mRNAs showed low expression and correlated with protein expression. In tumor cells, mRNAs of TFF1 and TFF3 were found increasingly compared to normal tissues (P = 0.008, P = 0.067, respectively). Protein expressions of TFF1, TFF2, and TFF3 in tumor tissues were positive staining at 50.9%, 25.5%, and 49.1%, respectively. The significant association between mRNA and protein was found only in TFF3 (P = 0.028). TFF3 protein expressed widely in normal bile ducts and markedly increased in pre-malignant and tumor cells. Increased expression of TFF1 protein was found in pre-malignant and tumor tissues. TFF2 protein rarely expressed in normal bile ducts and pre-malignant cells but increasingly expressed in tumor. Furthermore, TFF1 and TFF2 proteins were associated with nerve invasion.

CONCLUSIONS: No significant associations between DNA copy number, mRNA expression and clinicopathological data as well as survival time were found. Our studies suggest that TFF3 may be the first and main TFF which plays beneficial effect in cytoprotective bile duct system, whereas TFF1 may play a role as an initiator of CCA development at the pre-malignant stage and promote tumor progression at tumor stage. The alternative expression of TFF2 may play a crucial role in the enhancement of tumor progression in CCA patients.

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Steroid metabolism gene CYP17, CYP1A1*2B, CYP1A1*2C and risk of breast cancer in mexican women

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Background. Breast cancer is the 2nd cause of women mortality in Mexico, increasing this rate over the past ten years. Functional polymorphisms in genes encoding steroid metabolizing enzymes may contribute to this understanding by serving as surrogate markers for altered long-term hormone exposure and, thus, as biomarkers of individual breast cancer susceptibility. In order to determine the impact of CYP17 and CYP1A1 genotypes on the risk to develop breast cancer, we realized a case-control study of breast cancer patients and healthy controls among women invited to participate in this study from a Public Hospital in Mexico City.

Methods. 90 breast cancer patients and 87 healthy contol, who had given their informed consent were included. All breast cancer patiens had pathologically confirmed as breast carcinoma, all were diagnosed and treated at the "1o de octubre" hospital. Epidemiological questionnaire and genotyping data were obtained. CYP17 and CYP1A1 were genotyped using PCR/restriction fragment lenght polymorphism. For CYP17 a single nucleotide polymorphism at the 5`untraslated region of the CYP 17 was done (MspA1 restriction sitie). Two polymorphism for CYP1A1 were analized: 2455 A>G (CYP1A1*2B) and 4889 A >G (CYP1A1 *2C).

Results. We found an increased risk of breast cancer in women carrying the allele CYP1A1*2B. The odds ratio was 2.6 (CI95%= 1.08-6.4; p <0.032). In the stratified analysis, this risk was increased when CYP1A1*2B and CYP1A1*2C were presented together. The odds ratio was 3.4 (CI95%= 1.2-9.3; p<0.017). Regarding the CYP17 genotype, it was not preliminary associated with breast cancer risk. Conclusions. These results suggest that CYP1A1*2B and CYP1A1*2C genotype may be a biomarker for breast cancer risk in our general Mexican population.

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p53 gene alterations and HPV16 infection in early stages of cervical carcinomas in Serbia

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Background: Cervical cancer is the second most common malignant disease among women. Incidence rate (age standardized) of cervical carcinoma in Serbia is the highest in Europe. p53 is mainly inactivated at protein level in carcinomas associated with human papilloma virus (HPV) infection, such as cervical carcinomas. These tumors contain low rate of p53 mutations. It isn't clear if p53 mutations additionally confer impact to prognosis of disease. The role of polymorphic variant at codon 72 of p53 gene as a risk factor for cervical cancer development and patient's prognosis is controversial. The aim of study was to determine the frequency of p53 mutations and polymorphic variants of codon 72 among cervical carcinomas.

Patients and methods: 53 cervical carcinomas patients, FIGO stage I (50) and II (3) were included in study. The majority of cases (n=49) were squamous cell carcinoma. 30/32 patients who received adjuvant radiotherapy were followed-up. DNA was isolated by salting out method from tumor tissue (n=53) and blood (42/53). Mutations in exons 4 to 8 of p53 gene were detected by PCR-SSCP (polymerase chain reaction- single-stranded conformational polymorphism) electrophoresis and confirmed by direct sequencing. HPV16 was examined in 51/53 tumor by PCR-PAGE (polyacrilamide-gel) electrophoresis. Codon 72 polymorphism was assessed by RFLP (restriction fragment-length polymorphism) method.

Results: Five p53 mutations were detected in 4/53 patients in FIGO stage I squamous cell carcinoma (one patient had double mutations). 25/42 patients exhibited Arg/Arg genotype of 72 codon polymorphism. 3/5 p53 mutations were associated with Arg/Arg and 2/5 with Arg/Pro genotype. There was no statistically significant difference in the number of relapses among patients with different genotypes at codon 72. HPV16 type was detected in 29/51 cervical carcinomas. Statistically significant difference in the frequency of Arg/Arg genotype between HPV-16 positive and HPV16 negative patients was not observed. Relapse of disease occurred only in two patients - both with Arg/Arg genotype and HPV16 positive. One of them exhibits p53 mutation.

Conclusion: Results showed low incidence of p53 mutations and prevalence of Arg/Arg genotype polymorphic variant of codon 72 of p53 gene in early stages of cervical carcinomas in Serbia.

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Genetic polymorphism of CYP1A1 & CYP2D6 in Indian chronic myeloid leukemia patients

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BACKGROUND: Chronic myeloid leukemia (CML) is a clonal hematopoetic stem cell disorder. Genetic polymorphism of genes encoding carcinogen-metabolizing enzymes, namely, phase I cytochromes P-450 (CYPs) have been shown to influence the risk to develop cancer. It has been suggested that individuals possessing a modified ability to metabolize carcinogens are at increased risk of cancer. The cytochrome P450 (Phase–I) system is involved in the metabolism of both endogenous and exogenous molecules, CYP1A1 and CYP2D6 are two such genes which effect individual susceptibility towards the risk for cancer from environmental agents. Hence the present study was designed to find out the allelic frequency of CYP1A1 gene (*2A,*2B,*4 alleles) and CYP2D6 gene (*4 allele) in North Indian CML patients and racially matched controls.

AIM: Owing to the importance of CYP1A1 and CYP2D6 genetic polymorphism as risk factor in various cancers, the study was aimed to detect the prevalence of their genetic polymorphism in North Indian CML patients and racially matched controls. Further, it will help to determine the association of these allelic variants if any, as risk factor to develop CML.

METHODS: DNA isolation was carried out by standard proteinase K and phenol chloroform method. The prevalence of CYP1A1 *2A,*2B,*4 alleles and CYP2D6*4 allele was carried out by PCR-RFLP method (Krajinovic et al, 1999). PCR products were separated using 2% agarose gel. The relationship between these alleles and risk of CML was assessed by means of chi square test. The odds ratio (OR) with 95% confidence limits was calculated by logistic regression.

RESULTS: CYP1A1 mutations T6235C (m1), A4889G (m2) and C4887A (m4) were characterized by PCR-RFLP. These mutations were then used to define 3 distinct alleles, CYP1A1 *2A (presence of m1 only), *2B (both m1 and m2) and *4 (m4 only). The frequencies of CYP1A1 alleles *2A *2B and *4 in cases were 21.8% (12/55), 18.1% (10/55), and 9% (5/55), respectively. The allelic frequencies of CYP1A1 genes (*2A,*2B and *4(in controls were 32% (24/75), 16% (12/75), and 4% (3/75), respectively.

The allelic frequencies of CYP2D6*4 in CML patients of homozygous wild, heterozygous and homozygous mutant alleles, were 77% (35/45), 13% (6/45) and 8% (4/45). In controls these frequencies were 75% (42/56), 14% (8/56) and 10% (6/56) respectively.

CONCLUSIONS: A higher frequency of CYP1A1*2A was observed in controls as compared to CML patients. Thus the study provides an evidenced based data, which indicates a reduced risk for CML in individuals carrying the mutant allele CYP1A1*2A.

The results did not support the hypothesis that mutant alleles of CYP2D6*4 gene which are actively involved in activation of carcinogens, will be at greater risk to develop CML. Our attempt to study role of CYP2D6*4 allelic variants in CML is promising, however, study needs to be taken further with larger sample size to validate the results.