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Research and analysis of genes associated with hereditary predisposition to Crohn's disease and reconstruction of the gene network using bioinformatics tools

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Motivation and Aim: Genomic association studies and computerized meta-analyses have identified and confirmed 71 loci of susceptibility to Crohn's disease on 17 chromosomes [1]. Understanding the role of the innate immune response in Crohn's disease was the result of the discovery of the corresponding susceptibility loci in genetic studies, which still explains only a little more than 20 % of the heritability of Crohn's disease [2]. In this work, we compiled a list of genes associated with the development of Crohn's disease, analyzed the categories of gene ontologies for such a list and reconstructed the gene network. For the key genes of the disease obtained by analyzing the structure of the gene network, options for the search for drugs interacting with the studied proteins could be considered.

Methods and Algorithms: To build a list of genes associated with hereditary predisposition to Crohn's disease and to analyze the disease genes, the online resource OMIM (Online Mendelian Inheritance in Man, https://omim.org) was used [3]. To search and analyze significant categories of gene ontologies for this group of genes, the resulting list of human genes was downloaded via the DAVID interface (Database for Annotation, Visualization and Integrated Discovery) (https://david.ncifcrf.gov/summary.jsp) and PANTHER [4]. The categories of gene ontologies for molecular functions were also calculated. GeneMANIA (https://genemania.org) and STRING-DB (https://string-db.org/) tools were used to reconstruct the gene network of interactions of genes associated with Crohn's disease. We had follow scheme of applications of online tools recently published in [5] for glioblastoma analysis.

Results: The GO analysis revealed that the most significant categories for genes associated with Crohn's disease are signaling pathways mediated by tumor necrosis factor and caused by cytokines, as well as reactions to the drug and cytosolic processes. DAVID and PANTHER for Crohn's disease genes confirm the categories of gene ontologies of protein binding, membranes and intracellular processes. The most significant categories of gene ontologies for molecular functions are the categories of protein binding, binding of enzymes and cytokines, and other binding of protein-containing complexes. The usage of online bioinformatics tools [6] proved be reliable approach for Crohn's disease genes analysis. The presented bioinformatics techniques were discussed at the master-classes and students workshops at I.M. Sechenov First Moscow State Medical University.

Conclusion: Due to the identification of susceptibility loci, it is possible to conclude about violations of immune regulation in the intestine, as well as the presence of categories of cytosolic processes and signaling pathways allows us to determine the relationship of the disease with intracellular inflammation. The resulting gene network is quite coherent, although the connections were exposed only by the parameters protein-protein interactions and co-expression.

Current treatments are ineffective at counteracting disease progression. Overall, search for novel drug targets in Crohn's disease remains challenging problem [7].

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