Dr. Amalia Gastaldelli

Institute of Clinical Physiology (IFC) of National Research Council (CNR) &

Institute of Life Sciences of Sant'Anna School of Advanced Studies

Pisa, Italy

Current positions: Research Director at the Institute of Clinical Physiology (IFC) of National Research Council (CNR) and Affiliate Professor at the Institute of Life Sciences of Sant'Anna School of Advanced Studies in Pisa, Italy. Adjunct Professor of Medicine at the Diabetes Division of University of Texas Health, in San Antonio, TX, USA. President of the NAFLD study group of EASD and of the EGIR study group (European Group for the study of Insulin Resistance).

Research focus: physiological mechanisms that regulate glucose and lipid metabolism, and that are altered in metabolic diseases as NAFLD and diabetes. I am leading a multidisciplinary group (biologists, chemists, mathematician) and we use a translational approach to the study of human physiology, e.g., mass spectrometry coupled with stable isotope tracers for the evaluation in vivo of glucose and lipids metabolism and imaging tools as PET to study organ metabolism in collaboration with many institutions in Europe and United States. PI in national and international scientific projects, participation di clinical trials, partner of several EU grants. Member of the EASL EASD EASO committee for writing the European clinical guidelines for management of NAFLD (2016)

Bibliometric indicators: more than 300 original articles and 30 book chapters with >21000 citations; **H index** of 74 in Scopus and 87 in Google Scholar and a **total impact factor** IF>2400
https://www.scopus.com/authid/detail.uri?authorId=7004210893

Insulin resistance and NAFLD

The prevalence of non-alcoholic fatty liver disease (NAFLD) is now 25% in the general population but increases to more than 55% in subjects with obesity and/or type 2 diabetes. Simple steatosis (NAFL) can develop into more severe, i.e., non-alcoholic steatohepatitis (NASH), cirrhosis, hepatocellular carcinoma and death.

Several metabolic mechanisms have been indicated as primary promoters of NAFLD and of progression to NASH, in particular insulin resistance, mitochondrial dysfunction, synthesis and accumulation of lipotoxic lipids. Impaired insulin action in NAFLD is not limited to the liver but also occurs in other organs. Insulin resistance in the adipose tissue is the main driver of NAFLD due to excess release of fatty acid that are the primary source of hepatic lipids. In addition to triglycerides, other lipids are bioactive or toxic to liver cells and increase in relation to the degree of insulin resistance not only in the liver but also in muscles and adipose tissue.

Not only lipids, but also amino acid metabolism is impaired in NAFL / NASH due to reduced insulin action in muscle and excess catabolism and release of amino acids into the circulation. Increased plasma levels of branched-chain and aromatic amino acids, glutamate, serine and glycine, are associated with an increase in liver fibrosis.

In conclusion, insulin resistance induces metabolic changes not only in lipids but also in the amino acid profile that are linked to a more severe NAFLD phenotype. The causal relationship has yet to be fully clarified.