Detection of hub genes and protein complexes in gastric cancer cell line AGS exposed to mycophenolic acid by network-based analysis

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Abstract: Inosine monophosphate dehydrogenase, a rate-limiting enzyme for the de novo synthesis of guanosine nucleotides, is over-expressed in many type of tumor cells, hence it has been chosen as a target for cancer therapy. Mycophenolic acid is an uncompetitive inhibitor of this enzyme. Previous studies have shown anticancer activity of mycophenolic acid on several cancer cell lines. Some molecular mechanisms have been described, as well. In here, we dissected molecular mechanisms in AGS cells treated with mycophenolic acid and determined hub genes and modules involved in responding of the cells. In order to do this, we made a list of differentially expressed genes from GSE46671 data set utilizing GEO2R tool of NCBI by filtering the list for genes with a p-value < 0.05 and a Log2 fold change of ±0.6. The list were submitted to STRING database and only experimentally validated interaction between proteins were chosen. Resulted networks were analyzed for detecting hub and modules. Annotation were performed by DAVID database to determine function of the genes list and modules. We found 1837 differentially expressed genes, 968 and 869 up- and down regulated, respectively. Based overlapping neighborhood expansion, we found 23 modules (p-value < 0.1) sized from 6 to 32. Among top 5 percent nodes in degree and betweenness centrality factors, we determined 31 hubs including CDK1, CDK4, HSPA5 and NEDD4. Annotation analysis of differentially expressed genes revealed transcription, apoptotic, cell proliferation, and cell adhesion are remarkable processes affected by them. In conclusion, these data could be useful for better understanding of the mechanisms and important genes involved in cancer therapy by immunosuppressive drugs.

Keywords: cancer; network; differentially expressed genes hub genes; annotation