2. PDI and TF are co-located (shown by co-immunoprecipitaion)
3. TF is located on microparticles
4. No truncated TF can be found
5. TF in malignant effusions is coagulatory active (shortening time)

We found a loose inverse correlation between tissue factor activity and PDI levels.

Conclusions: These insight and the development of new, more specific coagulation inhibitors such as FXa-inhibitors will help to treat hypercoagulabilitiy with all negative consequences for cancer patients.

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1127 POSTER

Expression of HER-2 and Its Relation With Pathological and Clinical Features in Differentiated Thyroid Cancers

W. Madah[1], R. Mzalbat[1], P. Gilbey[1], W. Basher[1], A. Sharabi[1], J. Zidan[1]. *[1]Ziv Medical Center, Oncology, Zefat, Israel*

Background: Human epidermal growth factor receptor2 (HER-2) is a well recognized prognostic and predictive factor in breast cancer. Its overexpression in other human cancers may have prognostic significance. The role of HER-2 in thyroid cancer is controversial. The aim of this study is to evaluate HER-2 expression in a large retrospective series of non-metastatic differentiated thyroid cancers (DTC) and to compare it with other clinical and pathological features of the patients.
Methods: We have studied 69 patients with DTC; 58 papillary and 11 follicular carcinomas. HER-2 was detected by immunohistochemistry (IHC) test on sections from formalin-fixed, paraffin-embedded tumour tissues. Dako test was used and results were scaled by Hercept test criteria. Tumours with HER-2 +2 were retested with chromogenic in situ hybridization (CISH) test. All clinical and pathological data was summarized from the hospital files of the patients.
Results: HER-2 overexpression was found in 4 (6.9%) of 58 patients with papillary carcinoma. There was no HER-2 overexpression in 11 cases of follicular carcinoma. No association of HER-2 expression was found with tumour size, pathological grade, age, gender and cervical lymph node metastases.
Conclusion: There were no HER-2 positive cases of follicular carcinoma. The incidence of HER-2 overexpression in papillary carcinoma is very low. HER-2 cannot be used routinely as a prognostic or predictive factor in DTC. The expression of other epidermal growth factor receptors in DTC merits further future studies.

1128 POSTER

Mutations in CHEK2 and TP53 Genes in High-Risk Hereditary Breast and Ovarian Cancer Patients in the Czech Republic

I. Tichá[1], J. Stribrna[1], J. Soukupova[1], P. Pohlreich[1]. *[1]Charles University in Prague First Faculty of Medicine, Institute of Biochemistry and Experimental Oncology, Prague, Czech Republic*

Background: Germ-line mutations in *BRCA1* and *BRCA2* genes account for only 40% of inherited breast or ovarian cancer cases. Thus, mutations in additional susceptibility genes also influence the risk of cancer. In this study we focused on the role of mutations in *CHEK2* and *TP53* genes in families at high risk of breast and ovarian cancer.
Material and Methods: Mutation analysis was performed in a series of 626 unrelated patients previously tested negative for *BRCA1/2* mutations. The complete coding region of *TP53* gene was analyzed by sequencing of cDNA; multiplex ligation-dependent probe amplification (MLPA) was used for the detection of the two most frequent Czech alterations in the *CHEK2* gene: c.1100delC and genomic deletion of 5395 bp comprising exons 8−9 that is probably of Slavic origin. All identified gene alterations were confirmed and characterized by direct DNA sequencing.
Results: In our cohort, 10 (1.6%) patients carried pathogenic mutations in *CHEK2* (5 carriers for each tested mutations) and 4 (0.6%) patients carried mutation in *TP53.* The two *TP53* mutations (c.818G>A and c.815T>G) have been repeatedly identified in sporadic breast tumours and seem to be pathogenic. The clinical importance of the third sequence variant (c.760A>G) which was found in two patients is not known. One of these mutations was detected in a woman with a familial breast cancer that also carried large deletion in the *CHEK2* gene. The 2 pathogenic *TP53* mutations were identified among hereditary cancer cases (2/296; 0.7%), whereas the majority of CHEK2 mutations was found in non-familial cancer cases (7/330, 2.1%).
Conclusions: Pathogenic mutations in *CHEK2* and *TP53* genes were much less frequent than mutations described in major predisposition genes *BRCA1/2*. However, our results indicate that testing for locally prevalent recurrent mutations in *CHEK2* gene may be of an important clinical relevance in our population. On the other hand, families with mutation in *TP53* gene were rare and the role of this gene in breast tumorigenesis is limited. Two pathogenic mutations were detected in cases of breast cancer prior to age 28 years. Analysis of *TP53* may be restricted to cases of early onset breast cancer.
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1129 POSTER

DNA Repair Enzyme, O6-methylguanine DNa Methyltransferase, Modulates Therapeutic Efficacy of Platinum Drugs With Radiation and Its Clinical Significance

S.H. Chen[1], Y.N. Yang[1], C.F. Li[2], H.Y. Huang[3], J.F. Liu[1], C.C. Kuo[1], J.Y. Chang[1]. *[1]National Health Research Institutes, National Institute of Cancer Research, Tainan City, [2]Chi-Mei Medical Center, Department of Pathology, Tainan City, [3]Chang Gung Memorial Hospital-Kaohsiung Medical Center, Department of Pathology, Kaohsiung City, Taiwan*

Background: In this study, we were aiming to evaluate the role of DNA repair enzyme, O^6-methylguanine–DNA methyltransferase (MGMT) in regulating the therapeutic efficacy of platinum drugs and radiation, and also investigate its clinical significance.
Materials and Methods: Tetracycline-regulated Tet-On system and RNA interference method were used to investigate the correlations between MGMT expression and platinums/radiation-induced DNA damage and cytotoxicity in cultured cells. Furthermore, 83 NPC patients received cisplatin (CDDP)-based concurrent chemoradiotherapy (CCRT) were analyzed the relationship of MGMT expression and survival.
Results: CHO-derived Tet-On-inducible cells (S12+) showed MGMT overexpression and statistically significant more resistance to CDDP, carboplatin and oxaliplatin than parental CHO cells. Knockdown of MGMT expression with small interfering RNA in HONE-1 cells conferred increased sensitivity to those platinum drugs as compared with scrambled control. Further study showed that the amount of CDDP-DNA adduct and double strand DNA breaks after CDDP exposure were significantly lower in MGMT-proficient cells than that of MGMT-deficient cells in both Tet-On and RNAi system. Host reactivation assay revealed that protection of CDDP-induced DNA damage and cell death by MGMT is through enhanced global DNA repair capacity. Otherwise, Resistance to X-ray irradiation was observed in MGMT-proficient cells, and *vice versa* in MGMT-deficient cells. The result from clinical specimens revealed that the NPC patients, who received CDDP-based CCRT, with lower level of MGMT expression had a better disease-free survival (DSS) ($P = 0.015$) and local recurrent-free survival (LRFS) ($p < 0.05$) than patients with high expression of MGMT. Multivariate analyses indicated that high expression of MGMT is an independent predictor for poor survival, with a risk ratio of 2.14 for DSS (95% CI=1.14–4.02), and 3.62 for LRFS (95% CI=1.33–9.88).
Conclusion: Our results suggested that MGMT plays an important role in determining the therapeutic efficacy of platinum drugs and radiation, and may have a relevance to clinical use of CCRT.

1130 POSTER

Spectrum of Mutations in BRCA1 and BRCA2 Genes in Families at High Risk of Breast and Ovarian Cancer in the Czech Republic

P. Pohlreich[1], J. Stribrna[1], I. Ticha[1], J. Soukupova[1], J. Kotlas[2], A. Panczak[2]. *[1]Charles University in Prague First Faculty of Medicine, Institute of Biochemistry and Exp. Oncology, Prague, [2]Charles University in Prague First Faculty of Medicine, Institute of Biology and Medical Genetics, Prague, Czech Republic*

Introduction: *BRCA1* and *BRCA2* are major genes related to hereditary breast and ovarian cancer. The purpose of our study was to estimate the incidence and spectrum of inherited mutations in these genes in a large series of Czech patients.
Materials and Methods: We evaluated DNA and RNA samples from 820 high-risk breast or ovarian cancer patients for germline mutations in *BRCA1* and *BRCA2* genes. A complete sequence analysis of *BRCA1* and *BRCA2* coding sequence was performed by protein truncation test (PTT) and direct DNA sequencing of PCR products. A total of 640 patients tested negative for point mutations and small deletions or insertions were screened for large genomic deletions and rearrangements (LGRs) at *BRCA1/2* loci by multiplex ligation-dependent probe amplification (MLPA), long range PCR and genomic sequencing. The chromosome 17-specific aCGH was used to locate deletion breakpoints in regions flanking the *BRCA1* gene.
Results: Of the 820 analyzed individuals, PTT and sequencing identified 132 (16.1%) and 48 (5.8%) mutations in *BRCA1* and *BRCA2* genes,