ERK1 but not of ERK2 protein partially abrogated the proliferation inhibition by UDCA.
Conclusion: High and persistent ERK phosphorylation is the likely mechanism of proliferation inhibition by UDCA.

886 Information function, carcinogenic action and radioprotective properties of chemical compounds

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Background: Actual problem of modern chemistry of biologically active substances is the problem of produce of preparations that effective in the radio protective relation. The basic requirements to these preparations are small doses, low toxicity and absence of collateral action. Purpose of this to pay attention to possible linkage of radioprotective action and carcinogenic activity of preparations. Quantitative characteristics of this linkage are resulted. An attempt made to construct a quantitative model of relationship of the carcinogenic and radioprotective properties of biologically active compounds with their electronic and information factors.
Materials and Methods: In this work the method is offered for revealing linkage between carcinogenic and radioprotective properties of drugs with their molecular structure. In this work the method is offered for revealing linkage between carcinogenic and radioprotective properties of preparations with their molecular structure. The approach uses the factorial characters: the mean quasivalency number Z of a molecule and information function H of Shannon–Wiener. We have analyzed more than 120 various chemical compounds.
Results: It is established that carcinogenic properties of chemical compounds and effective radioprotectors are overlapping with each other. Parameters Z and H statistically authentically separates the compounds having radioprotective effect from compounds do not having radio protective action. For overwhelming number of preparations having activity the parameters $Z < 3.0$ and $H < 1.79$ *bit*. Whereas for the chemical preparations which are not possessing protective activity $Z > 3.0$ and $H > 1.97$ *bit*. The suggested method of selection of preparations most effective for drugs which find out protective action at small doses ($\ll$1 mM/kg) and are inactive even at very large doses ($\gg$1 mM/kg). At the same time use of molecular characters Z and H for separating the carcinogenic compounds also leads to statistically authentic results. The information function for the chemical preparations possessing carcinogenic activity $H < 1.41$ *bit* and not possessing ones $H > 1.86$ *bit*.
Conclusions: Within the framework of an information approach and the statistical method of comparison of quality characters, a systemic factor is proposed that permits to reliable distinguish highly radioprotective agents and carcinogenic compounds among a series of chemical substances. It was shown that the correlation relationships are able apply to studies of the mechanism of action of the preparations and for the purposeful synthesis of new effective radioprotectors.

887 Alterations of copy number of methylation pattern in MMR genes by MS-MLPA methodsin cases of colon cancer

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Background: Like other tumour types, colon carcinoma is thought to arise following the activation of oncogenes and inactivation of tumour suppressor and DNA-repair genes. In addition to genetic alterations, epigenetic abnormalities, such as changes in genomic DNA cytosine methylation patterns, are associated with all cancer types. The syndrome is caused by germline mutations in DNA mismatch repair (MMR) genes, predominantly MLH1 and MSH2.1. More than 1,500 different variants in MMR genes have been reported, approximately half of which may be pathogenic.
Material and Methods: In our study with a diagnosis of colorectal cancer tissue samples embedded in paraffin were used. With total 70 samples were studied, adenocarcinoma is 49 (70.0%) of samples, carcinoma is 21(30.0%) of total consists of samples. A modification of the MLPA technique, MS-MLPA (methylation-specific multiplex ligation dependent probe amplification) allows the detection of both copy number changes and unusual methylation levels of 10−50 different sequences in one simple reaction. MLPA probes for methylation quantification are similar to normal MLPA probes, except that the sequence detected by the MS-MLPA probe contains the sequence recognized by the methylation-sensitive restriction enzyme HhaI. Gene methylation status was evaluated by (MS-MLPA), using the ME001 tumour-suppressor kit (MRC Holland). A total of 24 genes were studied, using 20–200 ng of sample DNA. The amplified products were analyzed by sequence-type capillary electrophoresis (ABI 310; Applied Biosystems, Foster City, California, USA). The peak sizes and areas were exported to an Excel file, and the normalized areas from the digested and undigested samples were compared to determine the methylation status of the genes in colon cancer patients.
Results: According to the results of this amplification mean MLH1 methylation rates (97.14%), MSH2 (24.28%), MSH6 (67.14%), MSH3 (78.57%), MLH3 (75.71%), PMS2 (65.71%), MGMT (82.85%) were found to be.
Conclusions: The Mismatch Repair (MMR) system is critical for the maintenance of genomic stability.

888 In vivo genotoxicity of deltamethrin, a synthetic pyrethroid

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Deltamethrin, an alpha-cyano class of pyrethroid insecticide is widely used in agriculture, public health and livestock due to its high activity against a broad spectrum of insect pests and low toxicity to humans. In the present study, by taking into consideration of the consumption risk of deltamethrin by mammals, the in vivo cytogenetic effect of deltamethrin was evaluated by assessing the ability of the insecticide to induce micronucleus formation in bone marrow and peripheral blood erythrocytes and splenocytes.
Deltamethrin was administrated to adult mice as i.p. doses of 50, 100, 200 mg/kg/bw in %10 tween 80. To the positive control group, Mitomycin C, which is a mutagenic agent, prepared in saline, was given in 2 mg/kg bw doses. Samples were taken 48 h after the treatment.
All doses of deltamethrin significantly ($p < 0.001$) increased the frequency of micronuclei in erythrocytes and splenocytes, compared with the control group. A linear relationship was evident between the doses of deltamethrin used and the frequencies of micronuclei. The micronucleus induction suggets a clastogenic potential of deltamethrin and indicates the in vivo susceptibility of mammals to the potential genetic toxicity of deltamethrin.

889 The involvement of miR-483 and its host gene IGF2 in development of adrenal cortical carcinoma

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Patients with tumours of the adrenal cortex may present incidentally detected or hormonally overproducing adenomas (ACA), or uncommonly the very aggressive carcinoma (ACC). Recent genome-wide studies of gene expression have revealed significant alterations in the different tumour entities of possible diagnostic and prognostic relevance. Of special interest is the frequent finding of *IGF2* over-expression, observed in the ACC entity only. The aim of this study was to identify molecular signatures of ACC based on microRNA (miRNA) expression profiling, and to determine the role of specific miRNA in the development of ACC and its relation to *IGF2*.
Global miRNA expression profiles were determined in a series of ACC, ACA and normal adrenal cortical samples by using two different platforms (miRNA oligoarray and miRNA qRT-PCR array respectively), and the results were confirmed by qRT-PCR. Distinct miRNA expression signatures were observed between the three sample groups. Over-expression of *miR-483−3p* was frequently observed in ACC samples, but not in their normal or benign counterparts. Interestingly, *miR-483−3p* is located within an intron of the *IGF2* gene. Given that in an extended series of 63 samples (ACCs, ACAs of incidentaloma, Cushing and aldosteronoma types; and normal adrenal) we showed striking co-expression of *miR-483−3p* and *IGF2*. Subsequent knocking down of *miR-483−3p* in the ACC cell line NCI-H295R resulted in significantly decreased cell proliferation as compared to the non-targeting sequence Anti-miR-transfected cells used as negative control. Current efforts are directed to analyzing the biological function of *miR-483−3p* in ACC development, which may lead to the identification of an important target for clinical intervention in ACC.

890 IDH1 and IDH2 mutations in Bulgarian patients with glial tumours

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Background: Gliomas, the most common type of primary brain tumours, include distinct disease entities that affect patients of different age and vary in prognosis. In the recent years many comprehensive studies were focused on genomic characteristics of gliomas. This led to the discovery of a variety of genes that were not associated with glial carcinogenesis before. Mutations in genes encoding isocitrate dehydrogenase isoforms 1 (*IDH1*) and 2 (*IDH2*) have been found in a large proportion of gliomas. *IDH1* and *IDH2* genetic alterations occurred early in tumour progression of brain neoplasias, but very rarely in other solid tumours and were associated with better outcome.