Metabolic View on Human Healthspan: A Lipidome-Wide Association Study

JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

ID 4621229
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Year 2021
Title Metabolic View on Human Healthspan: A Lipidome-Wide Association Study
Journal Metabolites
Volume 11
Number 5
Pages / **Article-Number** 287
Keywords healthspan; healthy population study; lipidomics; metabolic phenotyping; serum lipid signature
As ageing is a major risk factor for the development of non-communicable diseases, extending healthspan has become a medical and societal necessity. Precise lipid phenotyping that captures metabolic individuality could support healthspan extension strategies. This study applied 'omic-scale lipid profiling to characterise sex-specific age-related differences in the serum lipidome composition of healthy humans. A subset of the COmPLETE-Health study, composed of 73 young (25.2 ś 2.6 years, 43% female) and 77 aged (73.5 ś 2.3 years, 48% female) clinically healthy individuals, was investigated, using an untargeted liquid chromatography high-resolution mass spectrometry approach. Compared to their younger counterparts, aged females and males exhibited significant higher levels in 138 and 107 lipid species representing 15 and 13 distinct subclasses, respectively. Percentage of difference ranged from 5.8% to 61.7% (females) and from 5.3% to 46.0% (males), with sphingolipid and glycerophophospholipid species displaying the greatest amplitudes. Remarkably, specific sphingolipid and glycerophospholipid species, previously described as cardiometabolically favourable, were found elevated in aged individuals. Furthermore, specific ether-glycerophospholipid and lyso-glycerophosphocholine species displayed higher levels in aged females only, revealing a more favourable lipidome evolution in females. Altogether, age determined the circulating lipidome composition, while lipid species analysis revealed additional findings that were not observed at the subclass level.
Publisher MDPI
ISSN/ISBN 2218-1989
edoc-URL https://edoc.unibas.ch/83498/
Full Text on edoc No;
Digital Object Identifier DOI 10.3390/metabo11050287
PubMed ID http://www.ncbi.nlm.nih.gov/pubmed/33946321
ISI-Number WOS:000654287400001
Document type (ISI) Journal Article