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Progression and control of tumorigenesis in F1 mice from the ethylnitrosourea exposed mothers involve miR-21 and PI3K/PTEN/Akt pathway along with apoptotic events

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Lung cancer is a most common form of the cancer and is among the leading causes of cancer associated deaths in adults and is increasing in younger population as well. In view of this, we studied the transplacental lung tumor development in the offspring's from the ethylnitrosourea (ENU) exposed mothers and the preventive effects of inositol hexaphosphate (IP6) in the F1 mice at 30 and 240 days representing early and late stage of tumorigenesis. Progressive time-dependent increase was observed in the development of lung tumor in F1 mice. Number of tumors on the lung surface was 101 (6.73 tumors/ tumor bearing mouse), and 378 (31.5 tumors/ tumor bearing mouse) at 30, and 240 days which was reduced to 81 (5.06 tumors/ tumor bearing mouse), 201 (15.46 tumors/ tumor bearing mouse) at 30 and 240 days in presence of IP6. During the tumorigenesis, overexpression of miR-21 activated the phosphorylation of Akt via targeting PTEN and inhibits apoptosis as revealed by down regulation of caspase-3 and cleavage of PARP1 in F1 mice. We also observed the upregulation of MMP-9 protein as well as its enzyme activity in F1 mice. Alterations in these molecular events were also prevented in presence of IP6. In conclusion, our findings show the progression and control of tumor development in F1 mice from the ENU exposed mothers possibly by affecting apoptosis via modulating the expression of miR-21, PI3K/PTEN/Akt pathways and MMP-9. The sensitivity of the molecular alterations to the IP6 makes them the potential targets for the cancer control.

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