

glandular hyperplasia in reproduction period (mean percentage of reactive cells – Labeling Index-LI $14,8 \pm 0,4\%$), menopause period (LI $18,2 \pm 0,8\%$), atypical hyperplasia (LI $15 \pm 0,5\%$) and well differentiated carcinoma (LI $22,6 \pm 0,3\%$). All specimen of glandular hyperplasia were negative for p53 expression. P21 expression was observed in 50% cases of glandular hyperplasia, but LI was low (<7) P16 expression was lower in hyperplastic endometrium of reproduction period (LI $30 \pm 0,3\%$), increased in menopause (LI $41 \pm 0,6\%$), decreased in atypical hyperplasia (LI $33,2 \pm 0,2\%$) and high differentiated carcinoma (LI $14,9 \pm 0,2\%$). It was observed over expression of both p53 and p21 (LI $91,0 \pm 0,9\%$ and $28,5 \pm 3,2\%$ accordingly), lowering of expression p16 (LI $28,0 \pm 0,3\%$) in one case of atypical hyperplasia, other specimen of atypical hyperplasia were negative for p53 and p21 expression. In groupe of patients with high differentiated adenocarcinoma was determined increasing expression of p53 (LI $35,9 \pm 0,8\%$), p21 (LI $7,8 \pm 0,2\%$) and decreasing expression of p16 (LI $14,9 \pm 0,2\%$).

Conclusion: The most of cases of hyperplastic endometrium were characterized high proliferative activity, which was increased in patients with glandular hyperplasia in menopause and atypical hyperplasia. Patients with high proliferative potential, high expression of Ki-67, p53 p21 genes and lowering expression of p16 form high group of risk for malignant transformation and require especial dynamic observation.

P21

Nucleolar organizer regions (NOR's) of chromosome as marker of endometrial proliferation

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Objective: The evaluation of NOR's in patients with glandular hyperplasia (GH) and endometrial cancer (EC).

Material and methods: Cultivated peripheral blood lymphocytes (PBL) and the surgical material of 106 patients with GH and EC were used. The NOR's analysis in metaphase chromosomes of PBL and histological sections of endometrium, stained with AgNO₃ according Howell and Black was performed. DNA content in endometrial epithelial cells was carried out using scanner microcytospectrophotometer MCSU-2MT.

Results: The estimation of PBL NOR's revealed the significant increasing of NOR's level of expression in 13, 21 and 22 chromosomes and elevated association index in EC patients in comparison with the same in GH patients. The biggest frequency of 13 and 21 chromosomes association was determined in cancer patients.

The study of NOR's in endometrial interphase cells revealed reliable increasing of mean quantity AgNOR's in tumour cells in comparison with GH of endometrium. It was determined progressive increasing of expression of NOR's in high-, middle- and low differentiated carcinomas (LI= $2,91 \pm 0,27\%$; $4,63 \pm 0,41\%$; $8,57 \pm 0,4\%$, accordingly) in patients with endometrial cancer. The analysis of cell number with more than 5 AgNOR's, that reflects the cell fraction in S-phase of cell cycle demonstrated the increasing of proliferating epithelial cells population in the line from high- to low-differentiated EC. The last correlated with increasing level of Ki-67 expression (LI= $22,6 \pm 0,3\%$ in high- in comparison with $47,6 \pm 0,4\%$ in

low differentiated carcinomas) and p53 (LI= $35,9 \pm 0,8\%$ in high- compared with $57,4 \pm 0,6\%$ in low differentiated carcinomas) and with elevated aneuploidy and predomination of nearly-triploid (56,6%) cells in patients with low level differentiated cancer. The correlation between mitotic activity and mean quantity of AgNOR's in nuclei in endometrial tumour cells was determined ($r=0,63$).

Conclusion: The obtained data give evidence that the level of expression of ribosome cystrons correlates with structural peculiarities of endometrium and can be a cytogenetic marker of genome instability. Activity AgNOR's with indicator expression of Ki-67 and p53 are objective criterions of proliferative potencial and can be used for differential diagnostics of glandular hyperplasia and endometrial cancer and as an additional marker of malignancy degree of tumour process in uterus.

P22

Cysteine proteases as biomarkers in murine tumors sensitive and resistant to cyclophosphamide

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The expression, activity and concentration of cysteine proteases in tumor tissue and serum can be used as prognostic and diagnostic biomarkers in several types of human cancer (Kos et al., 2002).

Aim: to evaluate the cysteine proteases as biomarkers in murine tumors, sensitive or resistant to cyclophosphamide (CPA) treatment.

Methods: DBA/2 mice with leucosis P-388 and L1210 (less aggressive) and CBA mice with lymphosarcoma LS, sensitive or resistant to cyclophosphamide (CP) were treated by CP (25, 30, 50 and 100 mg/kg) or/and new immunomodulator sulfoethylated glucan (SEG, Institute of Chemistry, Slovak AS, Bratislava, 10, 25, 50 mg/kg, single or three times). Cysteine protease activity was measured by fluorometrical method (Barrett, Kirshke, 1980).

Results: In murine leukosis P-388 as compare to leucosis L1210 (less aggressive) solid tumor development was characterized by lower cathepsins B, L and D activity in tumor tissue. The effective treatment by CPA and SEG was followed by tumor growth suppression and increased activity of proteases studied. In comparison to sensitive variant the resistant variant of lymphosarcoma LS was characterized by aggressive development, faster tumor growth, poor condition of mice and their shorter survival. Activity of cathepsins B, L and D in tumor tissue in resistant type was significantly lower comparatively to susceptible type of lymphosarcoma LS, during combined therapy activity of proteases increased. Preliminary to CPA administration of SEG enhanced therapeutic action of CPA both susceptible and resistant type of lymphosarcoma LS. In the both cases the significant synergistic effect of SEG was revealed at the lowest dose applied (10 mg/kg). The results obtained imply a possibility of application of low doses of SEG during combined tumor therapy with cytostatics. Similar doses SEG were effective in combination with CPA as preventive (preliminary administration of SEG). Moreover, SEG (10, 25 mg/kg) alone revealed antitumor activity in lymphosarcoma LS

model, revealing inhibition of tumor node. SEG like other b-1,3-glucans is perspective in treatment and prevention of tumor development as host defense modifiers

Conclusion: We can conclude that cathepsins B and L and aspartic protease cathepsin D are biomarkers of murine tumor development and SEG is perspective in prevention and therapy of murine tumors as immunomodulator, host defence modifier.

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Epidemiology/Screening

P24

Serial cytological assay of buccal exfoliated cells as technology for mass screening of individuals with risk of oral cancer for monitoring and cancer prevention

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The analytical epidemiology associated oral cancer with long-term smoking tobacco and drinking alcohol and exposure to various carcinogens. The aim of our study was to investigate the state of distant oral mucosa in patients with oral squamous cell carcinoma (SCCs) and in patients with risk of oral cancer that depends on age, social-demographic parameters, smoking-drinking status, clinical stage, tumor stage, DNA content, p53 expression, serum levels of VEGF. Buccal scrapes, biopsy specimens of tumors and squamous epithelium in tumor-distant mucosa were taken from 30 patients with SCCs. Buccal scrapes of patients with risk of oral cancer were studied in 20 volunteers living in the 5 km area from Rivne NPS. Buccal scrapes from 10 volunteers (age 19 years, nonsmoking, no drinking) were used as controls. Buccal scrapes were stained by Pap with some modification by Rudenko. Cytological changes in buccal mucosa were estimated by the dimension of nucleus, the structure of chromatin, the colouring of cytoplasm of epitheliocytes and differentiation index. DNA content was analyzed using Feulgen staining. P53 staining was performed with monoclonal anti-p53 antibody. Serum levels of VEGF (ng/ml) were measured by an enzyme immunoassay. The analysis of the buccal epithelium and tumor-distant mucosa epithelium showed, that normal epithelium was not detected in patients with SCCs. Progression of the histopathological phenotype in buccal and tumor-distant mucosa depended on clinical stages, p53 status and serum levels of VEGF. Similar alterations in differentiation and maturation of epitheliocytes, significant decrease of differentiation index, and transition to hyperplastic and dysplastic epithelium were revealed in buccal epithelium scrapes from both patients with SCCs and patients with risk of oral cancer. It was concluded, that oral tumorigenesis in men from Ukrainian population has not been correlated strongly with long-term smoking. Revealed similar alterations in buccal epithelium may be used in serial cytological assay of exfoliated cells for screening of individuals with risk of oral cancer. This technique is easy reproducible, economical and non-invasive.

P25

Participation rate and related socio-demographic factors in the National Cancer Screening Program

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Background: Cancer is the leading cause of death and one of the largest burdens of disease in Korea. In 1996, the 'Ten year Plan for Cancer Control' was formulated and the government then adopted the plan as a national policy. As part of this plan, the National Cancer Screening Program (NCSP) for Medicaid recipients was formulated, and the government adapted this in 1999. For low-income beneficiaries of the National Health Insurance Corporation (NHIC), the screening program has been in place since 2002. In 2002, the target cancers of NCSP were stomach, breast and cervical cancer. This study was conducted to examine the relationships between the participation rate, the abnormal screening rate and the socio-demographic factors associated with participation in the screening program.

Methods: To analyze the participation rate and abnormal rate for the NCSP, we used the 2002 NCSP records. The information on the socio-demographic factors was available from the database of the beneficiaries in the NHIC and Medicaid.

Results: The participation rate of the Medicaid beneficiaries for the stomach, breast and cervical cancer screening were 9.2%, 15.5% and 15.0%, respectively, and 11.3% and 12.5%, except cervical cancer which wasn't be included in the NCSP, for the beneficiaries of the NHIC. The abnormal rate of stomach, breast and cervical cancer screening were 25.7%, 11.2% and 21.0%, respectively, for the beneficiaries of Medicaid and 42.6% and 19.4% for the beneficiaries of the NHIC. On the multiple logistic regression analysis, gender, age and place of residence were significantly associated with participation rates of the NCSP. For stomach cancer, women participated in the NCSP more than men. The participation rate was higher among people in their fifties and sixties than for those people in their forties and those people over seventy years in age. For the breast and cervical cancer, people in their fifties were more likely to participate in the NCSP than people in their forties and people over sixty. For the place of residence, people in the rural areas participated more than those people in any other places.

Conclusion: The above results show that the participation rate and abnormal rate were significantly associated with the socio-demographic factors. To improve the participation rate for the NCSP, more attention should be given to the underserved groups.