

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.

## P29

### 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.

## P30

### 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 <sup>60</sup>Co 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.

## P31

### 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