Microbial metabolites are associated with a high adherence to a Mediterranean dietary pattern using a 1H-NMR-based untargeted metabolomics approach

Almanza-Aguilera E^{1,2*}, Urpi-Sarda M^{1,2#}, Llorach R^{1,2}, Vázquez-Fresno R¹, Garcia-Aloy M^{1,2}, Carmona F³, Sánchez A^{3,4}, Madrid-Gambin F^{1,2}, Estruch R^{5,6}, Corella D^{5,7}, Andres-Lacueva C^{1,2#}

¹Biomarkers and Nutrimetabolomics Laboratory, Nutrition, Food Science and Gastronomy Department, XaRTA, Institut de Recerca en Nutrició i Seguretat Alimentària de la Universitat de Barcelona (INSA-UB), Campus de l'Alimentació Torribera, Faculty of Pharmacy and Food Science, University of Barcelona, Barcelona 08028, Spain.

²CIBER Fragilidad y Envejecimiento Saludable (CIBERFES), Instituto de Salud Carlos III, Madrid 28028, Spain.

³Department of Genetics, Microbiology and Statistics, University of Barcelona, Barcelona, Spain.

⁴Statistics and Bioinformatics Unit. Vall d'Hebron Institut de Recerca, Barcelona, Spain.

⁵CIBER Fisiopatología de la Obesidad y Nutrición (CIBEROBN), Instituto de Salud Carlos III, Madrid 28028, Spain.

⁶Department of Internal Medicine, Institut d'Investigacions Biomediques August Pi Sunyer (IDIBAPS), Hospital Clinic, University of Barcelona, Barcelona, 08036, Spain.

⁷Department of Preventive Medicine, University of Valencia, Valencia 46010, Spain.

*Presenting autor and #Corresponding authors

Background and objectives:

The study of biomarkers of dietary patterns including the Mediterranean diet (MedDiet) is scarce and could improve the assessment of these patterns. We aimed to determine a robust and accurate biomarker associated with a high adherence to a MedDiet pattern that included dietary assessment and its biological effect.

Methodology:

In this cross-sectional study we included 56 and 63 individuals with high (H-MDA) and low (L-MDA) MedDiet adherence categories, respectively, all from the Prevención con Dieta Mediterránea trial. A ¹H-NMR-based untargeted metabolomics approach was applied to urine samples. Multivariate statistical analyses were conducted to determine the metabolite differences between groups, as well as to build and evaluate the prediction model for H-MDA.

Results and conclusions:

Thirty-four metabolites were identified as discriminant between H-MDA and L-MDA. The H-MDA included higher excretion of food metabolome metabolites, and decreased amounts of metabolites related to glucose metabolism. The microbial metabolites: phenylacetylglutamine, p-cresol and 4-hydroxyphenylacetate were included in the prediction model of H-MDA, thus being the biomarker

that defined high adherence to the MedDiet. The overall metabolite profiling identified reflects the metabolic modulation produced by H-MDA. The proposed biomarker may be a better tool for assessing and aiding nutritional epidemiology in future associations between H-MDA and the prevention or amelioration of chronic diseases.

Acknowledgements:

M.U.S. would like to thank the "Ramón y Cajal" program from MINECO and the Fondo Social Europeo (RYC-2011-09677). E.A.A. would like to thank CONACYT (México) for the Ph.D. fellowship. F.M.G. acknowledges the APIF Ph.D. fellowship (University of Barcelona).