Curing of mice by K-48 in low doses after chemical and irradiation influence promoted regeneration of bone marrow cellularity (karyocyte), restoration of mass of body, spleen, hemopoiesis (leukocytes and granulocytes) and immunity, and makes terms of their restoration lesser.
The anti-tumor drugs Decocine and Decovine also possess expressed radiosensitizing properties, exceeding the same action of 5-fluorouracil, that is reasoned their ability both to influence on DNA synthesis and synchronize cells in $M+G_2$ phase.
At present, clinical trials of Decocine are in process. It is revealed that it possesses ability to cure skin cancer; at it, negative affects on hemopoiesis and immunity has not been observed.
Among available synthesized compounds some new anti-tumor, immune-modulating, anti-inflammatory, anti-cirrhotic compounds are selected.

1038 POSTER

Correlation between frequency of BRAF V600E (T1796A) gene mutation and appearance of papillary thyroid carcinoma in a sample of Croatian population

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Papillary thyroid carcinoma (PTC) is the most common malignant tumor of the thyroid gland. There is several oncogenes as BRAF, RET/PTC, RAS, TRK which are involved in cancerogenesis of thyroid cells, but recently, BRAF oncogene, a serine-threonine kinase involved in the phosphorylation of MAPK signaling pathway responsible for cellular proliferation, has become a subject of great importance and interests. The BRAF gene mutations are found in 30−70% of all variants of PTC but there is no any data obout correlation between frequency of BRAF V600E (T1796A) mutation located in the exon 15 of BRAF gene (resulting in the substention of valine to glutamate at codone 600), with appearrance of PTC in a sample of Croatian examinees. We enrolled two group of patients: 59 subjects with PTC (mean age 39.6±3, range 28−56 years) and 68 healthy control subjects (mean age 40.2±2, range 25−55 years) without any history of malignancy in which the clinical evaluation including ultrasound of the neck and thyroid gland did not reveal any thyroid and neck pathology. Genomic DNA was isolated from peripheral venous blood while analysis of BRAF V600E (T1796A) gene mutation was performed using PCR-RLFP methode. The V600E (T1796A) gene mutation was detected in 21 samples in subjects with PTC (36.0%) compared to healthy group in which is mutation detected in 2 samples (2.9%). The difference was statisticaly significant ($p < 0.0001$). Our results indicate that the V600E (T1796A) mutation of the BRAF gene is genetic alteration with high frequency found in PTC amoung Croatian examinees and it could be used as a reliable genetic and preoperative marker but further investigation are needed to confirm these results.

1039 POSTER

Immunohistochemical staining of mammaglobin in breast cancer

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Background: Breast tumours are heterogeneous and new tumour markers are sought to improve patient diagnosis and prognosis. Mammaglobin A appears to be a suitable marker, as it is breast-specific and elevated in up to 80% of breast tumours. This study aims to examine the relationship between mammaglobin A expression in breast cancer specimens with pathological grades/markers.
Materials and Methods: 100 breast tumour specimens were analysed by immunohistochemistry for mammaglobin A expression. Stained sections were screened under the microscope with sections regarded as positive when >10% of lesional cells stained positive. For comparison purposes histological grade, tumour type, tumour size, ER, PR, Her-2 status and the presence/absence of nodal metastasis were recorded. Controls of benign breast conditions were also included.
Results: Mammaglobin was found to be absent in benign conditions and elevated in both invasive and in situ carcinoma. There was a positive correlation between ER positive status and mammaglobin A expression (57% correlation, $p < 0.05$, Chi Squared). There was also a positive correlation between lower tumour grades 1 and 2 (62 and 55% respectively) and mammaglobin A expression, whilst a negative correlation with grade 3 tumours, with mammaglobin protein expression decreasing as tumour grade increased. No correlation was found between presence/absence of nodal metastases, PR status, Her-2 status or tumour size.
Conclusions: Since positive ER status and lower tumour grade are associated with a better prognosis for breast cancer patients, then mammaglobin A protein expression may also be associated with a better prognosis. However, long-term follow-up is required to determine this.

1040 POSTER

KDR/Flk-1 expression in the tumor tissue vascular endothelial cells in two groups of breast cancer patients

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Background: Vascular endothelial growth factor (VEGF) is an endothelial cell specific mitogen which plays a role in pathogenic vascularity associated with carcinogenesis. Tumor cells and primary tumor tissues are known to express high levels of VEGF receptors. We try to evaluate VEGF receptor KDR (human homolog of Flk-1) or VEGFR2 expression in vascular endothelial cells of tumor tissue of the patients with sporadic breast cancer (BC) and pregnancy associated BC (PABC) of comparative age to suggest a bases of progression and dramatic tumor growth in PABC patients.
Material and Methods: Paraffin embedded tumor tissue sections from 12 sporadic BC patients and 12 PABC ones (250 and 300 vascular sections per each group in sum) were studied using image analyze by MatLab 7.0 algorithm. Representative images were confirmed by histopatological study. Immunohistochemical staining of tumor sections was made using pre-diluted antybodies for KDR/Flk-1, VEGF-A and DAP (Dako). KDR expression in fresh tumor tissues from three BC and three PABC patients was estimated also by RT PCR using primers for KDR encoding region (chr.4q11-q12) in comparison with GAPDH gene expression.
Results: Images obtained by Nicon digital microscope were studied for quantifying of VEGFR2 (KDR) expression revealed by immunohisto-chemistry. Preliminary automated image analysis of the receptor core number (density) in vascular endothelium sections of tumor tissue with comparative histological subtype and grade was revealed a significant difference in expression level between BC and PABC tumor tissues with receptor cores number 1.78±0.62 and 0.36±0.20 per vascular endothelium length unit in BC and PABC patients, respectively ($p < 0.002$). Over expression of KDR in PABC tumor tissues in comparison to BC ones was confirmed by RT PCR Automatic extraction of DAB-positive cores along vascular endothelium scatter plots showed more homogenous expression pattern in PABC tumors than in sporadic BC ones.
Conclusion: The data obtained suggest that VEGFR2 (KDR) expression in breast tumor vascular endothelium from PABC patients is higher than in sporadic BC tissues and it indicates on more intensive growth of the tumors and pathological evaluation of BC. Much higher VEGFR2 density and vascularity in PABC tumor tissue may induce activation of specific signal pathways, dramatic tumor progression and further angiogenesis in pregnancy – associated BC patients.

1041 POSTER

Use of tumor markers in a medicine department- a baseline and a post interventional study

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Background: Tumour markers (TM) are potentially useful in clinical practice, but seem to have a limited role in terms of diagnostic because of their poor sensitivity and specificity. Several guidelines exist on the appropriate use of TM, however they are frequently overused. The aim of the present study was to assess the impact of informative and audit activities about the correct use of TM on the use of TM in an internal medicine department in a baseline and in a post interventional evaluation.
Materials and Methods: A baseline study was conducted in an internal medicine department, with all patients to whom TM were requested, over a three month period. Clinical data were extracted from clinical files. The appropriate or inappropriate requests were determined according international guidelines. Results of this study were presented to the clinical staff and informative actions were performed. A post-interventional study was done, using the same methodology as the baseline study.
Results: At baseline TM were requested in 19.6% of patients from the evaluated period. After the intervention this figure dropped 42.6% to 10.2%. In the baseline study the main reason for TM request was diagnosis while in the post-interventional study it screening. In both studies the majority of appropriate requests were done for screening. In both studies most of inappropriate requests were done for diagnosis. In the baseline study 17, 5% of the requests were considered appropriate and there were an increase of appropriateness (TM appropriated in the post-interventional

study: 46%). There was an important decrease in the total costs related to TM, mainly due to a decrease in the costs of inappropriate requests.
Conclusions: The present study shows that informative and "self-audit" activities can have a positive impact in the clinical practice, with a decreased in costs.

1042 POSTER

Human homeobox gene (HOX) A10 is overexpressed in human ovarian clear cell adenocarcinoma and correlates with poor survival

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Human homeobox gene (HOX) A10 is a homeobox allotype gene of the HOXA family in the HOX family. HOXA10 may play an important role in cancer development. However, the role of HOXA10 in the carcinogenesis of ovarian clear cell adenocarcinoma (OCCA) has not been established. We have evaluated the prognostic significance of HOXA10 expression for human OCCA and the effects of HOXA10 on proliferation, motility, and invasion of OCCA cells. We found that HOXA10 was not expressed in normal ovarian epithelium, ovarian endometrial cysts, and ovarian serous carcinomas, but 20 of 29 (68.9%) OCCAs were positive for the expression of HOXA10. HOXA10 expression was negatively correlated to the 5-year survival of OCCA patients ($R = -0.442$, $P = 0.043$). When a HOXA10 expression vector was stably transfected into a human OCCA cell line, ES-2, the proliferation rate of ES-2-HOXA10 was much higher than the vector control, the motility of ES-2-HOXA10 cells was significantly increased compared to the control ($P < 0.05$), and the invasion of ES-2-HOXA10 cells was also much higher than the vector control ($P < 0.01$ at 5 hrs and 12 hrs after scratching). In conclusion, HOXA10 was overexpressed in OCCA and was correlated with poor survival. HOXA10 promotes proliferation, migration, and invasion of OCCA cells. HOXA10 could be a promising prognostic marker for OCCA.

1043 POSTER

BRCA1/2 mutation spectra in Serbia: preliminary results

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Background: Breast cancer is the most common female cancer worldwide, as well as in Serbia. The incidence of breast cancer increases in Serbia – it can be described with about 4000 newly diagnosed cases per year. Among them, up to 10% are present with a striking family history, suggestive of Mendelian inheritance, mostly associated with loss-of-function germline mutations in BRCA1/2 genes. BRCA1/2 mutation significantly elevates lifetime risk for the development of breast cancer (about 5 to 8 fold), as well as for ovarian cancer (10 to 20 fold) underling the importance of genetic testing in potential BRCA mutation carriers. This study was performed with the aim to estimate frequency and spectra of BRCA1/2 mutations in Serbian population.
Material and Methods: Complete or partial analysis of BRCA1/2 coding regions has been performed for 87 probands from 73 families. DNA was isolated by phenol/chloroform extraction from peripheral blood samples of the members of the high risk families. Whole gene screen was performed – coding regions of BRCA1 and BRCA2 genes were amplified by PCR, purified, labeled with fluorescent 3′-dye labeled ddNTPs and precipitated by EDTA/ethanol. These samples were bidirectionally sequenced on automatic ABI PRISM 310 genetic analyzer.
Results: 5 known (185delAG, C61G, 2138delA, 3447del4, 5382insC), as well as one novel BRCA1 deleterious mutations (4765del20) were found. 5382insC has been detected in 4 independent families. Novel BRCA2 deleterious mutation (4366insTT) has also been shown in 2 probands from the same family. The mutation frequency was 12.6%. Besides deleterious mutations, two probably damaging unclassified variant of BRCA1 gene (M1652I and R841W), as well as polymorphic variants of BRCA1 (n = 19 including intronic variants). Two BRCA2 unclassified mutations (S599F and IVS14+6 G>A) n = 16) and 21 polymorphisms, including intronic, were detected.
Conclusions: Slavic mutation 5382insC, found in 4 independent families, is probably founder mutation in Serbia. So far, we did not characterize any other mutation as founder for one population. Some of detected polymorphic variants can moderately modify cancer risk in BRCA mutation carriers and their possible impact has yet to be investigated. The presence of more than one polymorphism in several probands without deleterious mutations raises the question of their overall cumulative influence on breast cancer risk.

1044 POSTER

Comparative proteomics of the radioresistant phenotype in head and neck cancer: Gp96 as a novel prediction marker and radio-sensitizing target for radiotherapy

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Background: Radiotherapy is an integral part of the treatment modality for head and neck cancer (HNC). However, cancers can develop radioresistance (RR), leading to recurrence. In this study, we identified genes that may be involved in RR in HNC.
Materials and Methods: The radioresistant sublines from two HNC cell lines were established. Proteomic method were applied to identify the differential proteins between parental and subline cells. Molecular and cellular based studied were used to conform the role of Gp96 on radioresistance.
Results: A total of 64 proteins were identified as candidate RR genes, and those were subjected to analyzing functional network regulatory pathways. Three most significant of which were cellular response to stimulus ($P = 5.67E-26$), regulation of cell apoptosis ($P = 5.36E-22$) and glycolysis ($P = 1.14E-21$). RT-PCR analysis revealed 6 genes that were consistently differentially expressed in both RR sublines, with Gp96, Grp78, HSP60, Rab40B and GDF-15 being up-regulated and annexin V being down-regulated. Gp96 was further investigated for its functions in response to radiation. Gp96-siRNA transfectants displayed a radiation-induced growth delay, reduction in colonogenic survival, increased cellular ROS level, and increased proportion of the cells in G2/M phase. Xenograft mice administered Gp96-siRNA showed significantly enhanced growth suppression compared with radiation treatment alone ($P = 0.009$).
Conclusion: We have identified 64 proteins and verified 6 genes that are potentially involved in the RR phenotype. We further demonstrated that Gp96 knockdown enhances radiosensitivity, which may lead to a better prognosis of HNC treatment.

1045 POSTER

Human epidermal growth factor receptor 2 (HER2) testing in operable breast cancer: comparison of immunohistochemistry (IHC), fluorescent in situ hybridization (FISH), chromogenic in situ hybridization (CISH), and quantitative real-time polymerase chain reaction (qRT-PCR)

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Background: HER2 protein is overexpressed in approximately 15−30% of breast cancers. Amplification is the primary mechanism of HER2 overexpression. As it is not only a predictive factor but also a prognostic factor, HER2 testing should be routinely performed in patients with a new diagnosis of invasive breast cancer. However, approximately 20% of current HER2 testing may be inaccurate and the best method to assess HER2 status, in regards both to the type of assay used and the optimal method to perform each assay, remains controversial. So, we decided to compare IHC, FISH, CISH and qRT-PCR assays.
Material and Methods: This prospective study included 54 patients with a diagnosis of operable breast cancer whose fresh tumor tissues were obtained between 2005 and 2007. IHC, FISH and CISH analyses were performed on paraffin-embedded samples. Frozen tumor specimens were used for qRT-PCR assay. A positive HER2 result was IHC staining of 3+ (uniform, intense membrane staining of >30% of invasive tumor cells), a FISH result of more than 6.0 HER2 gene copies per nucleus or a FISH ratio (HER2 gene signals to chromosome 17 signals) of more than 2.2. For CISH assay, high HER2 amplification was defined as >10 dots or large clusters of the HER2 gene present per nucleus in >50% tumor cells. According to qRT-PCR method, final results were expressed as a ratio of HER2 gene expression value in the tumor sample normalized with