Enhancement of anti-inflammatory activities of reconstituted HDL by phosphatidylserine *in vivo* and *in vitro*

Anatol Kontush

INSERM Research Unit 1166 ICAN, University Pierre and Marie Curie - Paris 6, Hospital Pitié - Salpétrière, Paris, France

Emilie Tubeuf, Maryam Darabi, Wilfried Le Goff, Carolane Dauteuille, Isabelle Guillas-Baudouin, Marie Lhomme, Mili Patel, Thierry Huby, M. John Chapman, Kerry-Anne Rye, Philippe Lesnik

ISA 2015 - XVII International Symposium on Atherosclerosis, Amsterdam, May 23-26, 2015

Inserm
Institut national de la santé et de la recherche médicale

UPMC PARIS UNIVERSITAS

SORBONNE UNIVERSITY

UNSW AUSTRALIA

Anatol Kontush, PhD
Research Director

Disclosure potential conflicts of interest	
Research contracts:	CSL, Australia
Consulting:	-
Employment in industry:	-
Stockholder of a healthcare company:	-
Owner of a healthcare company:	-
Other:	Patents, UPMC, Paris, France

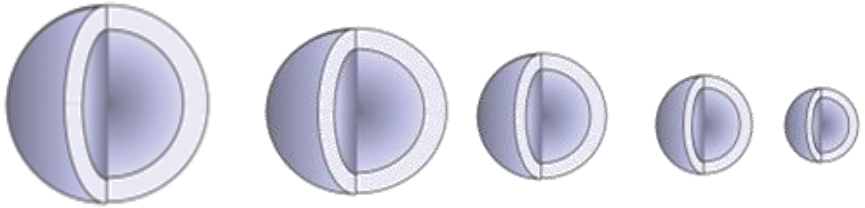
ISA 2015 AMSTERDAM

Physicochemical heterogeneity of HDL

Shape

Discoidal HDL Spherical HDL

Density and size



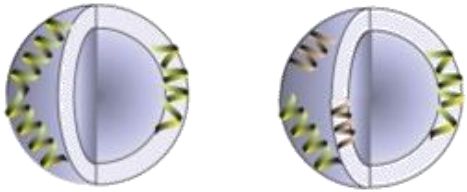
HDL2b HDL2a HDL3a HDL3b HDL3c

HDL2 HDL3

1.063 *Density (g/mL)* *1.21*

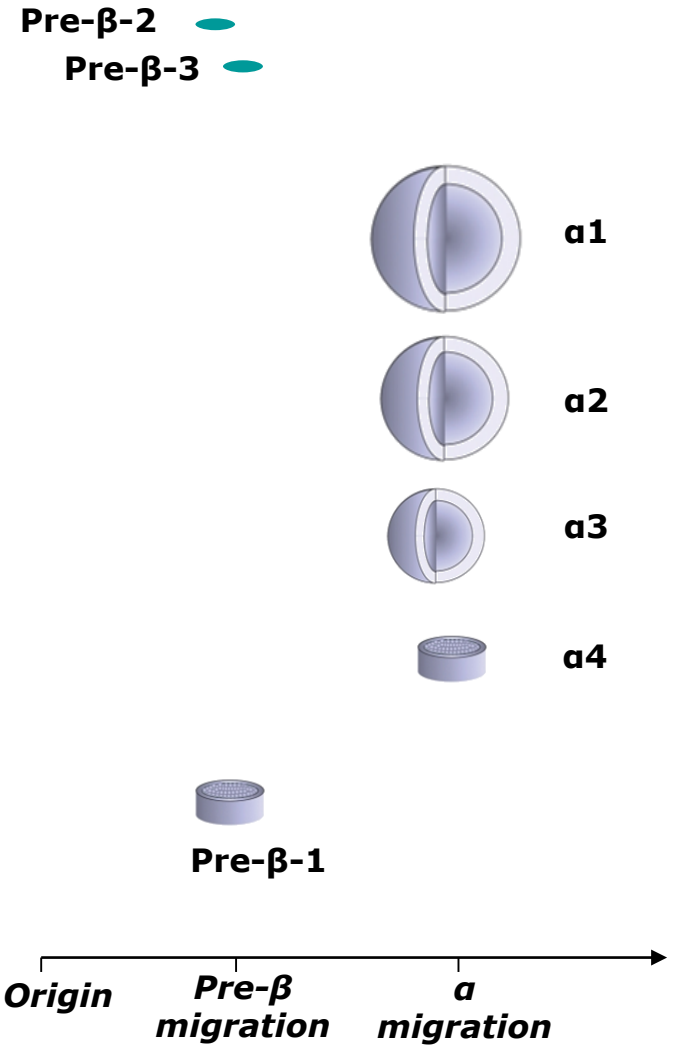
10.6 *Diameter (nm)* *7.6*

Apolipoprotein composition



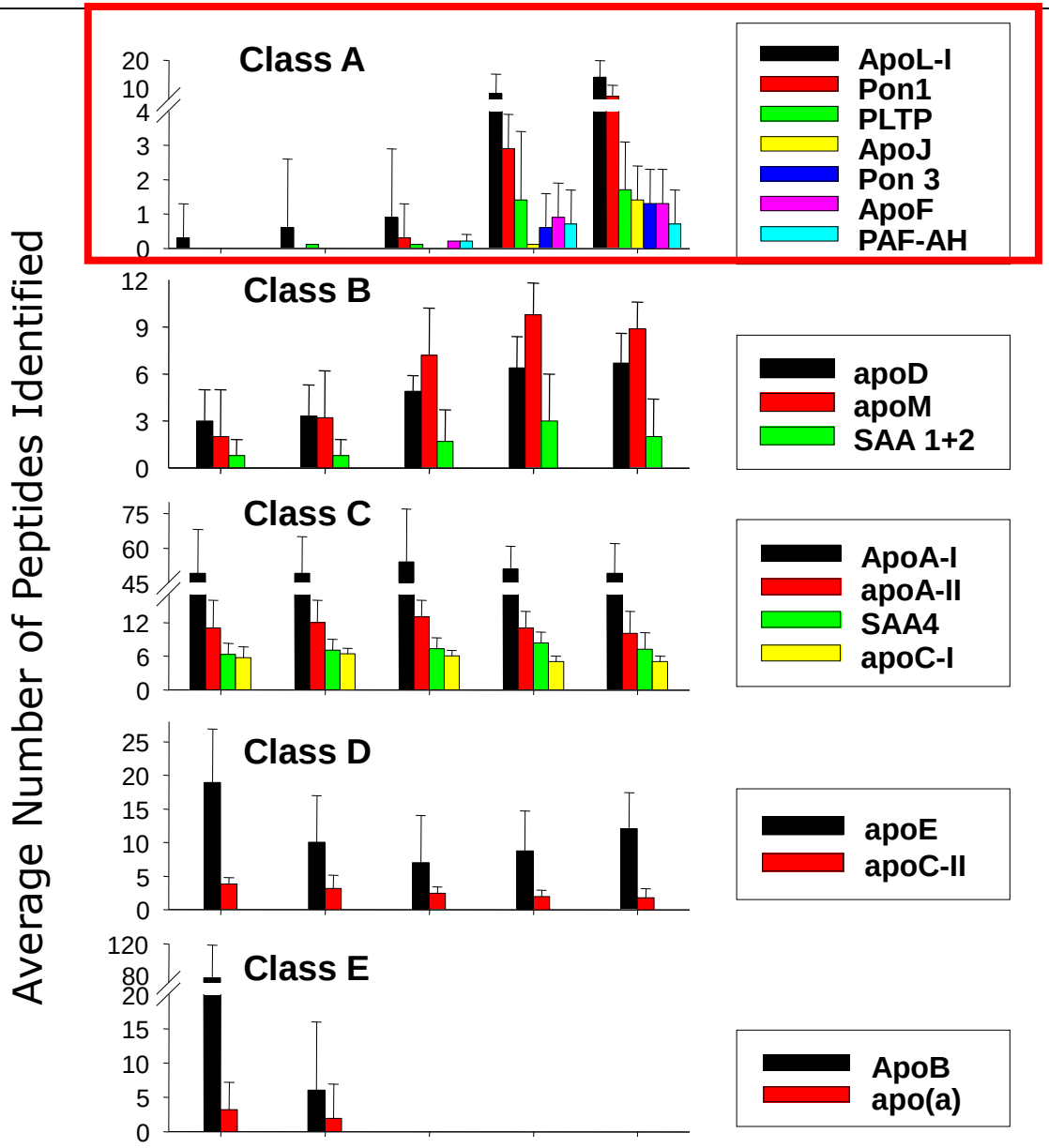
LpA-I LpA-I:A-II

Electrophoretic mobility



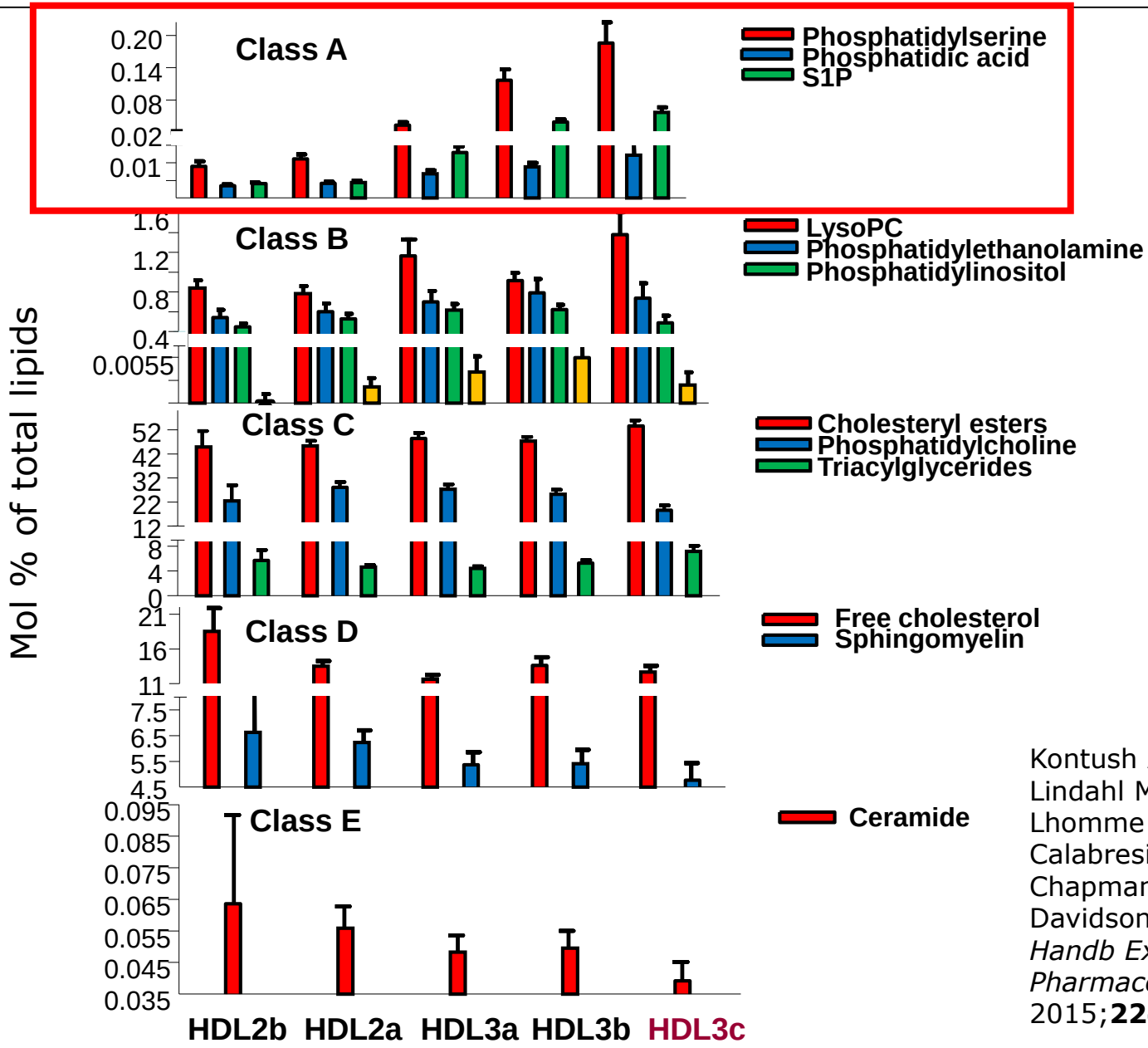
Camont L, Chapman MJ, Kontush A, *Trends Mol Med* 2011; 17: 594-603

HDL proteome is highly heterogeneous across five major HDL subpopulations



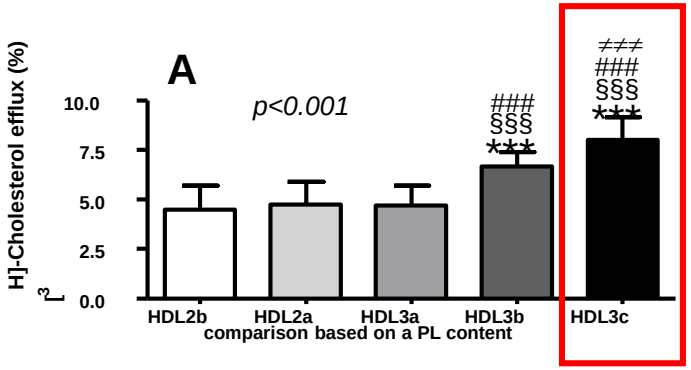
W.S. Davidson, R.A.G.D. Silva, S. Chantepie, W.R. Lagor, M.J. Chapman and A. Kontush (2009) *Arterioscler Thromb Vasc Biol.*, **29**: 870-6.

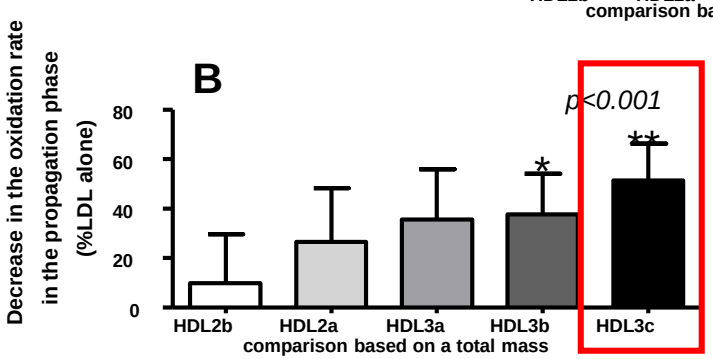
HDL lipidome is highly heterogeneous across five major HDL subpopulations

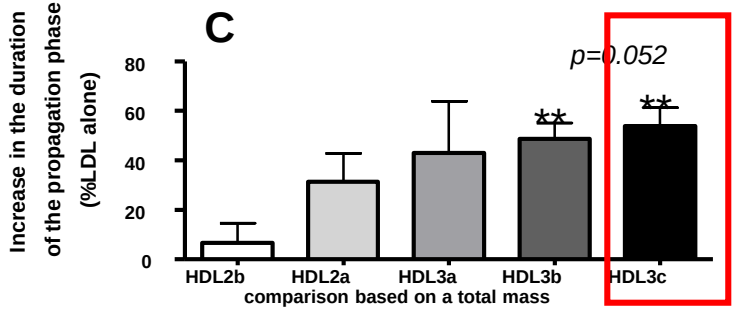


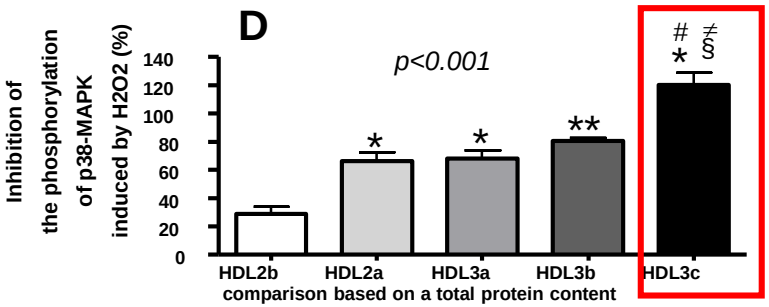
Kontush A, Lindahl M, Lhomme M, Calabresi L, Chapman MJ, Davidson WS. *Handb Exp Pharmacol.* 2015;**224**:3-51

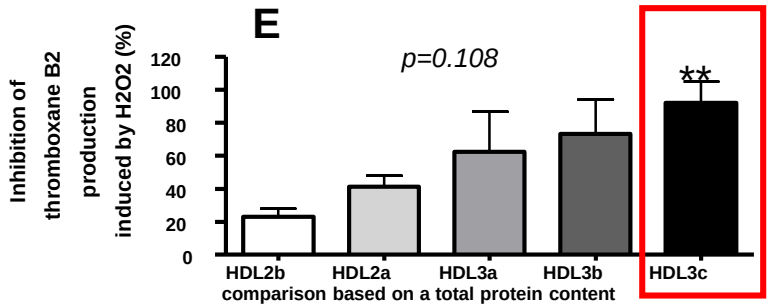
Biological activities of HDL are concentrated in small, dense particles

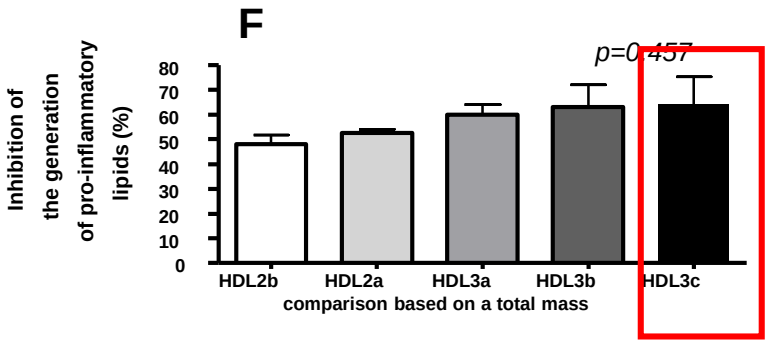


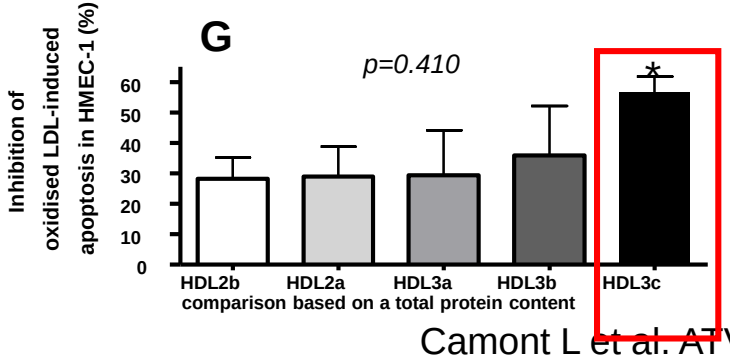






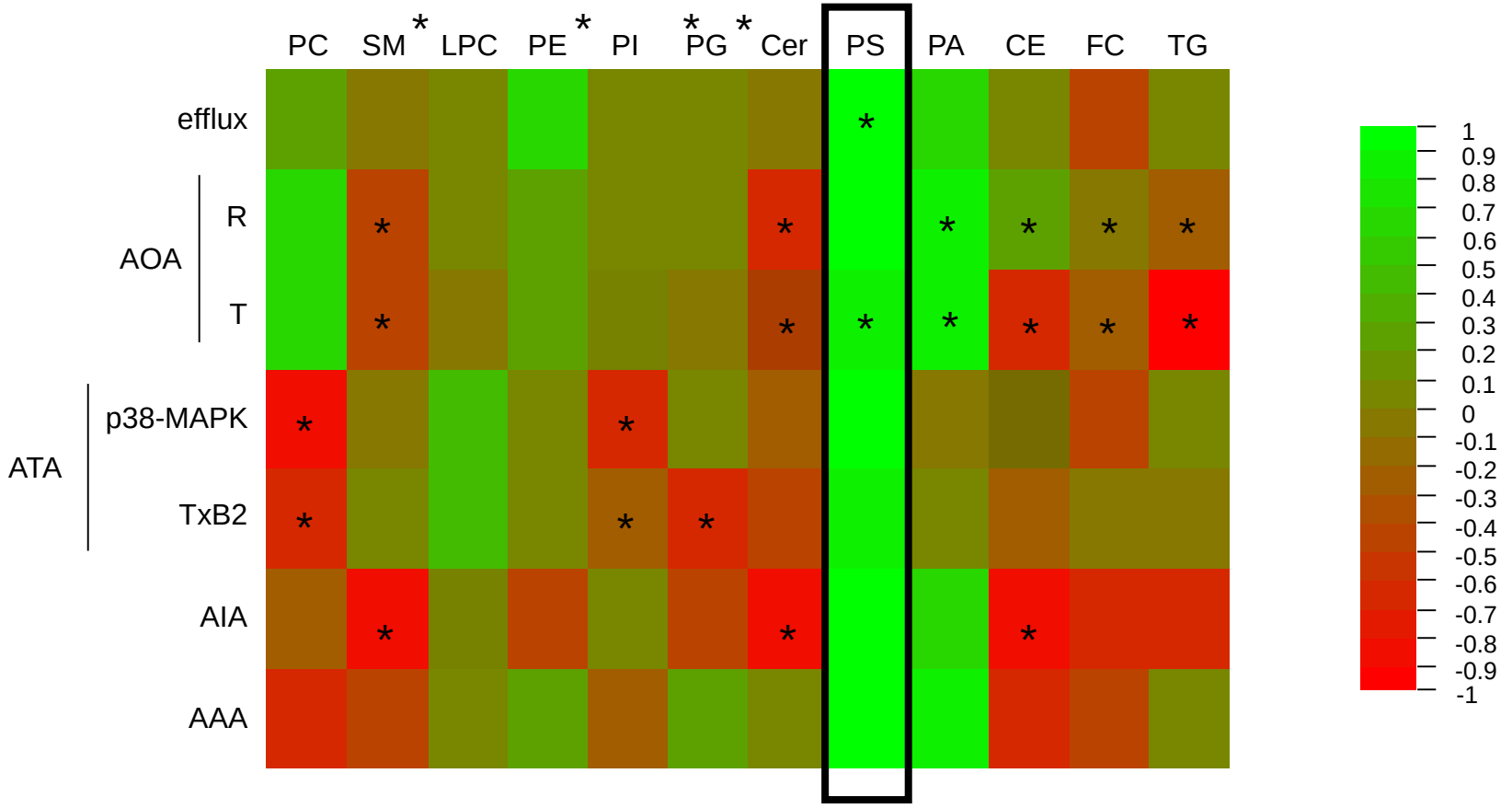






Camont L et al. ATVB 2013

Biological activities of HDL particles are positively correlated with the content of phosphatidylserine (PS)



Camont L et al. ATVB 2013

Working Hypothesis

- **Phosphatidylserine may represent an important determinant of anti-atherogenic activities of HDL**

- **Enrichment in phosphatidylserine may enhance anti-atherogenic activities of HDL**

Conclusions and perspectives

- Phosphatidylserine is enriched in small, dense HDL displaying elevated anti-atherogenic activities

- Phosphatidylserine enhances anti-inflammatory activities of rHDL both in vivo and in vitro

- Phosphatidylserine-containing rHDL may hold promise to reduce inflammation in rupture-prone, lipid-rich atherosclerotic plaques