Cooperation of Lipids and Genes during Differentiation of Human Subcutaneous Adipose Tissue Stromal Vascular Cells

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Exposition of cells to excess of energy substrates (high-fat diet), causes activation of evolutionarily conserved adaptive mechanisms such as unfolded protein response (UPR) called also ER-stress. In response to metabolic stress, ER changes his own activity, aiming to restore homeostasis of the cell. Our results on adipose tissue stromal vascular fraction (SVF) suggests that ER stress leads to preadipocytes differentiation.

SVF cells isolated from adipose tissue were incubated with MDI (dexamethasone (0.25μM), IBMX (0.5 mM) and insulin (66nM)) to cause the endoplasmic reticulum stress (ER-stress) and then incubated in basal medium up to 15 day (differentiation period). Analysis of the lipid profile by mass spectrometry and gene expression by microarray in cells was performed in cooperation with the center at Regensburg. The changes in gene expression was analyzed using Single Colored Agilent Array. The significant change of gene expression was estimated using GeneSpring software. The resulting MS data set as the amount of lipid/mg protein were analyzed as, the relative content of individual classes of lipids in cells and fatty acids with different carbon chain lengths in the various lipid fractions. The correlation of gene changed with significantly modified lipids was analyzed by bioinformatics.

The chosen incubation conditions lead to the activation of ER stress. This was connected with activation of the PAT proteins gene expression and lipid droplets (LD) formation in SVF cells. The predominant increase of the amount of phospholipids, plamalogens and cholesterol during the differentiation of cells indicates the demand of synthesis of lipid fractions needed to build the membranes able to form microvesicles. Used differentiation promoting conditions (MDI) resulted in stimulation of *de novo* synthesis of fatty acids which were incorporated into the ceramides, sphingolipids and caused an increase of the incorporation of unsaturated long-chain fatty acids into cellular lipids. Differentiation process was connected by the reduced amount of arachidonic acid incorporated in lipids. Released by phospholipase arachidonic acid could serve as a substrate for eicosanoids synthesis required for stimulation of preadipocyte differentiation by PPAR-gamma activation

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