ALTERATION OF INTRACELLULAR CHOLESTEROL IN SKIN FIBROBLASTS FROM ALZHEIMER'S DISEASE PATIENTS

S. Spolitu, S. Uda, S. Accossu, G. Diaz, F. Angius
University of Cagliari, Department of Sciences and Biomedical Technologies, Cagliari, Italy

Purpose: Free-cholesterol (FC) is in plasma membranes, cholesterol-esters (CE) are located in lipid-droplets. Changes in the organization of intracellular lipids can affect cellular functions as signal transduction and membrane trafficking. Recent studies showed that alterations in cholesterol homeostasis modulate the β-amyloid formation, responsible for AD senile plaques. Altered cholesterol levels lead to structural/functional destabilization of rafts and amyloidogenic enzymes activity associated with. Through the main intracellular lipid components identification by fluorescence-microscopy and molecular studies, we examined whether there are alterations in cholesterol metabolism also in peripheral cells of AD patients.
Methods: Fibroblasts isolated from skin tissue were stained with Nile Red, which marks lipids with low (NR590) or high (NR535) hydrophobicity, filipin and Oil Red O (ORO). The mRNA and protein expression were assessed by molecular biology.
Results: ORO showed higher neutral lipids concentration in AD. Lower ORO intensity after esterification-inhibitors treatment proved that CE increased in AD. Moreover, high NR535 was found in AD expecially in the perinuclear cytoplasm. Filipin revealed that high FC levels co-localized with high neutral lipids concentrations. Gene expression showed increased ACAT1 in AD, whereas SREBP2, nCEH, ABCA1, neprilysin, BACE1 were decreased; HMGCoA R, LDLR, caveolin1, APP were unchanged.
Conclusions: Our results show that also AD fibroblasts have an higher content of FC and CE that leads to an anomalous FC transport to the membranes and structural/functional rafts destabilization and consequently activity of APP and BACE1 here localized. These observations suggest these cells as potential model to study the cytopathological AD features biomarkers and therapies.