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