

the last year. The causal relationship between HPV and cervical cancer was known by 71% of the participants. From the participants, 43% had heard of the HPV vaccine, principally by mass media like newspapers, television, radio and 66% of these knew the correct age group for which the HPV vaccine was recommended in France. 98% were aware that only females were eligible for the HPV vaccine and 77% that the vaccine has to be administered before the onset of sexual activity. Only 4% of the participants had received at least one HPV vaccine dose. Fifty-two percent of the women, despite vaccination, knew that population-based screening for cervical neoplasia needs to be continued.

Conclusion: One year after introduction of the first two HPV vaccines in France, only 43% of women in our study knew HPV causes cervical cancer and that women can get vaccinated against it.

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Modulation of mRNA and protein levels of CYP1A1, 1A2, and 1B1 in nontumorigenic breast epithelial cells (MCF10A) by cabbage juice and its active components

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Epidemiological migrant studies have shown that consumption of raw or short cooked cabbage and sauerkraut is connected with significant reduction of breast cancer incidences. Concurrently, some of the active components of cabbage juices like indole-3-carbinol (I3C), 3,3'-diindolylmethane (DIM) – a major in vivo acid-catalyzed condensation product of I3C, and sulforaphane (SUL) were determined as potential anticancer agents.

Our previous study showed that cabbage juice and its isolated active ingredients affected the expression of the estrogen metabolism key enzymes including cytochrome P450 1A1/1A2 and 1B1 in MCF7 breast cancer cell line. The aim of the present study was to investigate the effect of cabbage and sauerkraut juices of different origins and I3C, DIM and SUL on the expression profile of CYP1A1, CYP1A2, CYP1B1 mRNA and proteins level in nontumorigenic human breast epithelial MCF10A cell line.

Cells were treated with the pure compounds at the concentrations relevant to those observed in human plasma. After 72 hours of incubation the screening of cDNA from total RNA was performed using real-time PCR assay with specific primers for CYPs and protein level was determined by Western blot analysis. The increased expression of CYP1A1 was found as a result of cabbage juices treatment. Sauerkraut juice has stronger effect than raw one. Similar effect was exerted by I3C and DIM. The CYP1A1 protein level was increased as result of I3C treatment at the dose of 30 µM. In contrast, a decreased level of protein was detected after treatment with lower dose of this compound (10 µM), both doses of DIM, and SUL at the dose of 5 µM. The decrease in CYP1B1 mRNA was observed after sauerkraut juice treatment. In contrast, expression of CYP1B1 was increased by both indoles and SUL at the concentration of 108 µM. CYP1B1 protein was decreased as result of DIM treatment at the dose of 5 µM. Up-regulation of CYP1A1 and CYP1A2 results in the reduction of active estrogens and might prevent breast carcinoma development. Thus the increase of CYP1A1 and CYP1A2 mRNA levels as a result of treatment of MCF10A breast epithelial cells with indoles or CYP1A1 and CYP1A2 mRNA and protein levels with cabbage juices observed in this study, may explain in part the epidemiological observations linking the cabbage consumption with decreased risk of breast cancer development.

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Purification and characterization of an N-acetyllactosamine specific lectin from tubers of *Arisaema utile* having anti-proliferative effect on human cancer cell lines

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Objective: Lectins are defined as carbohydrate binding proteins other than enzymes and antibodies. Lectins have emerged as very important macromolecular tools to recognize carbohydrates on cell surfaces. The present work is designed to purify and characterize monocot lectins with interesting biological properties from Indian monocot plants.

Methods: On the basis of sugar specificity determined by hemagglutination, asialofetuin-linked affinity was used to purify monocot lectins. Anti-proliferative potential were determined through sulphorhodamine-B assays.

Results: *Arisaema utile* lectin (AUL) gave a single band in SDS-PAGE at pH 8.3 corresponding to subunit Mr 13.5 kDa. The native molecular mass of 54 kDa suggested a homotetrameric structure. Like other monocot lectins, AUL gave multiple bands in isoelectric focusing and in native PAGE at pH 8.3. AUL was inhibited by N-acetyl-D-lactosamine (LacNAc), a disaccharide and asialofetuin, a complex desialylated serum glycoprotein. When treated with denaturing agents, the lectin was stable in the presence of urea (3M), thiourea (4M) and guanidine HCl (4M). The lectin had no requirement for divalent metal ions i.e. Ca²⁺ and Mn²⁺ for its activity. AUL was a glycoprotein with a carbohydrate content of 1.2%. Amino acid analysis revealed high content of aspartic acid, glutamic acid, glycine and threonine and a very low amount of methionine but complete absence of cysteine. Amino acid modification studies of AUL revealed the involvement of tryptophan and tyrosine residues involved in lectin-sugar interaction. AUL exhibited a fluorescence emission maximum (lambda max) at 340 nm upon excitation at 295 nm. Using Far UV CD spectra the estimated secondary structure was 37% alpha-helix, 25% beta-sheet and 38% random contributions. In vitro anti-proliferative activity of AUL was tested on eleven different human cancer cell lines viz. MCF-7 (Breast), SK-N-SH (CNS), 502713 (Colon), Colo-205 (Colon), HCT-15 (Colon), HT-29 (Colon), SW-620 (Colon), Hep-2 (Liver), IMR-32 (Neuroblastoma), DU-145 (Prostate) and PC-3 (Prostate). The concentrations of AUL which produced 50% inhibition (IC50) of cancer cell lines viz. SW-620, HCT-15, SK-N-SH, IMR-32, Colo-205 and HT-29 at 38, 42, 43, 49, 50 and 89 µg/ml, respectively.

Conclusion: The purified *Arisaema utile* lectin was found anti-proliferative on human cancer cell lines.

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Breast cancer: Molecular mechanisms underlying resistance to chemotherapy

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Breast cancer is the second leading cause of cancer deaths. This disease is estimated to be diagnosed in over one million people worldwide. Although chemotherapy is a successful treatment regime in many cases multidrug resistance (MDR) remains one of the main obstacles in treatment of these cancer patients. Several proteins have been identified that are able to prevent the intracellular accumulation of anticancer agents by efflux mechanism. Such drugs are exported in both ATP-dependent and -independent manners. To the ATP-dependent group belongs the ATP-binding cassette (ABC) transporter family, which includes P-gp, MRP, BCRP, etc. Another protein related to MDR, though not belonging

to the ABC transporter family, is lung resistance-related protein (LRP).

Since MDR requires one or combination of these genes expression, clinically relevant gene expression thresholds have been established and sequential samples from individual patients have been obtained for correlating MDR gene expression with the clinical course of disease. Studies in breast cancers, showed that expression of some of these genes correlates with poor response to chemotherapy.

In this presentation, I will provide an overview of the data (including ours) regarding the role of these genes in mediating drug resistance in breast cancer. In addition, I will briefly explain some of the strategies employed to overcome drug resistance in cancer cells.

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Hypothesis on targeted modification on human individual radiosensitivity as a new method of anti-cancer protection

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Goals: To represent and substantiate the hypothesis on targeted modification on human individual radiosensitivity on the genetic level. This is explained by the investigations which revealed that the formation of chromosomal aberrations in cell population is potentially an oncogenic event. Therefore, an increased individual radiosensitivity in comparison with mean population level value is the factor of radiogenic cancer and development of the risk. New candidate genes of human individual radiosensitivity connected with the formation of radiosensitive cell phenotype (BRCA1, BRCA2, XRCC1 etc.) are known today.

Methods: Analysis of chromosomes aberrations in culture of human lymphocytes, G2-radiosensitivity assay.

Results: The basis of the presented hypothesis is the position that targeted modification of individual radiosensitivity of human organism consists of the formation of normal mean population values of radiation effects and reactions. The proposed approach to modification on human individual radiosensitivity radically differs from the traditional 'radioreistance increasing', which assumes increased intensity of repair and other radioprotection systems functioning leading to their exhaustion in conditions of long-term irradiation and modification of individual radiation reactions. Pathology status is determined as the deviation from norm (increasing and reduction of parameter value is mean). Thus it is expedient to modify hypo- and hypersensitivity of human cells, tissues and organism in case of radiation therapy, the strategy of which is directed to maximal lesion (deviation) of tumor cells and protection of surrounding normal tissues.

Conclusions: The proposed hypothesis on targeted modification on human individual radiosensitivity is aimed at lowering the level of cancerogenic risk. The suggested method would increase an efficiency of the primary prevention of the development of the radiogenic cancer.

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The experimental proof of the usage of radioprotector inosine for cancer prevention

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Goals: To study the modification effect of inosine on the frequency of the radiation-induced cytogenetic effects in human somatic cells.

Methods: The irradiation of lymphocytes in vitro received from healthy donors had been done on therapeutic apparatus "Rockus" (with ⁶⁰Co source) in range 0.1–1.0 Gy. The metaphase analysis of chromosome aberrations had been carried out with group karyotyping. The inosine was added to

the cell culture in the concentration of 0.01 mg/mL of blood 30 min before the irradiation.

Results: The highest radioprotective effect of inosine is observed when the cell culture is irradiated in the range between 0.1–0.2–0.3 Gy. The level of chromosome aberration decreases from 6.06±0.6; 7.06±1.6; 7.76±1.0 to 1.6±0.1; 2.6±0.4; 2.2±0.6 respectively and reaches the meanings of spontaneous level of genetic damages of human's cells. During this the coefficient of modification equals to 2.7–3.8. With a further increase in radiation up to 1.0 Gy, the radioprotective effect of inosine decreases and the coefficient of modification equals to 1.2. Under the effect of inosine the dose curve built on the basis of group-average frequency of chromosome aberration, is situated below the caliber curve with the same plateau in the range 0.1–0.3 Gy, which has been observed under the single radiation. Since the process of reparation always takes place with the usage of energy, inosine, which stimulates the processes of renovation in a genetic material of cells, thus decreases the level of chromosome aberrations, that mirror genome instability and may cause the development of radiation cancerogenesis.

Conclusions: The protective effect of inosine has been established on the genetic level of human somatic cells by using small doses of radiation. Inosine does not affect an abnormal form of the 'dose-effect' curve. Obtained data regarding inosine effect on human genome stability should be taken into account for a primary prevention of the development of radiogenic tumors as a remote negative effect of Chernobyl accident.

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Cardioprotection during cancer chemotherapy with the use of natural antioxidants: review of literature and results of own studies

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Cardiotoxicity is a frequent side effect occurring during cancer chemotherapy, often responsible for long term heart failure in surviving cancer patients. The abnormalities range from small changes in blood pressure and arrhythmias to cardiomyopathy. This type of toxicity has been most widely investigated in the case of anthracyclines, doxorubicin (DOX) in particular, the effective anticancer drugs whose clinical use is limited by cumulative dose-dependent injury to cardiac tissue, often jeopardizing patients' life despite successful cancer eradication. Though best described for DOX, cardiotoxicity as a side effect has been observed during chemotherapy with majority of antineoplastic agents displaying different mechanisms of action: mitoxantrone (cardiomyopathy), fluorouracil (myocardial infarction), cyclophosphamide and vinca alkaloids (cardiac necrosis), trastuzumab (cardiac disfunction), imatinib mesylate (congestive heart failure).

The cardiotoxicity of anthracyclines, at least in part, is attributed to their ability to redox cycle with molecular oxygen leading to the formation of superoxide radical that initiates cascade of reactive oxygen and nitrogen species. It has therefore been suggested that some phytochemicals with high antioxidant potential, when administered together with DOX (and perhaps other antitumor agents), could decrease the toxic side effects of chemotherapy and reduce the risk of heart failure. Cardioprotective properties have been shown for preparations obtained from such foods as grapes, garlic, tomato, spinach, as well as for melatonin (a hormone synthesized by the pineal gland, but also present in many edible plants), chalcones (precursors of all known