Increased fasting or post-OGTT glucose levels are used for the diagnosis of obesity-associated carbohydrate metabolism impairment in adults. However, in obese children hyperinsulinism as a consequence of insulin resistance (IR) is usually found much earlier than the rise in glyceria. In childhood obesity, huge variations in fasting and postprandial insulinemia are observed for a given BMI, even in age, sex and ethnic controlled comparisons. This suggests the existence of predisposing factors for obesity associated IR that remain unclear to date.

**HYPOTHESIS**

The use of metabolic techniques could be a suitable approach to investigate the relationship between obesity and IR.

**OBJECTIVES**

• Our aim was to use a multiplatform metabolomics approach to elucidate the metabolic alterations in obese children with or without IR. In addition, we aimed to employ this revolutionary strategy to interpret the interaction of genetic and environmental factors by studying the final process of IR.

**BIOLGICAL MODEL**

- Pre-pubertal obese children
- Between 5 and 13 years
- 30 males and 30 females
- 30 insulin and 30 non-insulin resistant

**METABOLITE IDENTIFICATION**

- GC and CE
- Accurate masses matched in public databases (METLIN, LIPID MAPS, KEGG) and CEU mass mediator
- Isotopic pattern distribution
- Formula matching
- MS/MS analysis (LC)

**DATA ACQUISITION**

- GC-MS
  - Small
  - Thermal stable
  - Volatile and volatile after derivatization

- CE-MS
  - Small and polar
  - Charged molecules

- LC-MS
  - Universal
  - Intermediate - low polarity
  - High molecular mass
  - Hydrophilic
  - Hydrophobic

**DATA TREATMENT**

1. Feature finding
2. Alignment and filter by frequency

**DATA QUALITY CHECK (PCA models)**

- GC-MS
- LC-MS
- Universal
- Intermediate - low polarity

**STATISTICAL DATA ANALYSIS**

- Univariate data analysis (MATLAB) & Multivariate data analysis (SIMCA-P 12.0.1.0)
- IR vs. No IR
- Only girls IR vs. No IR

**SUMMARY & CONCLUSION**

- Bile acids and their derivatives represented the most prominent changes indicating the great impact of the gut microbiota on the host metabolism
- Central carbon metabolism and inflammation were the most altered processes in obese children with IR
- Subtle differences were highlighted between groups; these changes were unexpectedly magnified by pre-pubertal sex differences
- Metabolomics is a powerful tool to unveil alterations in metabolic conditions even at their early stage in order to provide new information for an adequate monitoring of predisposing factors in the obesity associated IR condition.

**REFERENCES**