SUMMARY

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Cancer is the second deadliest disease in the world. Amongst all the cancers, lung cancer has been reported to cause maximum number of deaths followed by breast cancer and head and neck cancer. The major cause of lung cancer is the presence of hazardous chemicals in the environment. These chemicals are also known as environmental carcinogens. Two most potent environmental carcinogens are BaP and NNK which belong to PAHs and TSNAs categories respectively. In this study, we have tried to identify the most potent biomolecular targets of BaP and NNK using systems biology approach.

With the help of T3DB database, the BaP perturbed genes were identified and protein-protein interaction network was generated. Genes affected by NNK were identified from literature survey and PPIN was generated. For both the environmental carcinogens biomolecular targets were separately identified by screening the proteins on the basis of their topological properties and molecular binding affinities towards BaP and NNK respectively. For BaP, the top 3 biomolecular targets identified were QSOX1, PTGS2 and NOS2. Based on the recent studies, QSOX1 and NOS2 are also emerging as potent biomarkers for different types of cancers while PTGS2 is directly linked with the cell cycle regulatory machinery. For NNK, CDK7 showed the highest binding affinity, followed by CCNA1 and CDKN1B. All the three bio-molecular targets play important

roles in the regulation of cell cycle and any perturbation in them may result in hampering of the normal cell division process.

Model of cell cycle regulatory machinery was designed and then simulated to find the fluctuations in the concentrations of proteins involved in the process of cell division. Separate time course analysis was done for both BaP and NNK perturbed cell cycle regulatory machinery. For BaP, time course analysis was done only for PTGS2 as it is directly linked with the cell division process while time based concentration fluctuation analysis of all the three bio-molecular targets of NNK was performed. From the time course analysis, it is very clearly visible that when CDK7 gets hampered, whole cell cycle gets perturbed severely.

Apart from finding the most probable biomolecular targets for BaP and NNK, the study also aimed at finding the use of carbon based nanoparticles as protective agents against these environmental carcinogens. For this, SWCNTs, MWCNTs and Fullerene rings were designed using *in silico* tools and their scavenging potentials against BaP and NNK were analysed using molecular docking simulation analysis and adsorption load analysis. From the molecular docking and adsorption load analysis, MWCNTs showed the highest binding affinity against BaP while it adsorbedaround 11 BaP molecules/NT while SWCNTs showed highest binding affinity for NNK and an adsorption capacity of 10 NNK molecules per nanotube.