Obesity is a serious health problem generally associated with diseases such as type 2 diabetes, hypertension, cardiovascular diseases and various types of cancer. A better understanding of the molecular mechanisms underlying obesity is essential. Adipokines and microRNAs are potential targets for therapeutic strategies. Adipose tissue secretes adipokines and microRNAs which are involved in mechanisms regulating adipose tissue metabolism (1, 2). Obesity leads to hyperadipose tissue due to tissue mass expands, with adipocytes becoming distant from the vasculature. Such variation in oxygen pressure has drastic effects on inflammation and modulation of adipokines and miRNA secretion (3, 4). Primary cell culture is the best in vitro model to mimic the physiological state of tissues. Adipocytes with specific Body Mass Index (BMI), have been cultured at 21% or 1% of oxygen. We compared the biomarkers secretion from different adipocytes in hypoxic and normoxic conditions by the analysis of cell supernatants using a Human Obesity Antibody Array and an innovative 3D structure microarray technology.

II / Profiling of secreted adipokines

Table 2: Fold change of secreted adipokines. The fold change was calculated as the ratio of the protein level obtained in hypoxic conditions to that obtained in normoxic conditions. The fold change over and below 1 show an increase or decrease of adipokine secretion under hypoxia, respectively. Fold changes higher than 2 and lower than 0.5 are considered as significant. Adipocytes secrete a number of adipokines as adiponectin, IL-6, IL-8, leptin, TNF-alpha, MCP-1, MIF, VEGF and PAI-1 (4, 5). In this array, ANGPTL4, IL-6, IL-8, TNF and VEGF were detected and their calculated fold changes must be considered carefully. Adiponectin, leptin, ANGPTL4, IL-8, VEGF, PAI-1 and TIMP-2 were clearly detected (data not shown). Hypoxia up-regulates the secretion of leptin, OPG, MIF, IL-6, IL-8, TNF-alpha, VEGF and PAI-1 and had no clear effect on TNF-alpha and adiponectin secretion. These data confirm some previous studies (4, 5). TIMP-1 were also secreted by adipocytes (6) as well as TIMP-2 which is not involved in the regulation of oxygen oxidative stress (7). These fold change levels are strongly dependent on donor without clear connection to BMI.

III / Profiling of secreted microRNA

The 3D Gene microarray technology was made with black resin substrate which substantially decreases background noise and enables the detection of low expression genes or miRNA. The adoption of uneven columnar morphology and the acquisition of a uniform detected image. The microarray is made with black resin substrate (A). The structure of 3D Gene® microarray. The microarray is made with black resin substrate which substantially decreases background noise and enables the detection of low expression genes or miRNA. The adoption of uneven columnar morphology and the acquisition of a uniform detected image. The microarray is made with black resin substrate (A). A Log2 ratio of 1 means hypoxia 2 fold up-regulates the secretion of the miRNA. A Log2 ratio of -1 means hypoxia 2 fold down-regulates the secretion of the miRNA.

The combination of hypoxia cell culture models and biomarker profiling tools, for both proteins and miRNAs, opens new avenues for drug discovery. Such studies are suitable for a broad range of diseases such as type 2 diabetes, hypertension, cardiovascular diseases and cancer.