Abstract: Open Access

Identification of Hub Gene for Therapeutic Drug Target from Sorafenib Resistance Microarray Data and Virtual Screening with Phytochemicals of Indian Medicinal Plants

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ABSTRACT

Liver cancer is among the commonly occurring cancer it exists in various forms, among which hepatocellular carcinoma (HCC) is the most frequently occurring one. The treatment plan for HCC depends on the cancer stage, involving procedures like surgical resection, liver transplant chemotherapy, radiation therapies, etc. One of the major concerns associated with the chemotherapy of HCC treatment is the development of resistance against the specified drug. Sorafenib is an FDA-approved drug commonly used in the treatment of HCC, reports are available that state the development of resistance against Sorafenib. In the present study, to determine the molecular factors contributing towards the development of the resistance against Sorafenib, microarray data of Sorafenib resistance HCC cells, HCC xenograft, and the corresponding counterparts is obtained from the GEO database (GSE121153). The microarray expression data was analyzed through GEO2R tool to extract the differentially expressed genes. Top differentially expressed genes were then exported to the STRING database to develop the Protein-protein interaction (PPI) network, the network was then analyzed on Cytoscape. cytoHubba module of Cytoscape was used to identify the hub genes, functional enrichment analysis of the hub genes was carried out at DAVID database. MAPK1 ranks first among the hub genes, further, it was considered for molecular docking. Phytochemicals from various Indian medicinal plants namely *Carica papaya*, *Neolamarckiacadamba* and *Ganoderma lucidum* were considered for docking against the identified Hub gene protein. Among all the taken phytochemicals, Rutin which is reported in *Neolamarckiacadamba* shows the best docking score -11.04 kJ/mol against MAPK1, further, the stability of the best docked complexes was examined through molecular dynamics simulation.

Keywords: Liver cancer, Sorafenib, PPI, Docking, Molecular dynamics simulation

Abbreviations: HCC: Hepatocellular Carcinoma; PPI: Protein-Protein Interaction

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