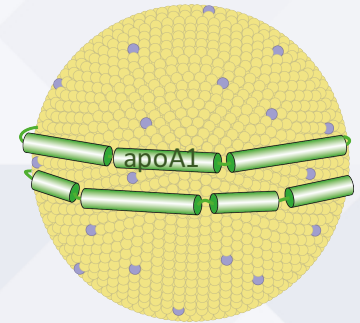
Lp(a) colocalises with the PlgRKT receptor



Plg-RKT deficient cells show reduced Lp(a) uptake



HDL As A Risk Factor for Heart Disease



Large clinical trials show low HDL-C to be an independent risk factor for CVD

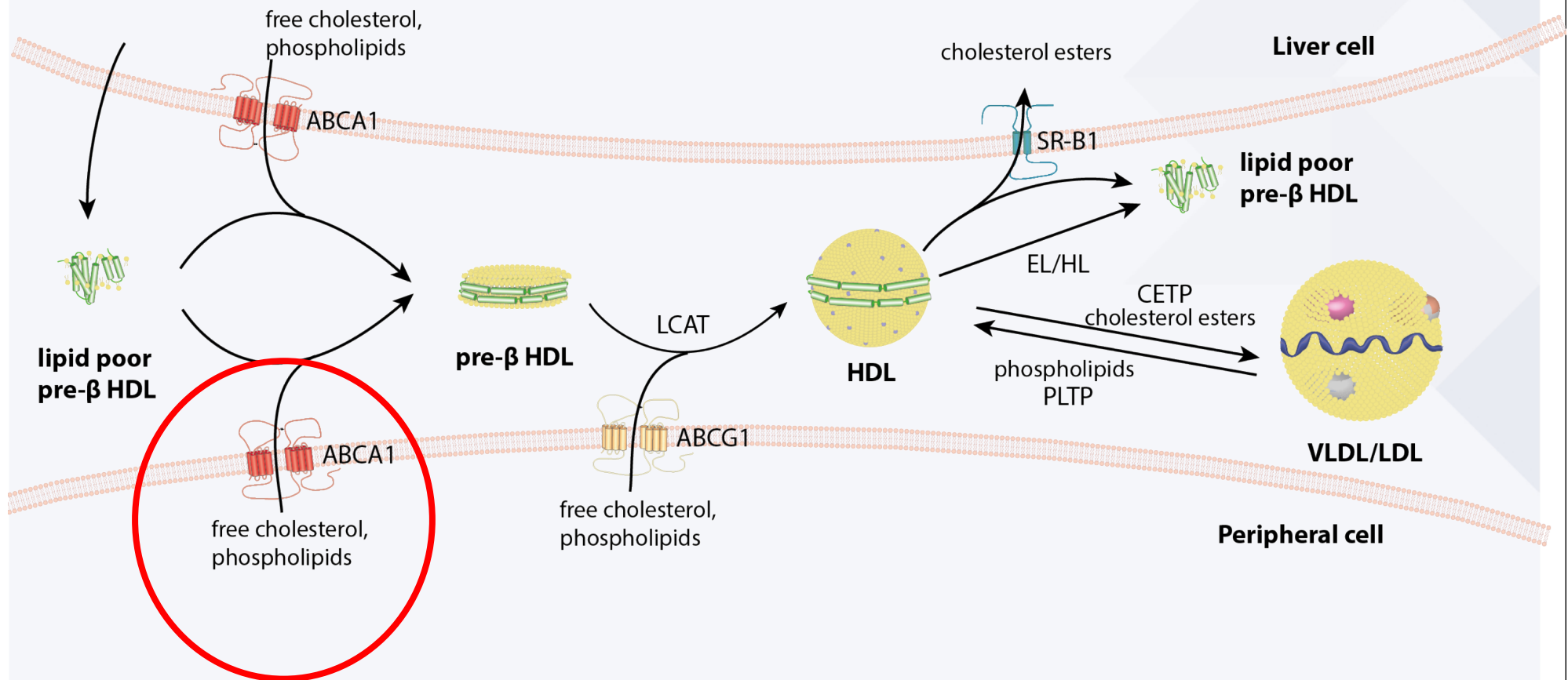
Transgenic animals studies show HDL to be protective

HDL has anti-oxidant, anti-inflammatory and anti-thrombogenic properties

Tangier disease individuals have virtually no HDL and develop premature heart disease

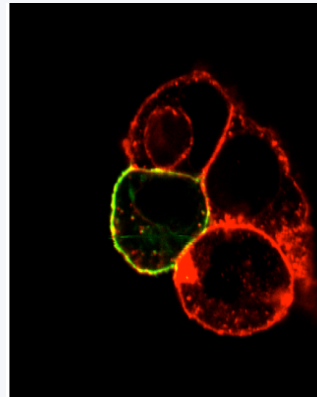
Intervention trials?

HDL Formation is Dependent on ABCA1

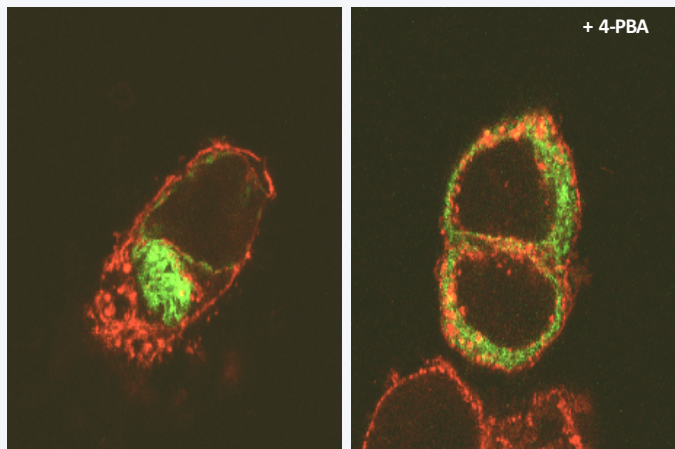


Rescue of ABCA1 Mutants with 4-Phenylbutyrate

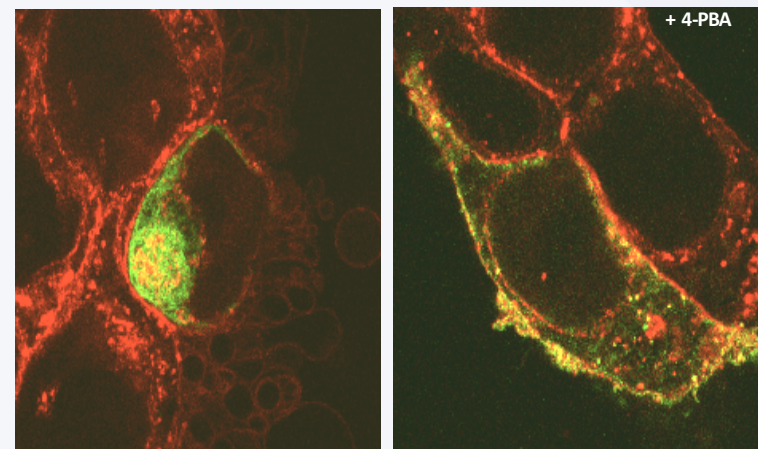
Wildtype ABCA1



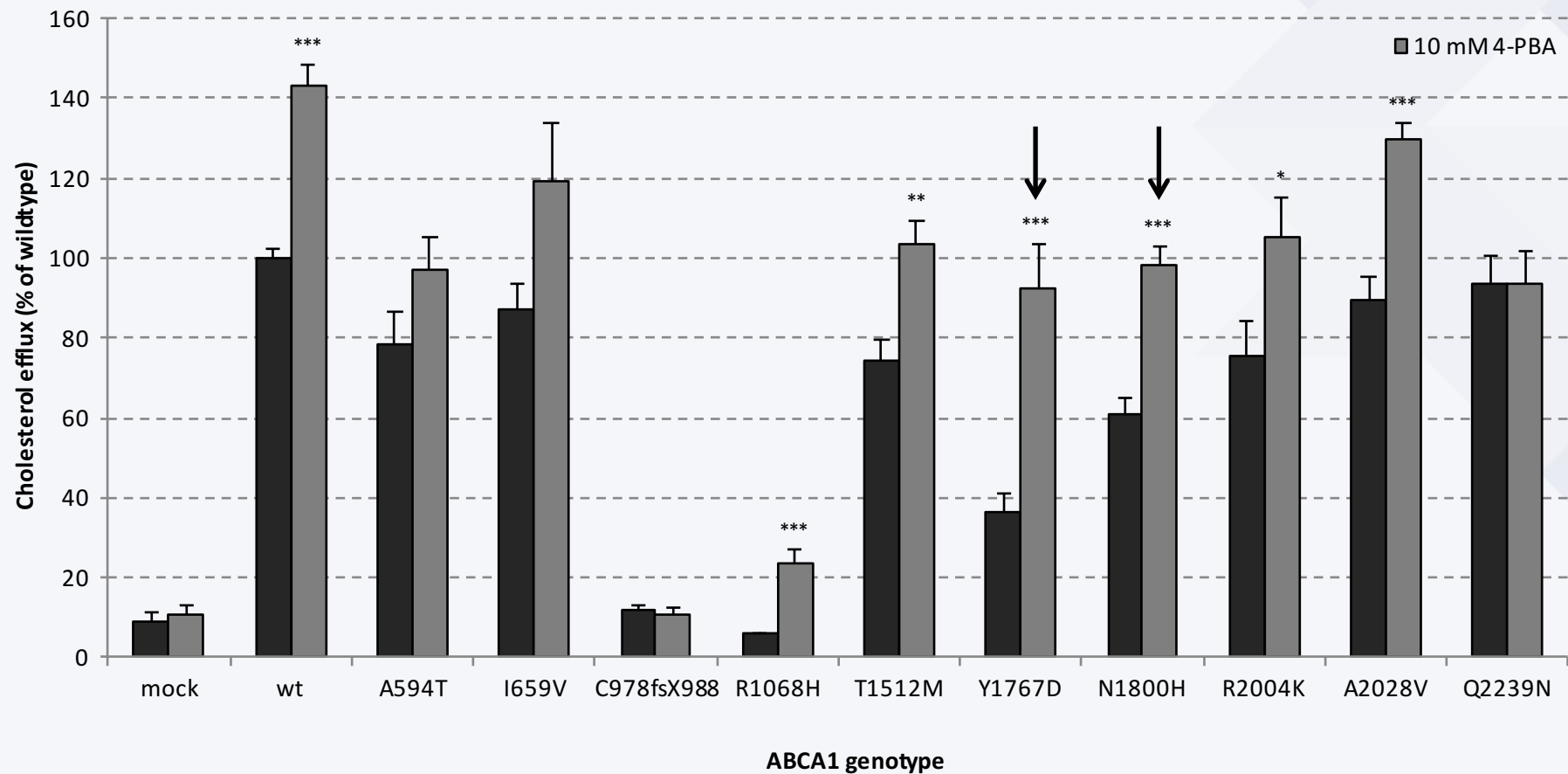
Y1767D



N1800H



Rescue of ABCA1 Mutant Function with 4-Phenylbutyrate





Otago Spotlight Series
Cardiovascular Disease

Acknowledgments

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Gregory Redpath

Research Fellow

Carolyn Porteous