



SPHINGOLIPID CLUB

## **XV SPHINGOLIPID CLUB MEETING**

3 -7 Sept 2024, Friedrich-Alexander-University Erlangen-Nürnberg

### **MEETING BOOK**



## The Relationship of Glucose Intolerance/Diabetes and Overweight/Obesity with Sphingolipidoma Alterations

C. Morano<sup>1</sup>, L. Centofanti<sup>2</sup>, M. Dei Cas<sup>2</sup>, S. Penati<sup>2</sup>, E. Bianco<sup>2</sup>, M. Bignotto<sup>2</sup>, C. Berra<sup>3</sup>, P. Zermiani<sup>2</sup>, R. Paroni<sup>2</sup>, P.M. Battezzati<sup>2,3</sup>, F. Folli<sup>2,3</sup>

<sup>1</sup> University of Milan, Department of Pharmaceutical Sciences, Milan, Italy

<sup>2</sup> University of Milan, Department of Health Sciences, Milan, Italy

<sup>3</sup> ASST Santi Paolo e Carlo, Ospedale San Paolo, Milan, Italy

The CA.ME.LI.A (CArdiovascular risks, MEtabolic syndrome, LIver, and Autoimmune disease) epidemiological study aimed at exploring the associations between cardiovascular, metabolic, hepatobiliary, and autoimmune diseases in a representative population from Northern Italy (n=2545, 1251 men), with the primary goal of identifying risk factors for cardiovascular disease. In this work, we examined whether a unique sphingolipid profile, potentially a new biomarker for *diabetes*, could be associated with overweight/obesity and glucose intolerance/diabetes.

A random sample of 368 individuals (n=367, 217 men, 150 women) underwent plasma lipid extraction and LC-MS/MS analysis and was stratified according to BMI (NBW < 25 kg/m<sup>2</sup>, OWO ≥ 25 kg/m<sup>2</sup>) and fasting glycemia (NFG <100 mg/dl, IFG 100 – 125 mg/dL, DM ≥ 126 mg/dL). By combining these two variables, six groups were created: 1. NFG/NBW; 2. NFG/OWO; 3. IFG/NBW; 4. IFG/OWO; 5. DM/NBW; 6. DM/OWO.

The most notable changes were observed when glucose intolerance occurred alongside overweight or obese individuals. Specifically, dihydroceramides were found to be higher in the IFG/OWO group (0.39±0.18 uM) compared to NGT/OWO (0.35±0.18 uM) and DM/OWO (0.32±0.2 uM), suggesting that the accumulation of these molecules may serve as an early marker of glucose intolerance. In diabetic patients, both those with obesity (DM/OWO, 13.9±7.2 uM) and those of normal weight (DM/NBW, 16.6±6 uM), hexosylceramides were significantly lower compared to the other groups (NGT/NBW, 19.9±6 uM). Foremost, sphingosine-1-phosphate, a biologically active sphingolipid with a remarkable signaling activity, was significantly reduced in IFG/OWO (1.8±0.5 uM) and DM/OWO (1.8±0.7 uM) patients compared to NGT/OWO (2.2±0.7 uM).

This study highlights notable shifts in plasma sphingolipid levels among individuals with diabetes and glucose intolerance, highlighting their role as promising biomarkers, particularly when glucose intolerance coincides with overweight or obesity, suggesting a potential synergistic effect. Moreover, these alterations may be identifiable even at glucose levels as low as ≥126 mg/dL (7.0 mmol/L), underscoring their diagnostic potential.