Systems Network Analysis of Protein Interaction Network (PIN) for deducing molecular mechanistic action of BaP induced carcinogenesis

Anukriti[1], Anupam Dhasmana[2*], Uma Bhardwaj[1]

[1]Department of Biosciences, School of Liberal Arts and Sciences, Mody University, Lakshamgarh-332311, Rajasthan, India.

[2] Department of Immunology and Microbiology, School of Medicine, University of Texas Rio Grande Valley, tx, USA

Abstract:

Background: Benzo[*a*]pyrene (BaP), a polycyclic aromatic hydrocarbon, has been placed in group 1 by IARC which indicates that it is a potential carcinogen to human beings. It has shown tumorigenic properties in approximately all animal model systems. In the current study, we have tried to identify the most probable biomolecular targets of BaP using systems biology approach.

Method: All the proteins that interact with BaP were extracted from T3DB. STRING-db was used to generate the Protein- protein interaction network (PPIN). Various apps of cytoscape software were used for network analysis, modulation and GO enrichment analysis. By developing biokinetic models, we then tried to find the impact of BaP on the top three most probable biomolecular targets and how whole of the cell cycle is getting perturbed which may ultimately lead to carcinogenesis. Apart from this, in this study we have also tried to propose a hypothesis of removing BaP from the cell vicinity by exploiting the scavenging properties of carbon based nanoparticles using *in silico* approach.

Result: 4000 genes were extracted from T3DB for which network was generated. On network analysis, 2058 nodes were obtained that were connected by 13850 edges. MCODE created 65 clusters which had 411 seed proteins and enrichment analysis showed that most of the proteins present in the network participate in cell cycle regulatory pathways. On molecular docking analysis QSOX1, PTGS2 and NOS2 emerged out to be top three most probable biomolecular targets of BaP out of which PTGS2 is directly involved in cell cycle regulatory pathways. Biomolecular kinetics showed that when PTGS2 gets hampered by BaP, cell cycle regulation gets disturbed and cell may become cancerous. On *in silico* analysis of the scavenging potential of carbon based nanoparticles, BaP showed higher binding efficiencies for SWCNT and MWCNT as compared with QSOX1.

Conclusion: Based on the in silico docking results we can hypothesize that carbon based nanoparticles can be used to scavenge BaP molecules from the cell vicinity.

Keywords: Benzo(alpha)pyrene, carcenogenesis, PPIN, systems biology