higher concentrations (at the micromolar range), Lam-D promoted a rapid cell death irrespective of its nuclear effect on topoisomerase-I. Using cancer cells lacking mitochondrial DNA we also showed that mitochondrial ROS were required for Lam-D-induced apoptosis. In conclusion, our study indicates that Lamellarin–D may act as a potent pro-oxidant agent responsible for both senescence and apoptosis in cancer cells.

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Polymorphisms in glutathione S-transferases increase colorectal cancer risk

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Background: Colorectal cancer (CRC) is one of the most frequent malignancies. CRC incidence in Czech republic ranks third worldwide. The majority of CRC are sporadic cases accounting for over 85% of all cases. High mortality is probably caused by diagnosis of CRC in advanced stages when prognosis is bad. Low-penetrance genes, e.g. genes coding xenobiotic-metabolizing enzymes (XME) belong to relevant factors modifying an individual susceptibility to CRC. This hospital-based case-control study followed functional polymorphisms in XME as potential CRC susceptibility factors.

Materials and methods: Polymorphisms in glutathione S-transferases GSTM1 (deletion), GSTT1 (deletion), GSTP1 (Ile105Val), NADP(H)-quinone oxidoreductase NQO1 (Pro187Ser), cytochrome P450 CYP1B1 (Asn453Ser and Leu432Val) and epoxide hydrolase EPHX1 (Tyr113His and His139Arg) were assessed by PCR RFLP in 784 CRC patients and 493 unrelated colonoscopy cancer-negative controls of Czech Caucasian origin.

Results: Heterozygous genotypes in CYP1B1 (OR=0.68, CI=0.52-0.90, P=0.007) and GSTP1 (OR=1.30, CI=1.00-1.67, P=0.049) and deletion polymorphism in GSTM1 (OR=1.31, CI=1.04-1.66, P=0.024) were associated with CRC risk. The risk was further enhanced in carriers of combination of variant alleles in GSTM1 and GSTP1 (OR=1.80, CI=1.24-2.60, P=0.002) and in smokers carrying the deletion in GSTM1 (OR=2.08, CI=1.42-3.04, P<0.001). Polymorphisms in EPHX1, NQO1 and GSTT1 were not associated with CRC risk.

Conclusions: The results of this study further support the concept that interaction between metabolism and environment contributes to colorectal carcinogenesis. Glutathione S-transferases should be further followed as candidate risk-associated genes in carefully controlled studies with special attention to exposure status of participants.

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Gene expression signatures in BALB3T3 fibroblasts exposed to cobalt micro/nano-particles and cobalt ions

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Nanoscale materials are increasingly employed in several industrial applications as well as in biology and medicine. Despite their wide predicted utilization, little research has been carried out on the potential toxicity of metal-based micro/nano-materials. To explore possible biological effects relevant to toxicity that could depend on the physical characteristics of compounds, we investigated the global gene expression patterns of BALB3T3 A31-1-1 cells exposed or not to 1 microM concentrations of cobalt microparticles (Co-micro), cobalt nanoparticles (Co-nano), and cobalt ions (Co++). All exposures were carried out at semi-confluence for 72 hrs, as determined based on toxicity assays performed for toxic metals. Global gene expression analyses were carried-out using 70 mer murine 13.443 oligonucleotide microarrays (Operon version 1.1). Data were normalized using the MIDAS program and elaborated using the SAM program. Molecular interaction networks were constructed applying gene ontology, canonical pathway and functional network analyses with the Ingenuity Pathways Analysis (IPA) tools software (http.//www.ingenuity.com).This showed that the involved molecular pathways differed according to exposure: the interferon, apoptosis, JAK/STAT and death receptor signalling pathways were involved following Co-nano exposure; nucleotide sugar metabolism, G1/S cell cycle check point, hypoxia signalling and ubiquitination following Co-micro exposure; no statistically significant alterations in molecular pathways were detected after exposure to Co++. Real-Time PCR analysis confirmed that exposure to Co-micro, Co-nano, and Co++ down-modulated Rab18, a member of the RAS oncogene family, and that Co-micro exposure down-regulated CAV2, a key constituent of caveolae, integral membrane components. Rab18 and CAV2 represent candidate biomarkers of possible effects on the regulation of intracellular membrane trafficking after Co-micro, -nano, and -ions exposure. In addition, our results show that exposure to Co-micro, Co-nano and Co++ differentially activates cellular pathways that control defense and repair mechanisms.

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Lung cancer in never smokers in Florida: 1981-2003

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Lung cancer is the leading cause of cancer death among men and women. (1) Recently there has been increased awareness of lung cancer in never smokers, especially women (2-5). It has been estimated that 10% of lung cancers occur among never smokers (2). Studies have been inconsistent however in finding gender differences in lung cancer risk (2, 6, 7).

The study investigated whether lung cancer is increasing among never smokers and if any increase is primarily among female never smokers. The study also considered the related issues of gender differences in age at diagnosis, stage, grade and histology.

This study included histologically confirmed primary carcinoma of the lung in the Florida Cancer Data System, 1981- 2003. Data in the de-identified file included gender, race, smoking status, age at diagnosis and tumor characteristics. Odds ratio were used to estimate relative risks, logistic regression was used to calculate adjusted odds ratios and ninety-five percent confidence intervals for the odds ratios.

In Florida, during the study period, 10618 histologically confirmed primary carcinomas of the lung were reported among men and 13134 among women. The number of lung cancers among never smokers increased from 4841 for 1981-85 to 6061 for 1996-2000. Despite this increase, the proportion of lung cancers that occurred in never smokers decreased over time for each major cell type, among men and women. Differences by gender remained however and a never smoker who developed lung cancer was more likely to be female than male. The odds ratio for being a never smoker if female was 1.93 (1.87-1.98) that of a male. Odds ratios were greatest for adenocarcinoma OR=2.28 (2.19-2.37) and least for small cell carcinoma OR=1.14 (1.06-1.23). Further analyses are underway.

As lung cancer continues to increase among women, the proportion of cases among never smokers decreases while the absolute number of lung cancers increases, resulting in the perception of increased risk of lung cancer among women who never smoked.

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