Influence of a high-fat diet in the cerebellar tissue of Cockayne Syndrome mice

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Cockayne syndrome (CS) is an autosomal recessive progeroid neurodegenerative disease. Cerebellum is the most affected brain's region with observed irregular myelination patterns. The syndrome is caused by mutations in both *CSA* and *CSB* genes, involved in DNA repair mechanism. Both mutations changes the activities of interacting proteins, like DNA repair signaling protein PARP. It was observed that PARP is overactivated in CS, resulting in ATP depletion and cell death. Recent data demonstrates that a high-fat diet (HFD) can rescue the CS symptoms and consequently improve cerebellar functions. However, the mechanisms of HFD-inducing cerebellar protection are unknown. Therefore, this work aims to understand the major genes that are modulated in cerebellum of a CS-model mouse fed with a HFD. Microarray data (GSE62194) was downloaded from Gene Expression Omnibus (GEO) into "R" statistical environment, being quality-assessed and statistically analyzed by a*rrayQualityMetrics and limma* packages, respectively. The gene expression comparison between HFD fed and standard diet fed CS-model mice generated a list of differentially expressed genes (DEGs) that was used as an input in the metasearch website STRING in order to generate an interatomic network. Additionally, the lipids found in HFD were utilized as an input in the website STITCH to draw chemical interaction networks. These networks were merged in a main network using the software Cytoscape, in which were performed clustering, centralities and gene ontologies (GO) analyses. The clustering and GO analysis indicated two main clusters associated to lipid transport and metabolism, as well as cell death regulation. It was also observed in the main network the presence of overexpressed genes associated to lipid metabolism and Krebs cycle, suggesting the positive regulation of lipid catabolism in CS. In addition, LINGO1, which is associated to myelination and oligodendrocyte differentiation, was found differentially expressed in HFD fed mice. The data supports the hypothesis that lipid catabolism could be necessary for providing a positive energetic balance for CS-affected neuron cells.

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