ABSTRACTS

Abstracts of posters and selected oral presentations

The abstracts are divided according to the following six tracks:
Mutational and epigenetic mechanisms
DNA damage responses
Environmental mutagenesis
Mutagenesis and health effects
Prevention of mutation-related diseases
Risk assessment

The abstracts are allocated in each track according to the indication of the authors, when available.

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time trying to open the cells of T. thermophila and T .pyriformis we can conclude that these cells are, just as the yeast cells, not suited for the comet assay. The work was supported by the Danish Society for Protection of Laboratory Animals and the Alternative Fund.

EM152
NONINVASIVE POLYORGAN KARYOLOGIC TEST FOR ESTIMATION OF CYTOGENETIC, CYTOTOXIC AND POTENTIAL CARCINOGENIC EFFECTS OF ENVIRONMENTAL FACTORS IN HUMAN STUDY

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Polyorgan karyologic test is founded on the microscopic analysis and quantitative account of karyologic end points in buccal, nasal, urothelial and bronchial epithelyocytes. It is designed categorization of end points on cytogenetic, proliferative and early and late nucleus destruction indexes. Integral cytogenetic index as amount of micronuclei, protrusion, nuclear bridges in 1000 cells of tissue is offered. Also integral index of proliferation (amount of bi-, polynucleated cells and double-nucleated cells) and apoptosis (amount of cells with nucleus destruction) is offered. Criteria of the determination and table diagnostic sign full spectrum of karyologic end points are designed. They are determined approximate normative levels of karyologic end points of buccal, nasal, bronchial and urothelial epithelyocytes of children and adults («Medical genetics» in Russian N° 11, 2007). It is revealed dependency of some indexes of proliferation and nucleus destruction from age, sex, smoking. Relationship the amount of congenital morphogenetic variants on one child with cytogenetic end point was revealed. It was shown dependency of karyologic indexes of buccal epithelium from local immunity. Polyorgan karyologic test was applied in Institute for estimation of the influence on the human populations (about 700 surveyed people) of the atmospheric air pollution in Tula; the working conditions of the large office centre; pollution of cellulose-paper plant; dioxin-contaminated regions of South Vietnam. Following laws have been revealed: air pollution induces significant (sometimes 10-times) increasing of the frequency of the exfoliated cells with cytogenetic damages and decreasing of apoptotic index. This trend is extremely disadvantage for human population, and promotes the accumulation genetic changed cells that can conduct to development of the cancer. It was revealed increasing of the rate of the cells with nuclear protrusions, atypical nucleus and in all studies integral cytogenetic indexes; indexes of proliferation; basically apoptotic index in patients with bronchial and lung pathology. It was shown possibility to correction of cytogenetic disturbances by means of acceptance vitamin A and C in recommended daily dose.

EM153
PERSISTENT DYSREGULATION OF DNA METHYLATION IN CELLS WITH ARSENIC-INDUCED GENOMIC INSTABILITY

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The mechanisms by which arsenic-induced genomic instability is initiated and maintained are poorly understood. In our previous studies, the long-term progression of chromosomal instability was typified by increasing aneuploidy in V79 Chinese hamster cells and human HaCaT keratinocytes treated with low doses arsenite for two cell cycles and maintained in arsenic-free medium up to 120 and 40 cell generations, respectively. In the current study, we evaluated DNA methylation levels in these cell cultures at several time points during the expanded growth. We have found altered genomic methylation patterns in cells that were briefly exposed to arsenic with evidence for widespread dysregulation of CpG methylation that persists for many population doublings after the treatment. In V79 cells increasing genomic instability characterized by aneuploidy, dicentric chromosomes and/or telomeric associations, complex chromosome rearrangements, and mutator and transformed phenotype correlated with modifications of global DNA methylation pattern evaluated by immunofluorescence with anti-5-methylcytosine antibody and MeSAP-PCR. The results show that short-term exposure to arsenite induced an apparent genome hypomethylating effect within a short time after exposure. In human HaCaT keratinocytes, genomewide methylation levels were measured by LINE1 pyrosequencing and gene-specific methylation status was assessed by Methylation-Specific-PCR. Global demethylation seen after treatment was followed by a renewal of DNA methylation. Moreover, the results from MS-PCR and determination of expression levels by RT-PCR of several genes (p16, hMLH1, hMSH2, DNMT1, DNMT3a and DNMT3b) demonstrated that hMSH2 gene was epigenetically regulated and that down regulation of DNMT3a and DNMT3b genes occurred in an arsenite dose-dependent manner. The results reported here demonstrate that acute arsenic exposure promptly induces genomewide DNA hypomethylation and support the hypothesis that the cells undergo epigenetic reprogramming both at gene and genome level, in the absence of further arsenite treatment; these DNA methylation changes are likely contributing to long-lasting genomic instability that manifests as aberrant chromosomal effects and mutator and transformed phenotypes.

EM154
POTENTIAL GENOTOXIC EFFECT OF DIFFERENT SUPERFICIAL MORPHOLOGY OF AMORPHOUS SILICA EVALUATED IN MURINE ALVEOLAR MACROPHAGES (RAW 264.7) CELL LINES BY COMET ASSAY AND MICRONUCLEUS TEST

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Exposure to crystalline silica may cause lung fibrosis, carcinomas and autoimmune diseases. Instead amorphous silica micrometer-sized is accepted as having low toxicity and is used as a food additive. No sufficient evidence exists about the health hazards caused by amorphous (non-crystalline) silica of lower dimension, nor as regard its superficial conformity. The aim of the study is to investigate the potential genotoxic effects of amorphous silica nanosized particles (250-500 nm diameter) with different superficial morphology, by *in vitro* experimental models. Murine alveolar machrophages (Raw 264.7) cell lines have been used as representative of occupational and environmental exposure. Genotoxicity was evaluated by Comet Assay and Micronucleus Test. Cytotoxicity was tested using both Trypan Blue and Crystal Violet methods. Cell lines have been treated with 5-10-20-40-80 $\mu g/cm^2$ of MCM-41 mesoporous silica particles (250, 500 nm) and SiO_2 dense spheres (250, 500 nm). Powders were suspended in complete MEM solution, and sonicated for 30 minutes at 37°C (35 KHz) to prevent aggregation. Comet assay was used to evaluate genotoxicity at 4 and 24 hours exposure. The same doses of exposure were tested by micronucleus test. Hydrogen peroxide was used as positive control for DNA primary damage in Comet assay, Mytomicin C for micronucleated cells. Preliminary Comet assay results only seem to indicate a weak genotoxic effetct except for the highest dose (80 $\mu g/cm^2$) of MCM-41 mesoporous silica particles, where a statistically significant effect was found at the highest time exposure (24 hrs) and dimension (500 nm). For the dense sphere of the same dimension of MCM-41 a statistically significant increase of DNA damage was also observed at the lowest dose after 24 hrs exposure. A different trend was showed by the smaller size compunds which displayed a statistical significant increase of DNA migration at the lowest time exposure (4 hrs) and dose. Generally, dense silica spheres appear to be more genotoxic at lower doses (5-10 $\mu g/cm^2$). Smaller ones (250 nm) induce an increase of DNA damage at 4h, while the bigger (500 nm) at 24h. Further studies are needed to better investigate silica particles genotoxic effects even after long lasting exposures.