LIPIDOMICS AS A TOOL TO UNRAVEL THE ROLE OF BONE MARROW ADIPOSE TISSUE IN AGING AND TYPE 2 DIABETES MELLITUS: STUDY ON SAMPLES DERIVED FROM HUMAN HIPS

1)De Metrio S.. 2)Accattatis F.. 3)Granata A.. 4)Maselli D.. 5)Ferland-mccollough D.. 6)Mangialardi G.. 7)Corsini A.. 8)Madeddu P.. 9)Spinetti G.. 10)Arnaboldi L..

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By 2030, 20% of the population of industrialized countries will have an average age of 65 years (or higher) and will develop cardiovascular diseases (CVD), mostly caused (80%) by type 2 diabetes mellitus (T2DM) and its consequences. If aging is an unchangeable variable, CVD could be reduced by healthy lifestyles and/or appropriate pharmacological treatments, aimed at correcting T2DM, metabolic syndrome and dyslipidemia.

Recently, Bone Marrow Adipose Tissue (BMAT) has gained attention as an attractive target because its mass (measured as the relative percentage) in Bone Marrow (BM) increases with age from 10-15% in young people up to 70% and more in elderly. BM is composed of several cell populations deriving from totipotent stem cells which can differentiate into hemopoietic and/or mesenchymal stem cells (MSC). The latter are stromal precursors that in physiological conditions undergo lineage-specific differentiation to repair damaged tissue and to modulate immune responses and inflammation. Moreover, BMAT may also be involved in T2DM and obesity, due to its ability to secrete various cytokines, including IL-6 and IL-8, and adipokines such as leptin and adiponectin, whose altered concentrations may exert systemic effects, thus activating inflammation and adipogenesis.

Based on this evidence, the purpose of this project is to understand the role of BMAT in aging and T2DM, by performing lipidomic studies (by chromatographic techniques) on BMAT derived from 27 old (70±12 years) patients undergoing hip replacement, 9 of those suffered from T2DM.

We first performed a qualitative analysis of the total fatty acid (FA) profile of the samples and we found significant differences nor between single FA composition neither between saturated and unsaturated FA of T2DM vs healthy controls. The fact that we did not find a significant presence of PUFA (characteristics of phospholipid) in all the samples, indirectly documents that these extracts are really BMAT, whose main components are triglycerides and cholesterol.

When we measured the composition and the mass of triglycerides (TG), free cholesterol (FC) and cholesteryl esters (CE) we found a non significant but slight increase in TG (1.5 fold) and CE mass (2.9 fold). In CE also a significant increase in 16:1 mass and a decrease in saturated/unsaturated (SFA/UFA) ratio was found in T2DM vs controls.

On the other hand, the increase in CE was balanced by a concomitant decrease in FC mass, which is reflected by a 4.7 fold increase of CE/FC in T2DM patients. Altogether, since these preliminary results suggest that T2DM is associated with variations in lipid profile of BMAT, our next goal will be the evaluation of enzymes involved in lipid metabolism, such as SCD-1, ACAT, lipases for future specific pharmacological approaches.

While the analysis of the activity of ACAT and lipases urges from data documenting the unbalanced FC/CE ratio, that of SCD-1 is related to the known increase in the lipid unsaturation index that causes bone fragility and osteoporosis in T2DM patients.

To better estimate the effect of BMAT on T2DM we will correct these data for body mass index, age, sex, drug treatment and duration of T2DM and correlate the same data with plasma cholesterol, triglycerides and glucose.

All these information may lead to a better understanding of the pathology and to the identification of novel pharmacological targets for the treatment of T2DM.