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Transcriptomic autophagy-related gene signature investigation for type 2 diabetes in Mediterranean subjects

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Abstract

Background: Autophagy (involving degradation and clearance of damaged organelles and compounds) plays a role in type 2 diabetes (T2D). There are three main types of autophagy and several genes involved. These genes have been well studied in animal models, but there are few transcriptomic studies in humans. Our aim is to analyze the differential gene expression, and the functional enrichment of the main autophagy-related genes (ARG) in T2D subjects from a Mediterranean population

Methods: We analyzed 120 White-European subjects (mean age 61,4 years; 50% women; 24 T2D) from Valencia, Spain. Clinical and lifestyle data were obtained. ARN was isolated from blood. Transcriptome-wide gene expression was analyzed with the GeneChip Human Gene 2.0 ST Array, according to standardized procedures. Differential gene expression between T2D and non-T2D subjects was estimated with multivariable models adjusted for covariates (sex, age, BMI, batch effect and leukocytes). A list of 111 ARG was selected to specifically study gene expression in terms of the log fold change. Gene ontology (GO) and pathway analysis using Kyoto Encyclopedia of Genes and Genomes (KEGG), were undertaken.

Results: For T2D vs. non-T2D subjects, we detected several differentially expressed ARG. The top-ranked genes were: HTT (p=0.0005), MTOR (p=0.0006), UVRAG (p=0.0028), NCOR1 (p=0.0031), APP (p=0.0034), AMBRA1 (p=0.0034), GABARAPL2 (p=0.0038), NFE2L2 (p=0.0111), BCL2 (p=0.0134) and ATG16L1 (p=0.0145). GO analysis showed that the 18 differentially expressed genes were primarily involved in regulation of catabolic process (p=1.19E-13), regulation of autophagy (p=5.80E-12) and response to starvation(p=2.88E-10). KEGG results revealed Autophagy (p=1.24E-12) and Autophagy-other (p=4.26E-09) as the hits.

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