Significant Upregulated Genes in Celiac Disease Cases

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Introduction

Celiac Disease is an autoimmune disease in which the immune system mistakes gliadin, a molecule found in gluten, as a threat to the body. Consequently, the immune system attacks and damages the lining of the small intestines and disrupts the body's ability to properly take in nutrients. It is estimated that 1% of the global population is affected by Celiac disease. This disease causes long-term digestive issues and contributes to other diseases such as Type 1 Diabetes, Thyroid disease, Liver disease, etc. Unfortunately, no cure currently exists and Celiac disease's inheritance pattern is unknown, although patients do often form familial clusters. This study investigates genes involved in Celiac disease.

Methods

The gene expression of peripheral blood mononuclear cells of celiac patients on a gluten-free diet as presented by dataset GSE113469, found in the NCBI's Gene Ontology Omnibus database, was analyzed. In total, 37 samples were analyzed and isolated into two groups: healthy control and patients with Celiac disease. A t-test was performed to identify the top 420 most statistically significant genes in the analysis pointing toward markers of Celiac disease. These genes were subsequently entered into the STRING database to analyze the pathways between their relevant proteins. We investigated the functions of certain genes in our data by combining the KEGG pathways and Gene Ontology terms that String-db provided with information from Genecards.

Results

After inputting the top 420 most significant genes into STRING, two pathways were highly active, natural killer cell-mediated cytotoxicity and antigen processing and presentation, each with a false discovery rate of 0.0262 and 0.0214 respectively. The following genes ICAM2, KLRD1, SH2D1A, MAPK1, and IFNAR1 were especially relevant to the cell-mediated cytotoxicity pathway and were found to be upregulated in Celiac disease. The genes HSPA8, HSPA6, HSPA1B, and HLA-C are the most relevant to the Antigen Processing pathway and were also found to be upregulated in Celiac Disease.

Conclusions

The gene ICAM2 mediates natural killer cell clearance and directly activates receptors in the Natural Killer cell to trigger immune responses. The gene KLRD1 releases cytokines and activates the immune response in the body. SH2D1A is a protein-coding gene whose protein product has a major role in activating the body's T and B cells. Celiac disease also increases the activity of MAPK1, which indirectly activates IFNAR1 in a pathway for cell apoptosis. As all of these genes are upregulated, we find that natural killer cells, T cells, B cells, and cell apoptosis are being overactivated by the increase in cytokines. Additionally, HSPA8, HSPA6, and HSPA1B are heat shock proteins that re-fold misfolded proteins in our body. In Celiac disease patients, these genes are up-regulated, promoting the proliferation of protein misfolding and induced apoptosis, causing reactions to the proteins and glutens. Lastly, HLA-C plays a vital role in antiviral immunity as it activates killer immunoglobulin receptors (KIRs) expressed in NK cells. Due to the over-expression of HLA-C, cytokines are released and the immune response is activated, which eventually damages intestine linings. Further research is needed to provide a clearer link between gluten digestion and the genes involved in Celiac disease and develop personalized medicine. We may also find alternative treatment solutions to adjusted diets and give Celiac patients more targeted treatments.