POLYUNSATURATED LIPID SPECIES OF HDL ARE MOST STRONGLY AFFECTED BY GENETIC APOLIPOPROTEIN A-I DEFICIENCY

Emile Zakiev [ac], Fabiana Rached [b], Marie Lhomme [a], Carlos V. Serrano Jr. [b], Raul D. Santos [b], John Chapman [a], Alexander Orekhov [cd], Anatol Kontush [a]

a – UMR-ICAN 1166, National Institute for Health and Medical Research (INSERM), Paris, France

b – University of Sao Paulo , Sao Paulo, Brazil

c – Institute of General Pathology and Pathophysiology, Moscow, Russia

d – Institute for Atherosclerosis Research, Moscow, Russia

UMRS 1166

Inserm
Institut national de la santé et de la recherche médicale

UPMC SORBONNE UNIVERSITÉS

UNIVERSIDADE DE SÃO PAULO

INSTITUTE FOR ATHEROSLEROSIS RESEARCH SKOLKOVO INNOVATIVE CENTRE

Sk Resident

- Authors declare that they have no conflict of interest to disclose

Rationale

- Both circulating levels of high-density lipoprotein (HDL) and its functionality are under genetic control
- Anti-atherogenic properties of HDL depend on the molecular composition of its lipidome and proteome
- Kindreds with genetically determined low HDL-cholesterol are characterised by markedly perturbed lipoprotein metabolism

Working hypothesis

- Hereditary familial hypoHDLemia features distinct alterations in molecular species of the HDL lipidome

Experimental strategy

recruitment

Subjects: Nonsense mutation at codon -2, Q[-2]X in APOA1

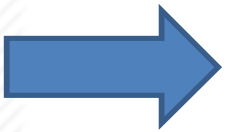
♂**=5** ♀**= 1**

Controls: Healthy normolipidemic controls

♂=9 ♀=0

Experimental strategy

recruitment



Blood sampling

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LC/MS/MS: Molecular lipid species (n=160)

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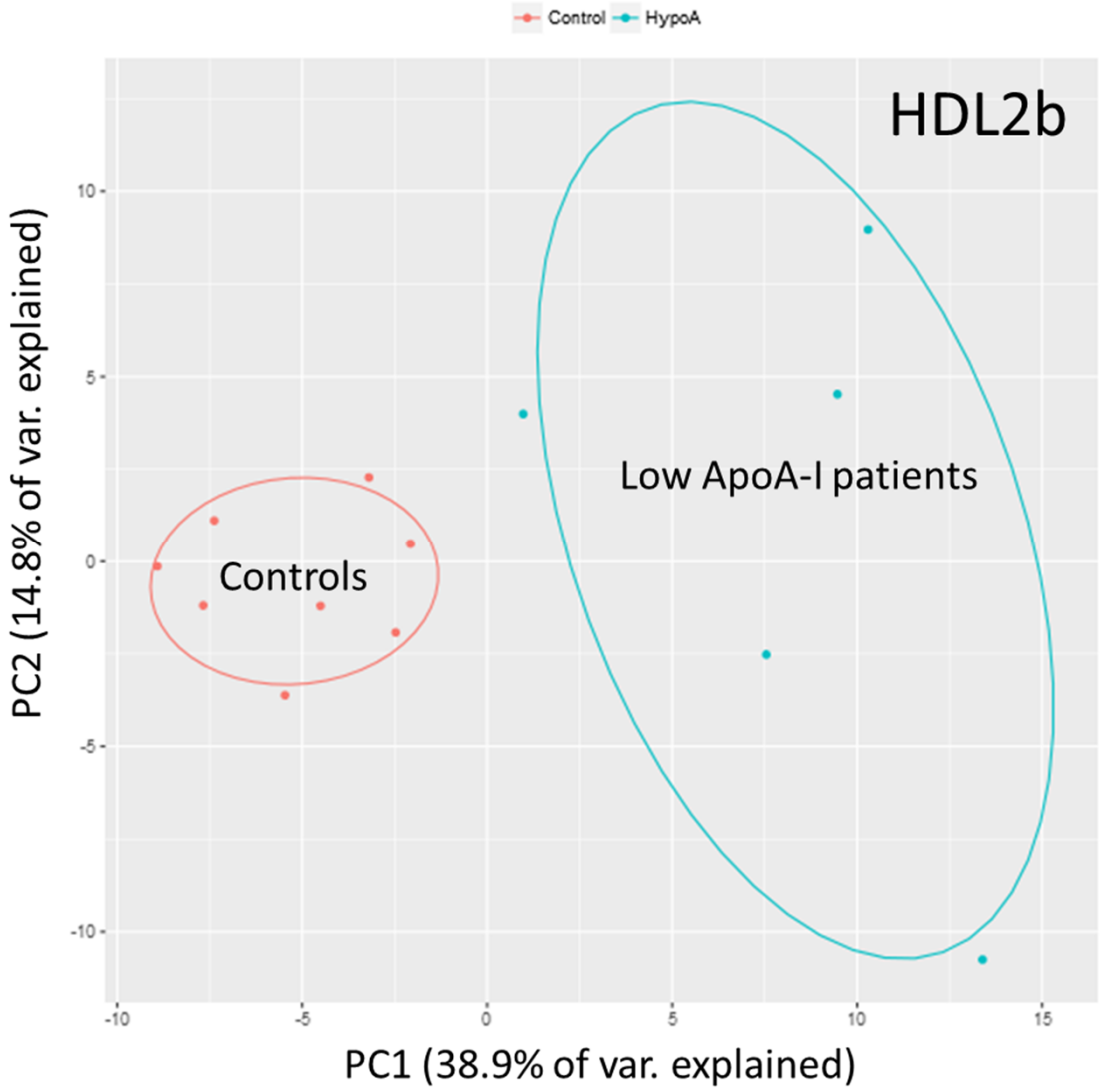
Data Analysis & Conclusions (R + plotly, ggbiplot, gplots)

Principal Component Analysis: Distinct lipidome of all HDL subpopulations in apoA-I deficiency



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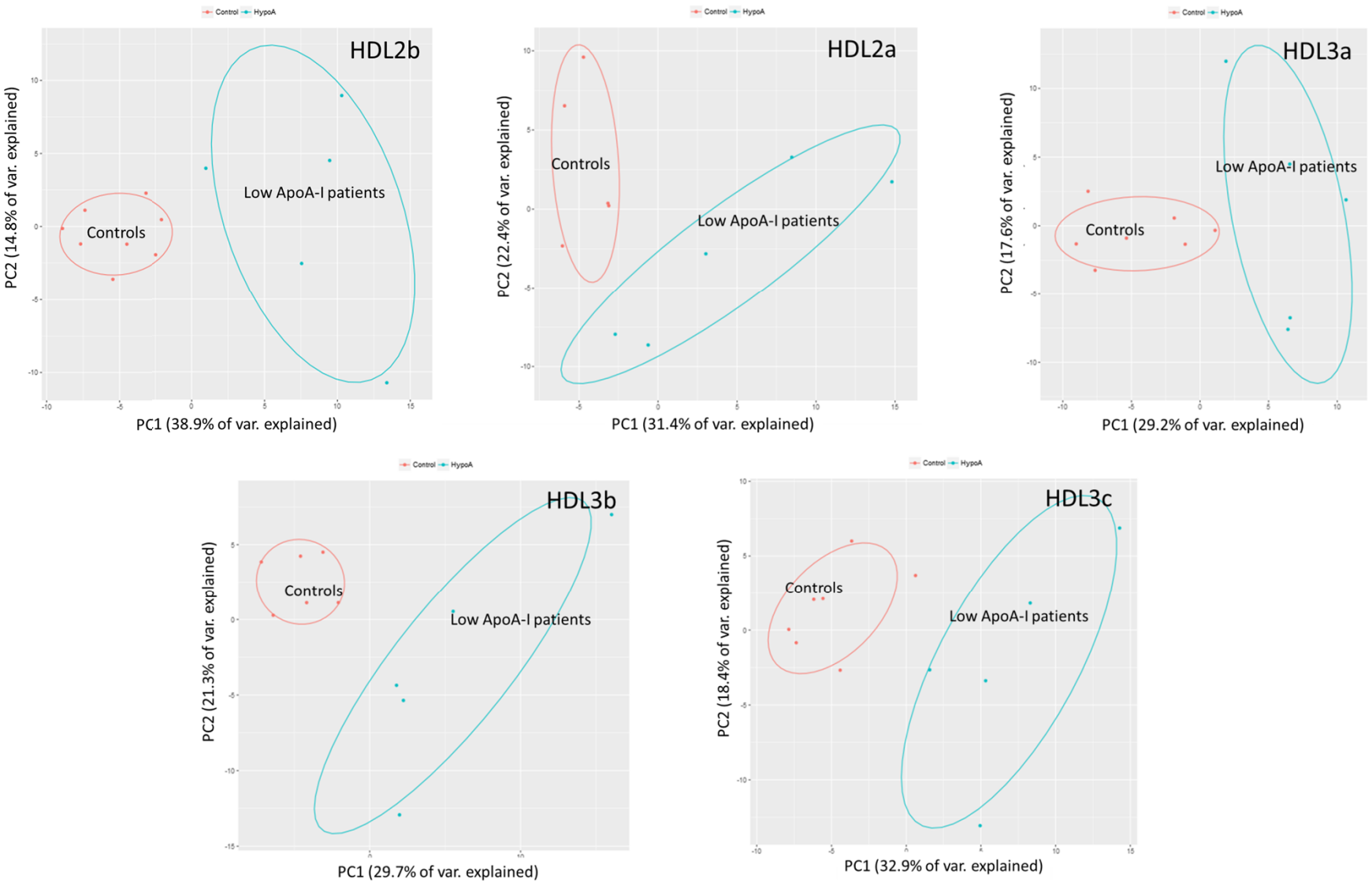
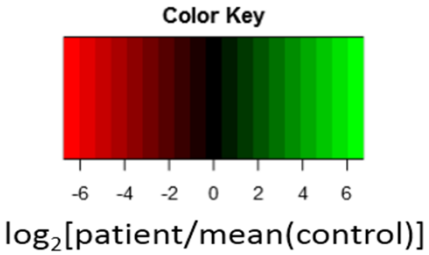
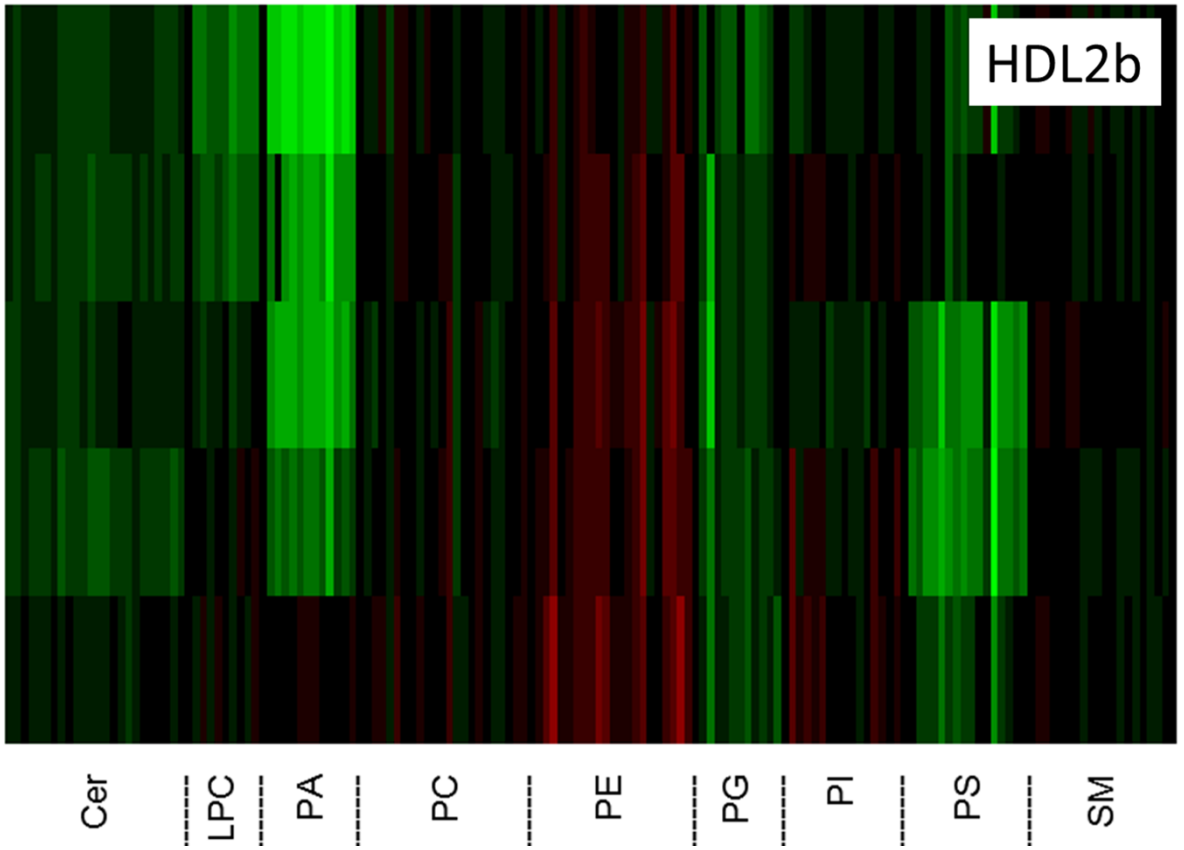
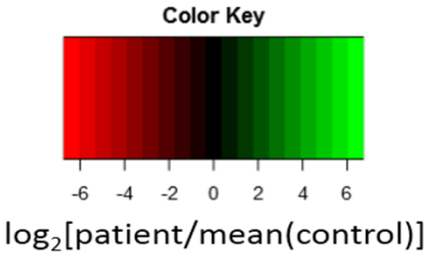




Heatmaps: Systematic alterations of molecular species of LPC, PA, PG and PE across HDL subpopulations in apoA-I deficiency





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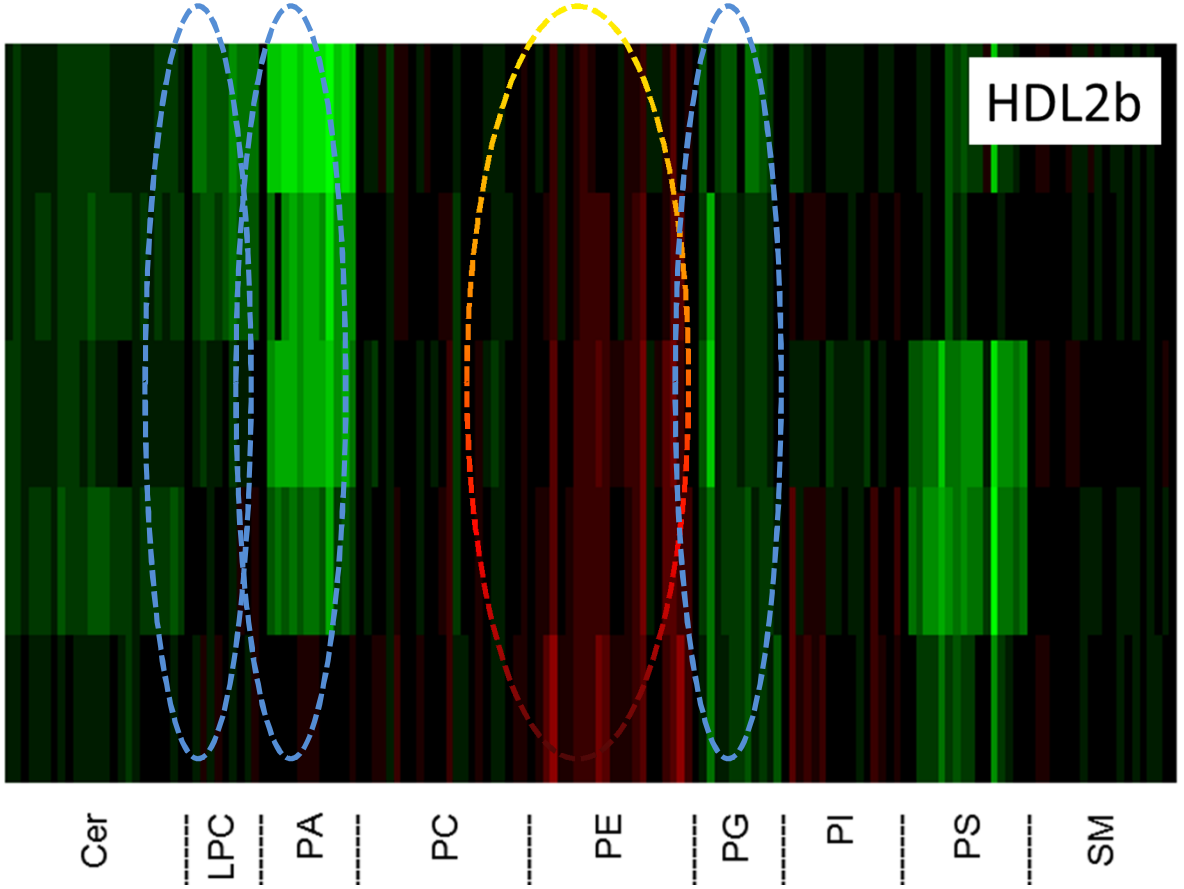

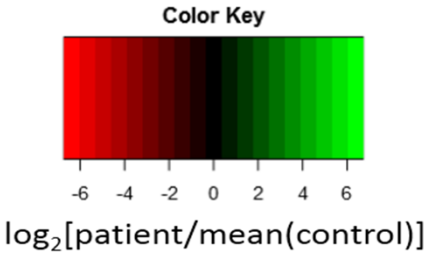

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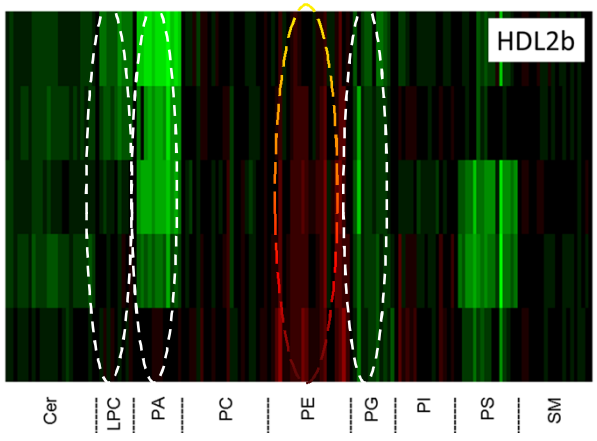
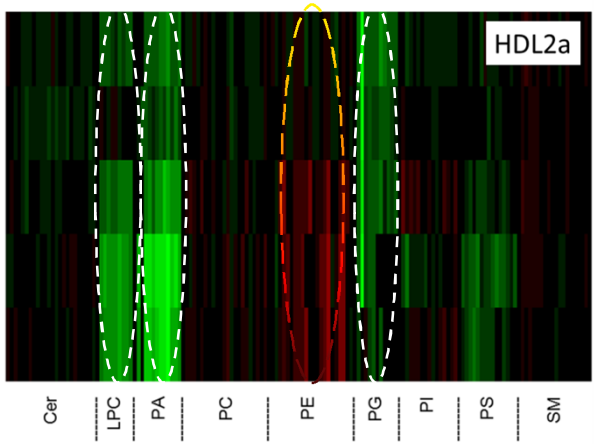
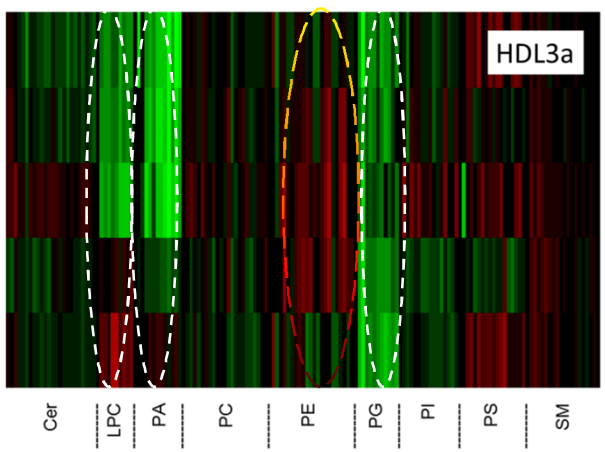
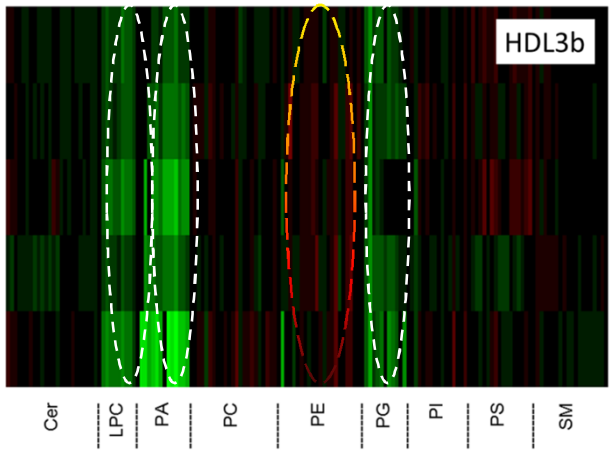
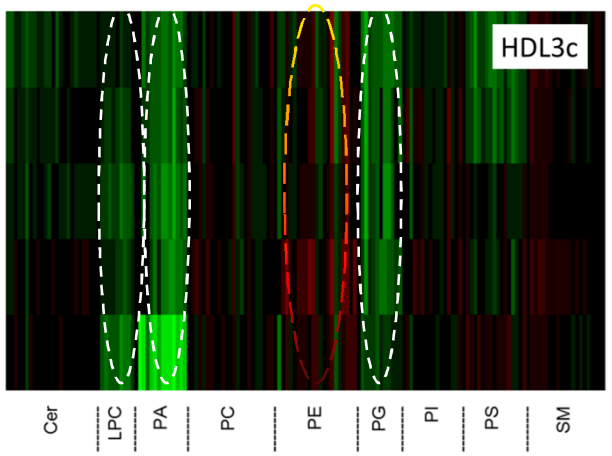


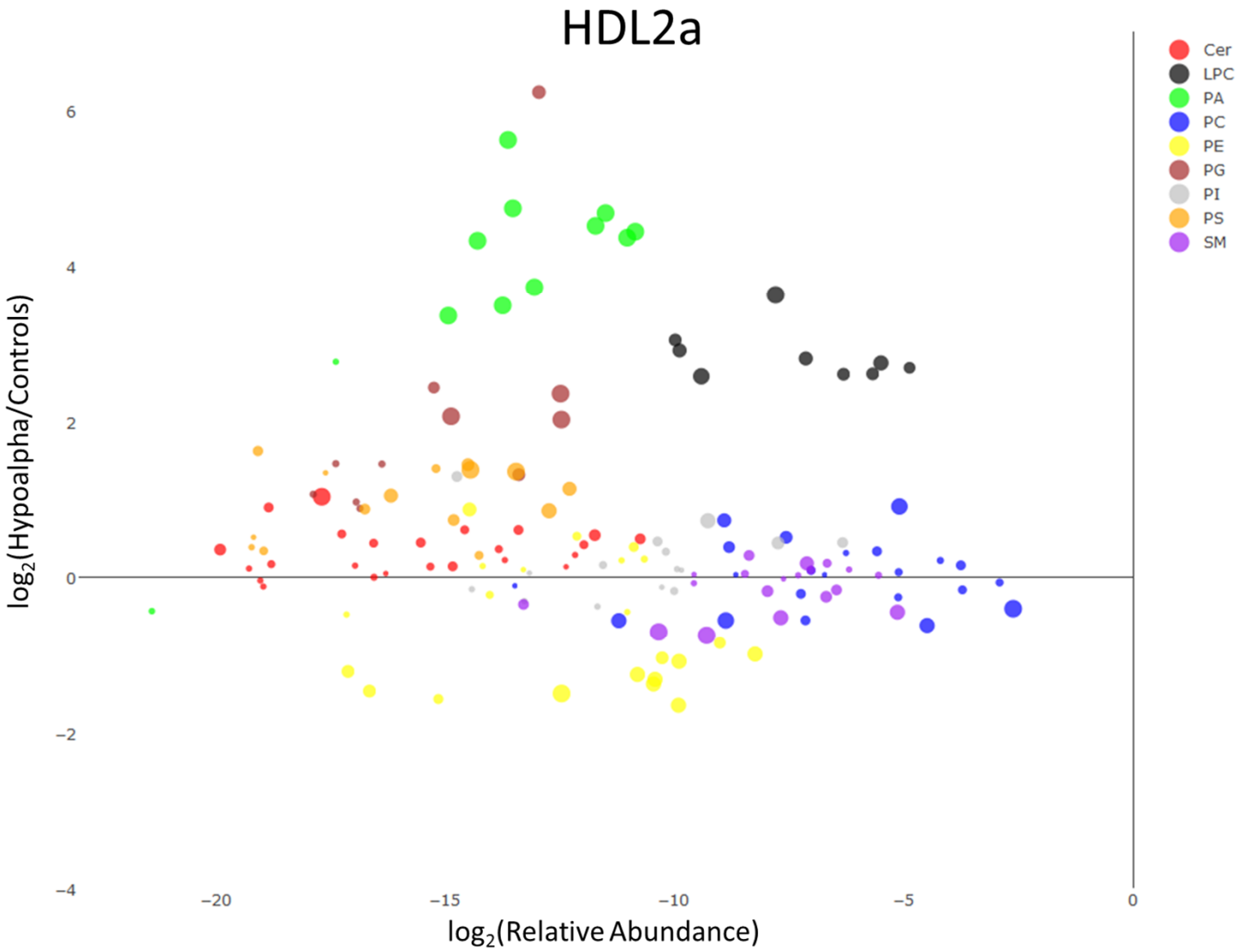








Bubble charts: Altered molecular species of LPC, PA, PG and PE are present in HDL at low-to-moderate abundance



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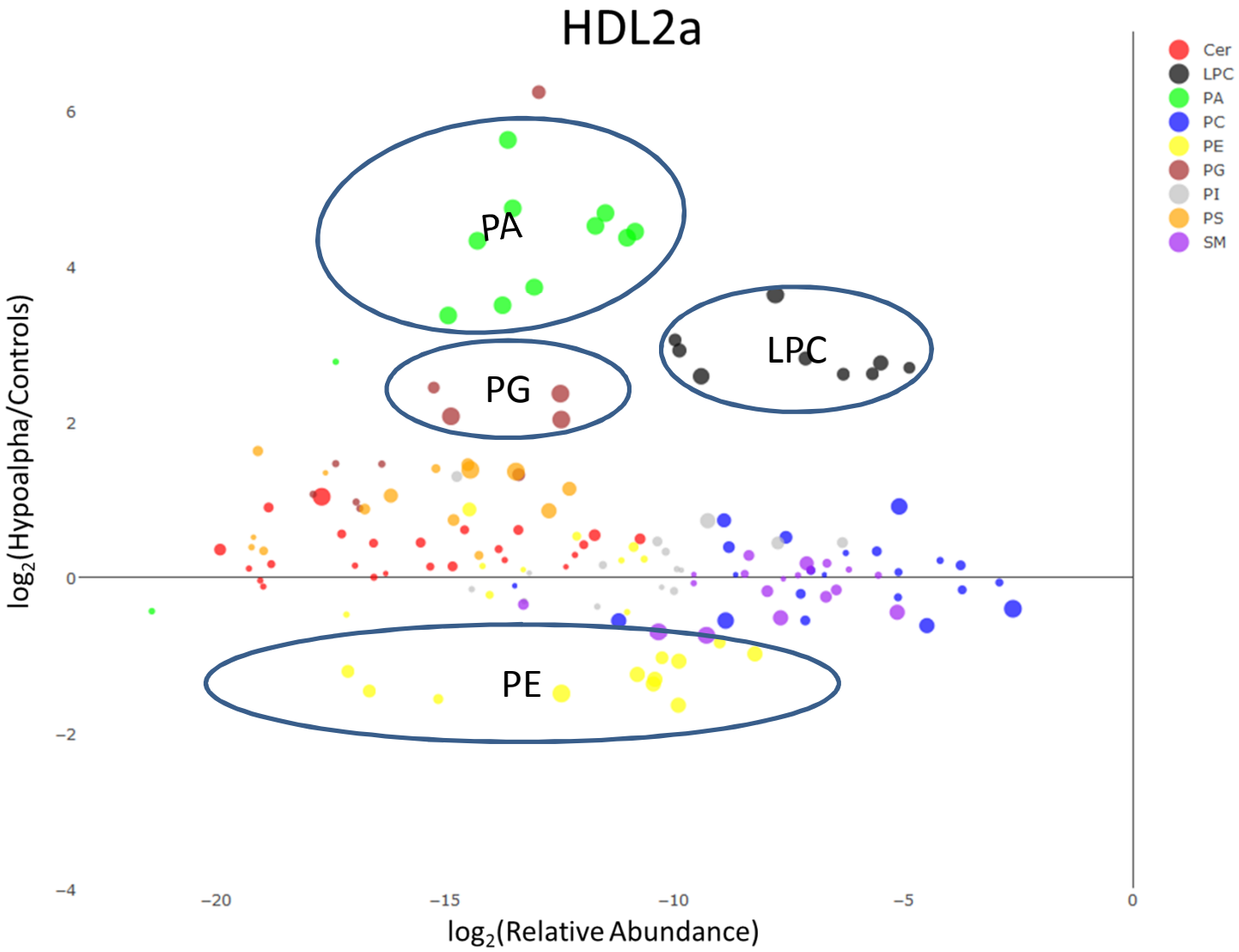

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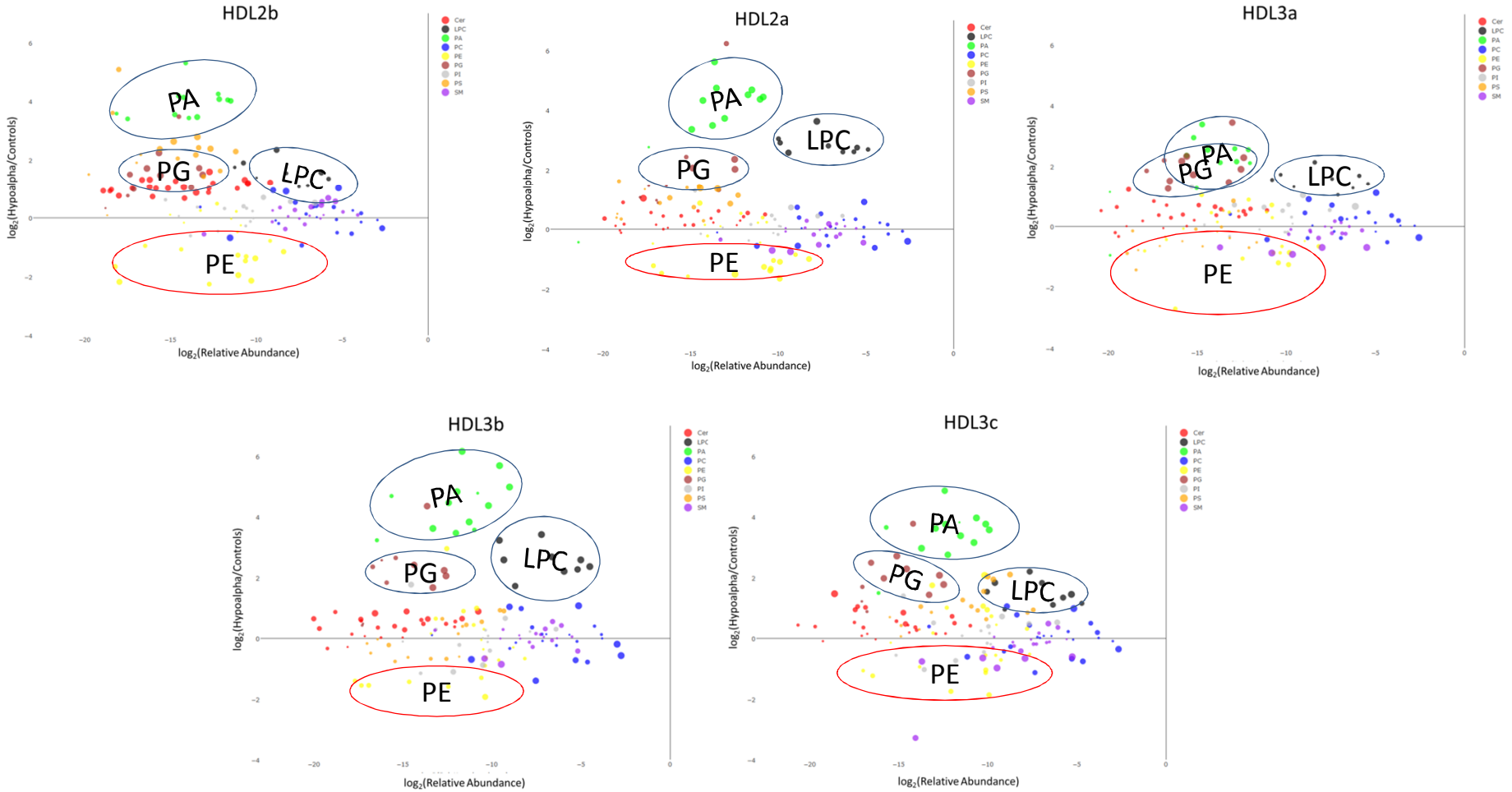
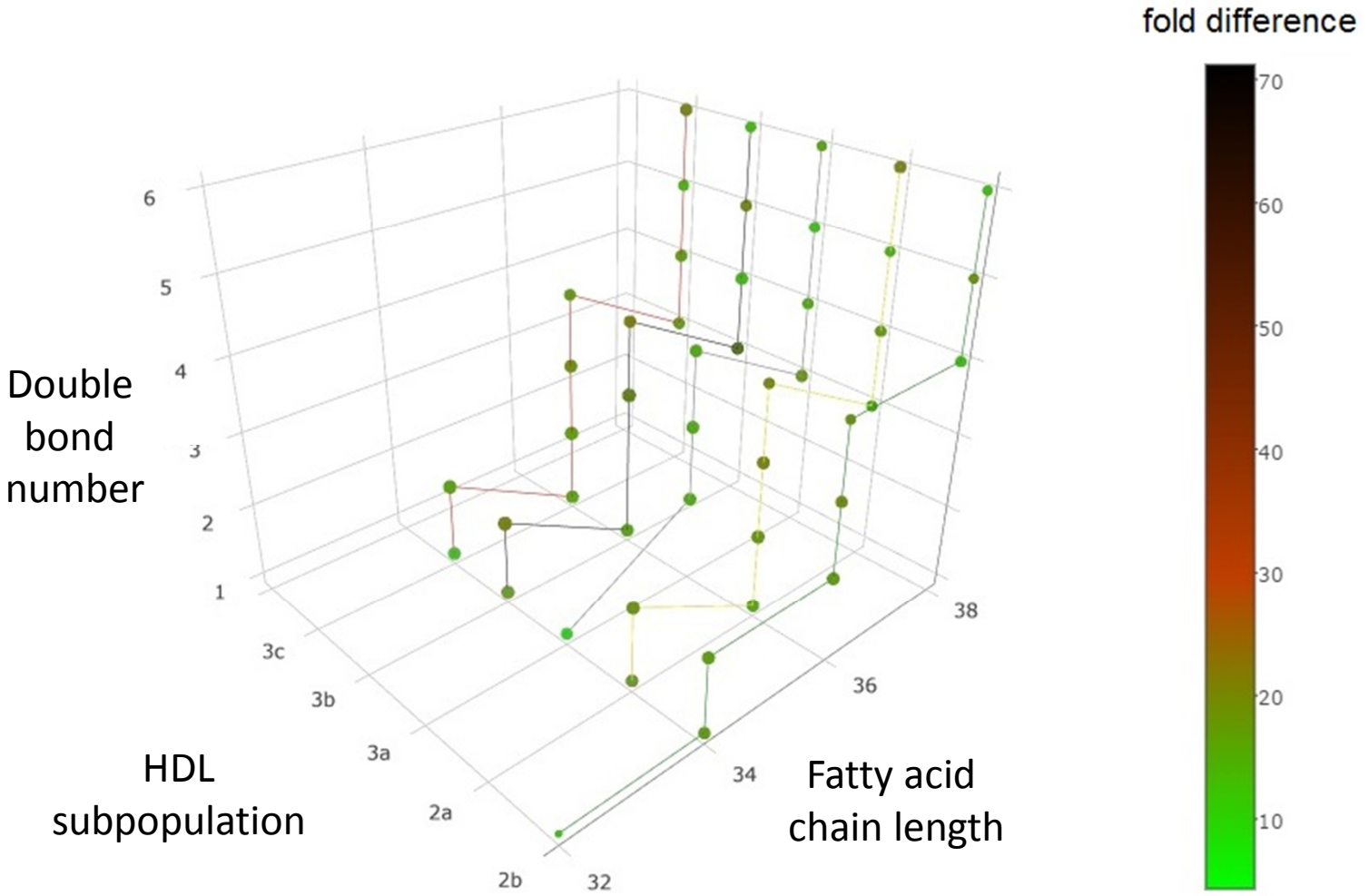
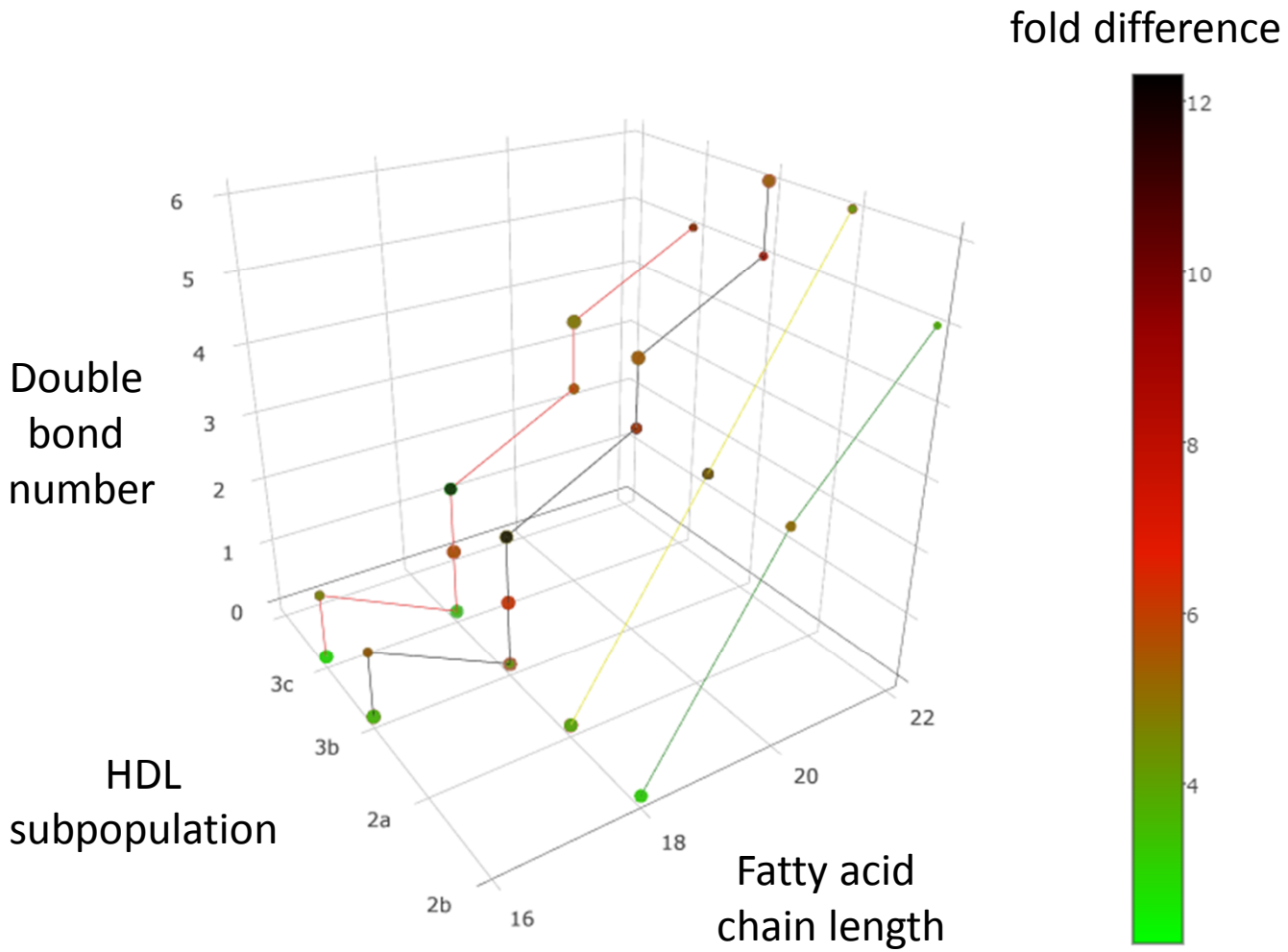


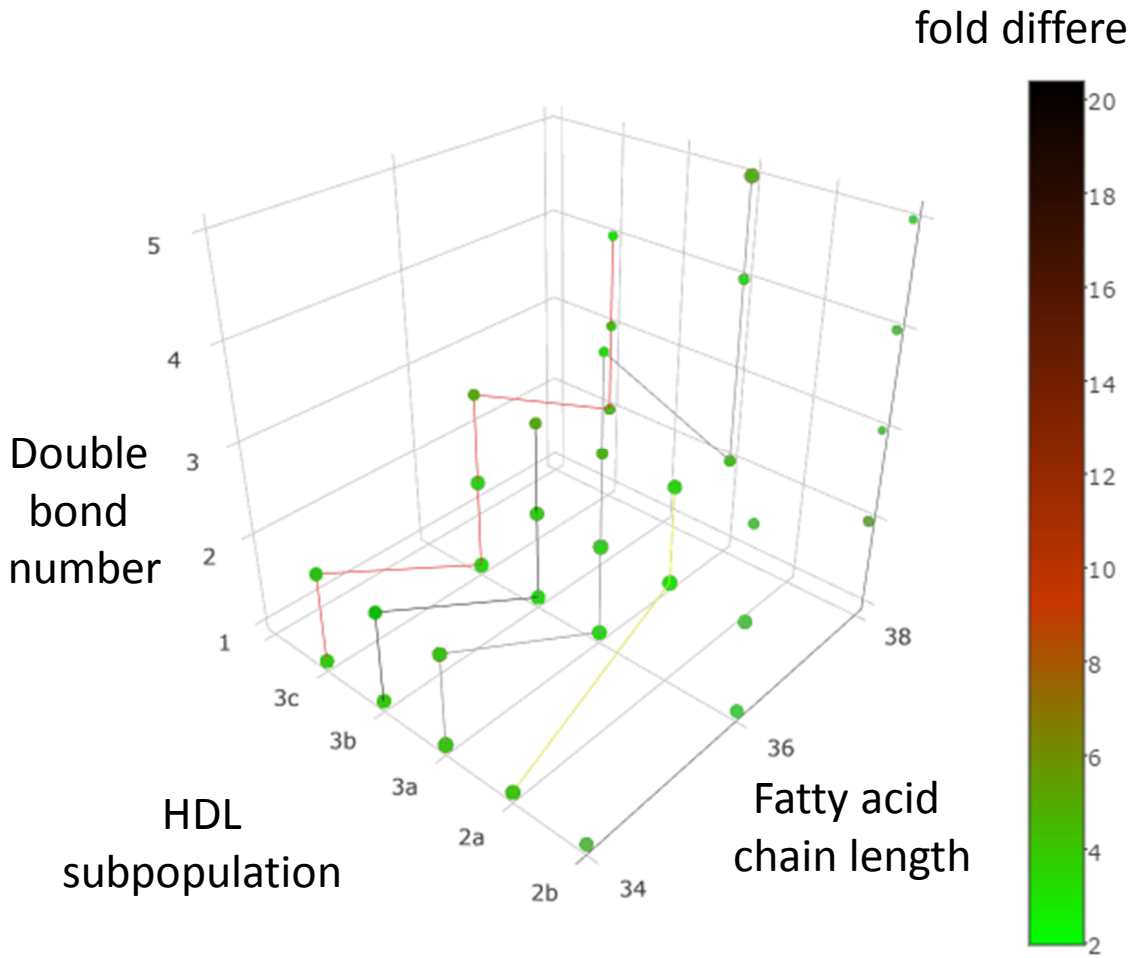
Structural analysis: PUFA-containing molecular species of **PA (36:3, 36:4, 38:4, 38:5, 38:6)** are markedly affected by apoA-I deficiency



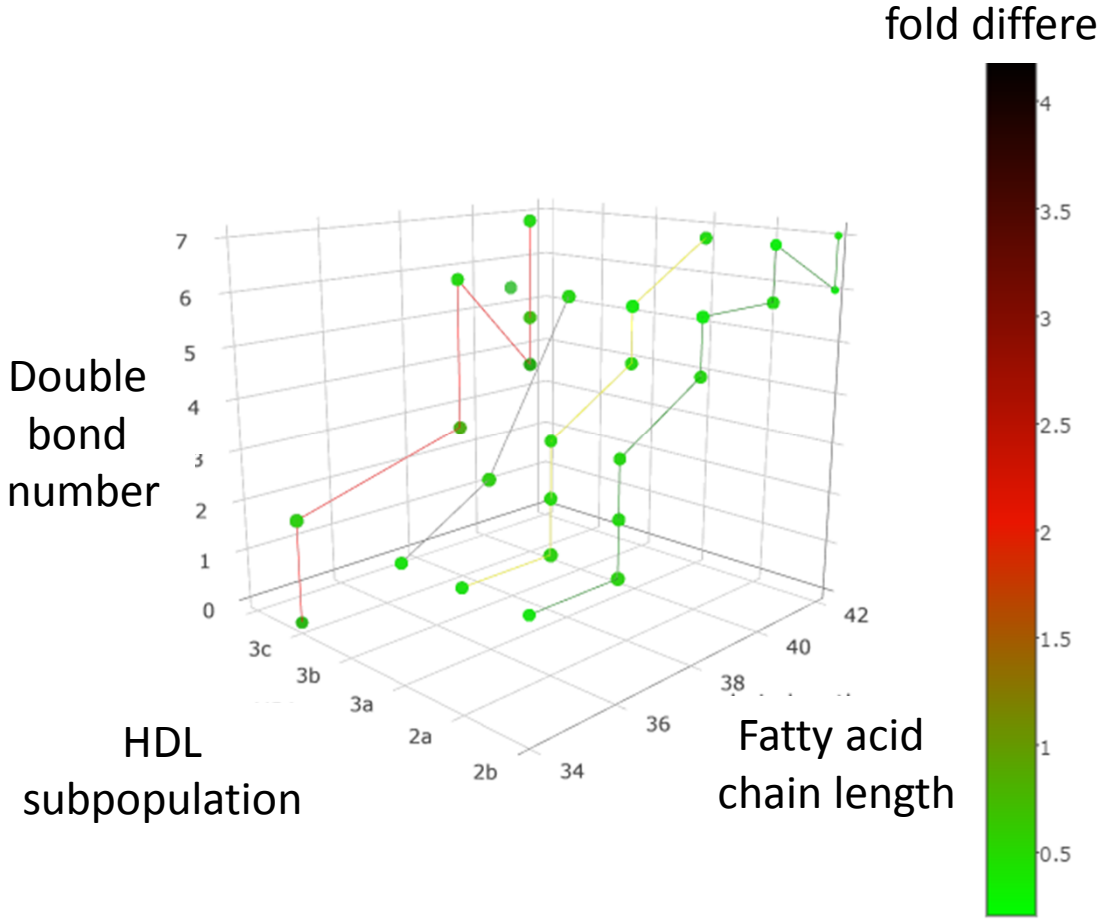
Structural analysis: PUFA-containing molecular species of LPC (18:2) are markedly affected by apoA-I deficiency



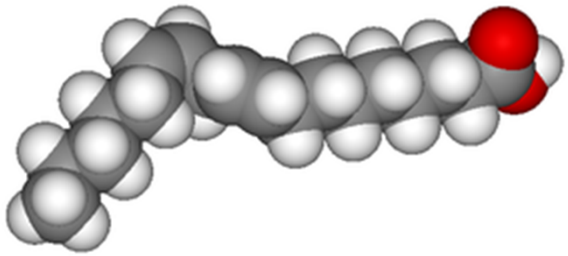
Structural analysis: PUFA-containing molecular species of PG (36:2 and 36:3) are markedly affected by apoA-I deficiency



Structural analysis: PUFA-containing molecular species of **PE (34:2, 38:6)** are markedly affected by apoA-I deficiency



Conclusions



- Low-to-moderately abundant, polyunsaturated fatty acid-containing phospholipid species of HDL, primarily PA(36:3), PA(36:4), PA(38:4), PA(38:5), PA(38:6), PG(36:2), PG(36:3), LPC(18:2), PE(34:2) and PE(38:6), are strongly affected by genetic apoA-I deficiency
- Elevated content of PA and LPC may reflect enhanced hydrolytic processing of HDL lipids
- Increased PA levels may result in activation of pro-inflammatory signalling pathways and may serve as biomarkers of impaired HDL function

Thank you for your attention!