PREDICTION OF ADVERSE EFFECTS OF SULFORAPHANE BY *IN SILICO* TESTING OF TARGETED GENES, PROTEIN- PROTEIN INTERACTIONS AND MOLECULAR CLASSES

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Alternative form of cancer treatment includes targeting natural compounds such as sulfur-rich dietary phytochemical sulforaphane (SFN). However, data on SFN safety, interactions on the protein level and target of SFN in human organism are limited (1). The aim of this study was to elucidate the target interactions of SFN in human body in order to rationalize possible side-effects and predict off-targets by using *in silico* approach. STITCH database (http://stitch.embl.de) was used to obtain the information about chemical–protein interactions, while Metascape (https://metascape.org/) highlighted protein-protein interaction enrichment (PPIE).

SwissTargetPrediction (http://www.swisstargetprediction.ch/) indicated the target molecule classes of SFN in human. Human genes that had the strongest interaction with SFN were NQO1, NFE2L2, CASP3, HSP90AA1, MAPK14, HDAC6, HPGDS, KEAP1, GSTA1 and GSTM1. PPIE analysis singled out fluid shear stress and atherosclerosis, NRF2 pathway and chemical carcinogenesis - reactive oxygen species (ROS) as the most significant interactions. The most represented class of SFN targeted molecules in human organism were enzymes (26.7%). Epidermal growth factor receptor erbB1, macrophage migration inhibitory factor, nitric oxide synthase (inducible) showed the highest probability target rate. In our previous study (2), we pointed out that the genome of cancer patients could affect SFN safety. The current study provides a set of target genes, emphasizes the importance of oxidative stress in the suggested genetic interactions and predicts classes of target molecules, which should further be examined.

References

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Acknowledgements

This research was supported by the Ministry of Education, Sciences and Technological Development of Republic of Serbia, International Serbia-China project: "Improving anti-cancer immunotherapy efficacy of CAR-T cells or PD-1/PD-L1 inhibitors by combining immune modulators" (451-03-1203/2021-09).

PREDVIĐANJE ŠTETNIH EFEKATA SULFORAFANA *IN SILICO* ISPITIVANJEM NJEGOVOG CILJANOG DEJSTVA NA GENE, PROTEIN-PROTEIN INTERAKCIJE I KLASE MOLEKULA

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Alternativni oblik lečenja raka uključuje upotrebu prirodnih jedinjenja kao što je fitohemikalija bogata sumporom, sulforafan (SFN). Međutim, podaci o interakcijama SFN na nivou proteina i ciljnih mesta dejstva SFN u ljudskom organizmu su ograničeni (1). Cilj ove studije bio je da se ukaže na ciljne interakcije SFN kod ljudi kako bi se racionalizovali mogući neželjeni efekti i predvidela nova ciljna mesta toksičnosti korišćenjem *in silico* pristupa. STITCH baza podataka (http://stitch.embl.de) korišćena je za dobijanje informacija o interakcijama između hemikalija i proteina, dok je *Metascape* (https://metascape.org/) izdvojio protein-protein interakcije (PPIE).

SwissTargetPrediction (http://vvv.svisstargetprediction.ch/) ukazao je na ciljana mesta dejstva SFN kod ljudi. Izdvojeni su geni koji kod ljudi imaju najjaču interakciju sa SFN: NQO1, NFE2L2, CASP3, HSP90AA1, MAPK14, HDAC6, HPGDS, KEAP1, GSTA1, GSTM1. Ateroskleroza, NRF2 signalni put i hemijska karcinogeneza - reaktivne vrste kiseonika (ROS) označeni su kao najznačajnije protein-protein interakcije. Najzastupljenija klasa SFN ciljanih molekula u ljudskom organizmu bili su enzimi (26,7%). Receptor epidermalnog faktora rasta erbB1, faktor inhibitora migracije makrofaga i sintaza azot oksida (inducibilna) pokazali su najveću stopu verovatnoće ciljnog mesta dejstva. U našoj prethodnoj studiji (2) istakli smo da bi genom pacijenata obolelih od raka mogao uticati na bezbednost primene SFN. Međutim, ova studija daje dodatni set ciljnih gena i naglašava važnost oksidativnog stresa u predloženim interakcijama između gena, kao i predviđenim klasama ciljnih molekula na koje deluje SFN i koje bi trebalo dalje ispitati.

Literatura

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Zahvalnica

Ovo istraživanje je podržalo Ministarstvo prosvete, nauke i tehnološkog razvoja Republike Srbije kroz međunarodni projekat između Republike Srbije i NR Kine: „Povećanje efikasnosti terapije karcinoma kombinacijom CAR-T ćelija ili PD-1/PD-L1 inhibitora pomoću imunomodulatora” (451-03-1203/2021-09).