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B3 vitamin component fights carcinogen action in human cells, says research

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Benzo[a]pyrene is a potent carcinogen and mutagen present in cigarette smoke, automotive exhaust, burnt wood fumes, barbecued and smoked meat etc.

Understanding the mechanisms whereby benzo[a]pyrene, which belongs to the class of polycyclic aromatic hydrocarbons (PAHs), may induce malignant transformation of human cells is the aim of a research project led by Ana Paula de Melo Loureiro, a professor at the University of São Paulo's School of Pharmaceutical Sciences (FCF-USP) in Brazil.

According to Loureiro, the idea is to identify the cellular pathways or sequences of biological reactions involved in the development of cancer and hence find possible targets for prevention or treatment of the disease. "Tests have shown that supplementing cell cultures with nicotinamide riboside, one of the components of vitamin B3, protects cells and prevents malignant transformation," she said. "We now want to find out exactly how this happens and whether the compound in question can be used in chemoprevention."

In experiments performed with regular lung cell cultures—more precisely, those of bronchial epithelial cells—were exposed to 0.5 and 1 micromolar (μM) benzo[a]pyrene for seven days. Recent data in the scientific literature suggests that the appearance of tumors is closely associated with genetic alterations and also with epigenetic alterations that may activate the expression of protumoral genes or silence protective genes, for example.

What most drew the scientists' attention, however, was a significant drop in the levels of metabolites involved in the production of energy for cells shortly after the first hour of exposure to benzo[a]pyrene. Throughout the exposure period, the cells readapted metabolically, and by the end of the period, the levels of metabolites had risen in exposed cells compared with the control group.

"It was for this reason that we had the idea of supplementing the cultures with nicotinamide riboside, a precursor to nicotinamide adenine dinucleotide [NAD+], which is essential to cellular metabolism and to the production of ATP [adenosine triphosphate, a molecule that stores energy for cell use]," Loureiro said.

Supplementation with nicotinamide riboside (1 μM) began 24 hours before exposure to benzo[a]pyrene and continued daily. Because benzo[a]pyrene is absorbed rapidly and biotransformed, it has to be replenished in the cell cultures every day, Loureiro explained.

At the end of the seven-day period, the cells were transferred to a semi-solid medium containing agarose, a polysaccharide obtained from algae, in order to prevent adhesion to the culture dish. The researcher says that a normal epithelial cell is unable to grow in this semi-solid medium without anchorage. "To make this possible, the expression of a number of genes and proteins must be altered so as to favor tumor development, for example by silencing the expression of cadherins [calcium-dependent adhesion molecules that form junctions to bind nearby cells together]," said Loureiro.

Analysis performed during the incubation period showed the occurrence of DNA alterations—both genetic (lesions that caused mutations in the nucleotide sequence) and epigenetic (increased levels of 5-methylcytosine, which alters gene expression). Cells grown in the semi-solid medium displayed global hypomethylation (reduction in levels of

5-methylcytosine), a characteristic of tumor cells.

Supplementing cells exposed to the carcinogen with nicotinamide riboside yielded positive results since they proved unable to grow in the agar medium, displaying similar behavior to the control cells, which were not exposed to benzo[a]pyrene.

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