Radiol Oncol 2002; 36(2): 154-5.

Genetic toxicology: from exposure detection to cancer prevention

Metka Filipič

Department of Genetic Toxicology and Cancer Biology, National Institute of Biology, Večna pot 111, 1000 Ljubljana, Slovenija

There is a general concern that many environmental chemicals to which humans are exposed are genotoxic and may cause cancer. The main problem is not only to identify the environmental genotoxic pollutants, but also to characterise their mode of action at cellular and molecular levels. To identify genotoxic environmental pollutants we are using selected in vitro short-term assays.

For fast screening for the presence of genotoxic substances in wastewater and fresh waters samples we use modifed SOS/*umu* test and Salmonella/microsomal assay. The modified assays are sensitive enough to detect low concentrations of genotoxic pollutants in non-concentrated water samples. We have demonstrated by using bacterial strains with elevated nitroreductase and/or O-acetyltransferase activity, that nitro polyaromatic hydrocarbons are important genotoxic contaminantns in water. We suggest to use the modifed SOS/*umu* for rutine controling the efficiency of wastewater treatment plants.

For detection of mutations, which are the consequence of DNA damage and the processing of the damaged DNA, we are using the Comet assay or single-cell gel electrophoresis (SCGE). This is a sensitive method for detecting DNA strand breaks at the level of individual cells. Cells embedded in agarose are lysed, subjected to alkaline unvinding, electrophoresed and stained. DNA, broken and relaxed in the electric field, migrates toward the anode, resembling a shape of a comet with bright fluorescent head and a tail region, which increases, as the DNA damage gets more severe. The "comets" are measured and analysed using video image analysis: DNA damage is quantified by tail length, tail moment and percentage of DNA in the tail. In our hands, the comet assay proved to be a valuable tool to study the biochemical and physicochemical mechanisms of DNA damage and repair. Based on the Comet assay we are developing a biomarker for detection differences in DNA repair capacity in populations exposed to heavy metals (Cd and Pb) compared to non-exposed. As heavy metals inhibit DNA repair, we supose that in populations exposed to heavy metals cellular DNA repair capacity is affected, leading to enhanced risk for cancer.

For identification of cancer preventive agents and potential antimutagens, we found, that the extract of *Salvia officinalis* inhibited UV induced SOS response and mutagenesis in bacteria. The results indicate that *Salvia officinalis* extract acts as an inhibitor of SOS functions as well as a promoter of DNA excision repair processes. For screening large number of samples we use SOS/*umu* test, modifed for detection of potential antimutagens. The samples that show antimuatgenic potential in SOS/*umu* test are than tested for antimutagenic activity in bacterial reverse mutation assay using different strains to allow insight in to the mode of action. Using this approach, we tested 121 mushroom extracts

for antigenotoxic activity. Seven of them inhibited UV induced SOS response by more than 50 % and three of them were effective also against oxidative damage.