

From Hazard to Risk

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The Micronucleus (Mn) test in rodents is an internationally recognised system for the detection of compounds that are potentially clastogenic and/or aneugenic. Micronucleus frequencies are usually determined manually by microscopy and this is both time consuming and labour intensive. The single-laser flow cytometer method (Dertinger et al 1996) has many advantages over manual scoring, including high speed analysis and improved throughput. As this is usually coupled with the analysis of larger cell numbers (20,000 cf. 2000 with manual scoring) flow cytometry analysis has the potential for improved sensitivity and consistency. Therefore, we have participated in a multi-laboratory validation study of the flow cytometry Mn test. The results of Phase 1 of the collaborative trial were published (Torous et al, 2001) and here we report our contribution to Phase II comparing Mn frequencies obtained in mouse peripheral blood by flow cytometry with manual scoring (using acridine orange staining). Rats were treated with methotrexate (0.5, 1, 2 and 4 mg/kg ip/po/iv) or vehicle daily for 3 days and peripheral blood sampled 24 hours after the final dose to determine Mn frequency. Methotrexate induced a dose dependent increase in reticulocyte Mn frequencies by flow cytometry and by manual scoring and overall, there was good concordance between both methods of analysis. These results support the conclusions of the Collaborative Study Group for the Micronucleus Test (Wakata et al, 1998) that the rat peripheral blood micronucleus test can be integrated into routine toxicology assays which assess the acute toxicity of chemicals.

Ecogenotoxicology

P128 Long-term monitoring of chromosomal aberrations in the population of a large industrial region of Western Siberia

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Constant genetic monitoring of the population of the ecologically unsuccessful area of Russia, Kemerovo region at the Laboratory of Genetics of the Kemerovo State University, Russia, has been carried on since 1987. Analysis of chromosomal aberrations (CA), sister chromatid exchanges and the micronucleus assay in cytokinesis-blocked lymphocytes have been used as a biomarker for DNA damage in human populations.

One of the important aspects is the investigation of cytogenetic effects in different groups of the population of Kemerovo region brought about local ecological circumstances. This problem is of great importance as Kemerovo region has the status of ecological disaster zone, because of a high concentration of chemical, machine-building, coal-mining and other plants. Most of them have out-of-date technologies and emit a great number of toxic, mutagenic and carcinogenic compounds.

In the present paper the results of the CA study in the peripheral blood lymphocytes of 925 inhabitants of the region (456 male and 469 female) aged 9 - 69 are presented. The proportion of metaphases with aberrations in this sample is $3.73 \pm 0.1\%$. The separate types of aberrations have the following frequencies: single fragments - 2.49 ± 0.08 ; chromatid exchanges - 0.04 ± 0.01 ; double fragments - 1.21 ± 0.05 ; chromosomal exchanges - 0.14 ± 0.02 . The modifying influence of the sex, age and the season of inspection were insignificant. Smoking caused an insignificant increase of the level of aberrations of all types in smokers in comparison with nonsmokers ($P > 0.05$).

All donors were divided into 4 groups: 1 - inhabitants of village districts ($n=110$); 2 - inhabitants of miners' towns ($n=157$); 3 - inhabitants of cities with a high level of chemical pollution ($n=378$); 4 - workers of coke-chemical and aluminium plants ($n=280$).

The average frequencies of metaphases with aberrations were the following: 1 - $2.86 \pm 0.26\%$; 2 - $3.79 \pm 0.24\%$; 3 - $3.29 \pm 0.28\%$; 4 - $4.65 \pm 0.21\%$.

A method of the mapping the cytogenetic effects for a regional examination of the toxico-genetic conditions of the environment has been proposed.

P129 The cyanotoxin cylindrospermopsin induces cell alterations without DNA damage visualized by the alkaline comet assay

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Eutrophication of brackish and freshwaters is commonly associated with blooms of cyanobacteria, most of them producing toxins. The cyanotoxin cylindrospermopsin has been involved in animal and human intoxications in different countries. Acute toxicity is due to liver necrosis but thymus and kidney are also affected. This toxic effect is caused by inhibition of protein synthesis. However, further research on its chronic toxicity is required. We focused our attention on