

# Bioactive lipids as potential markers of cardiometabolic health in young adults

Xinyu Di<sup>1</sup>, Lucas Jurado Fasoli<sup>2</sup>, Thomas Hankemeier<sup>1</sup>, Patrick Rensen<sup>3</sup>, Borja Martinez-Tellez<sup>3</sup>, Isabelle Kohler<sup>4,\*</sup>

<sup>1</sup> *Division of Systems Biomedicine and Pharmacology Leiden Academic Center for Drug Research, Leiden University, Leiden, The Netherlands*

<sup>2</sup> *Department of Medical Physiology, School of Medicine, University of Granada, Granada, Spain*

<sup>3</sup> *Department of Medicine, Division of Endocrinology, Leiden University Medical Center, Leiden, The Netherlands; Einthoven Laboratory for Experimental Vascular Medicine, Leiden University Medical Center, Leiden, The Netherlands.*

<sup>4</sup> *Division of BioAnalytical Chemistry, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands*

## Gold statement

- Understand the role metabolomics can play in cardiometabolic research
- Discover the relations between bioactive lipids and cardiometabolic health

## Introduction

The prevalence of cardiometabolic disease has gradually increased over the last years, posing a serious health and economic burden. Evidence shows that  $\omega$ -3 and  $\omega$ -6 polyunsaturated fatty acids intake can influence the cardiometabolic health, but little is known about the impact of circulating bioactive lipids levels on body composition and cardiometabolic risks. In this study, targeted metabolomics was used to investigate the possible associations between circulating bioactive lipids levels and cardiometabolic health in a cohort of young adults.

## Body

This cross-sectional study included 136 young adults. Clinical data collected included anthropometric and body composition, brown adipose tissue volume, and classic cardiometabolic parameters such as glucose and insulin levels, total cholesterol, apolipoproteins, liver enzymes activity, triglycerides, C-reactive protein, leptin and adiponectin, blood pressure as well as inflammatory markers. Targeted metabolomics experiments were performed using liquid chromatography – tandem mass spectrometry (LC-MS/MS), targeting  $\omega$ -3 and  $\omega$ -6 polyunsaturated fatty acids. A total of 50 bioactive lipids were detected in plasma samples at fasting conditions, most of them showing a variability lower than 15% (expressed a relative standard deviation) in quality control samples.

The  $\omega$ -6 lipids 8-HETrE, 15-HETrE, 8,12-iso-iPF<sub>2</sub> $\alpha$ -VI, and 14,15-EpETrE plasma levels were shown to be correlated with increased adiposity and an exacerbated cardiometabolic profile. On the other hands, the  $\omega$ -3 lipids 14,15-DiHETE, 17,18-DiHETE, and 19,20-DiHDPA plasma levels were associated with a lower adiposity and a better cardiometabolic profile. Moreover, obese individuals showed an upregulated  $\omega$ -6 lipid pathway compared to normal-weight individuals. Overall, the bioactive lipid plasma levels did not improve the prediction of adiposity compared with classical cardiometabolic factors, but they were better predictors of adiposity than classical inflammatory markers.

## Conclusion

Using LC-MS/MS-based metabolomics, we showed that the bioactive  $\omega$ -6 lipids 15-HeTrE, 5-HETE, 14,15-EpETrE and 8,12-iso-iPF<sub>2</sub> $\alpha$ -VI were related with increased adiposity and an exacerbated cardiometabolic profile in young healthy adults, while the bioactive  $\omega$ -3 lipids 14,15-DiHETE, 17,18-DiHETE, and 19,20-DiHDPA were related with less adiposity and a better cardiometabolic profile.