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Reconstruction and analysis of the network of interactions between genes that regulate human body weight

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Motivation and Aim: Obesity is a multifactorial chronic disease manifested in an excessive increase in adipose tissue mass and is a risk factor for many diseases. The prevalence of this pathology in the world is increasing, which makes this problem particularly relevant. In order to obtain additional information on the genetic and molecular basis of obesity, we built and analyzed a network of interactions between proteins encoded by genes involved in the regulation of body weight.
Methods and Algorithms: For the list of genes, which was formed earlier [1], information on protein-protein interactions (PPIs) from the GeneMANIA, STRING and BioGRID databases was searched and extracted. The reconstruction and analysis of networks were carried out using Cytoscape. For the reconstruction of networks specific for adipocytes and brain cells, expression information from publications was used [2] and [3]. Functional annotation of genes (GO analysis) was performed using DAVID tool. For finding potential transcription factor binding sites disturbed by GWAS SNPs collected in [1], UCSC Variant Annotation Integrator, dbSNP and PERFECTOS-APE were used.
Results: We obtained PPI networks involving proteins controlling body weight and/or feeding behavior (1) encoded by all genes from [1] and (2) (3) specific for adipocytes and brain cells. GO analysis of lists of genes involved in networks has shown that they are enriched with genes controlling transcriptional and hormonal regulation. 24 potential binding sites for transcription factors that are involved in the regulation of body weight [1], which may be affected by SNPs, were identified. We found that transcriptional regulators reliably more often corresponded to vertices with increased degree and high values of centrality and radiality, for transmembrane receptors, the opposite pattern was revealed. For proteins INO80E and DMXL2, protein-protein interactions have been identified that allow the construction of hypothetical mechanisms for their participation in the regulation of body weight.
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