**250** PUBLICATION

**Cytotoxic T lymphocyte antigen-4 promoter variants in breast cancer**

N. Erfani[1,2], M. Razmkhah[1], A. Talei[3], A. Pezeshki[1], M. Doroudchi[1,2], A. Monabati[4], A. Ghaderi[1,2]. [1]*Shiraz Institute for Cancer Research, Shiraz University of Medical Sciences, Shiraz, Iran;* [2]*Department of Immunology, Shiraz University of Medical Sciences, Shiraz, Iran;* [3]*Department of Surgery, Shiraz University of Medical Sciences, Shiraz, Iran;* [4]*Department of Pathology, Shiraz University of Medical Sciences, Shiraz, Iran*

**Background and Objectives:** CTLA-4 is a co-inhibitory molecule expressed mainly on activated T lymphocytes. To test the putative involvement of CTLA-4 in inhibitory state of immunity to breast cancer, we genotyped 283 patients and 245 healthy controls for −1722 T/C, −1661 A/G and −318 C/T polymorphisms in ctla-4 promoter region.
**Methods:** −1722 T to C dimorphism was genotyped by a Polymerase Chain Reaction with Confronting Two Pairs Primers (PCR-CTPP) method. −1661 A to G polymorphism was investigated by a PCR-Restriction Fragment Length Polymorphism (PCR-RFLP) method. −318 C to T polymorphism was genotyped by a PCR− Amplification Refractory Mutation System (ARMS) method.
**Results:** There were no significant differences in genotype, allele and haplotype frequencies in all three loci between patients and healthy controls. Moreover, the frequency of the most frequent haplotype combination (TAC/TAC, T-1722, A-1661, C-318) was only slightly higher among healthy controls than patients (68.4% vs. 64.8%, P = 0.2). However, this haplotype combination was associated with lower stages of the disease (P = 0.0007) and higher expression of Estrogen Receptor (ER) in patients (P = 0.006). Association with tumor prognostic/predictive factors was also observed in the case of certain genotypes: −1661 AA genotype was associated with less LN involvement (P = 0.017) and high ER expression (P = 0.004), and −318 CC genotype with less LN involvement (P = 0.007).
**Conclusions:** These results suggest that CTLA-4 promoter variants participate, at least partly, in the progression of breast cancer rather than its initial development.

**251** PUBLICATION

**Acute phase proteins in malignancy: role of CRP in the discrimination of infectious complications in cancer patients**

M. Ozguroglu[1], M. Bolayirli[2], T. Orhanoglu[1], O. Yildiz[1], H. Turna[1], S. Serdengecti[1]. [1]*Istanbul University, Cerrahpasa Medical Faculty, Medical Oncology, Istanbul, Turkey;* [2]*Istanbul University, Cerrahpasa Medical Faculty, Central Laboratory, Istanbul, Turkey*

**Background:** Acute phase response is one of the defense mechanisms that maintains organism against stimulants such as invasions of microorganisms, trauma, immunological diseases, and cancer. An increased acute phase response was found in patients with various malignant tumors and could be a sign of poor prognosis. The aim of this study was to determine the rate of acute phase response in cancer patients and comparing the response against healthy controls and patients with infectious disease(diseased control group).
**Materials and methods:** 104 cancer patients(45 male, 59 female), 25 healthy controls(14 male, 11 female) and 25 patients with infectious disease (11 male, 14 female) were included in the study. Serum levels of c-reactive protein (CRP), lactate dehydrogenase (LDH), ferritin, haptoglobin, fibrinogen, and erythrocyte sedimentation rate (ESR) were measured.

Table 1

| | CRP (mg/l) | Haptoglobin (mg/dl) | Ferritin (ng/ml) | Fibrinogen (mg/dl) | LDH (U) | ESR (mm/h) |
|---|---|---|---|---|---|---|
| Group I (cancer) | 25.3 ±47.37 | 216.54 ±131.33 | 171.58 ±234.55 | 484.32 ±177.09 | 416.54 ±371.83 | 36.36 ±29.64 |
| Ia (metastatic) | 39.25 ±62.12 | 252.13 ±151.23 | 209.42 ±260.22 | 546.02 ±201.04 | 484.98 ±515.24 | 47.52 ±33.07 |
| Ib (non-metastatic) | 10.72 ±11.66 | 172.95 ±87.33 | 119.13 ±166.37 | 408.89 ±120.81 | 334.28 ±64.76 | 26.31 ±19.20 |
| Group II (healthy control) | 2.21 ±0.94 | 126 ±44.05 | 152 ±73.71 | 270 ±56.22 | 279.32 ±44.11 | 8.7 ±4.37 |
| Group III (infection) | 42.26 ±65.63 | 180.04 ±92.57 | 285.54 ±416.10 | 533.78 ±201.2 | 334.28 ±64.7 | 26.73 ±19.36 |

**Results:** Cancer patients were found to have higher levels of CRP, LDH, haptoglobin, and fibrinogen than healthy control group($p < 0.001$). Serum levels of acute phase proteins were found to be similar between cancer patients and patients with infectious disease for all the checked parameters. Subgroup analysis of cancer patients showed that cancer patients with metastatic disease had significantly higher CRP, fibrinogen, and ESR levels than non-metastatic group.
**Conclusion:** All types of acute phase proteins increase in cancer patients and may be a marker of tumor burden in this group of patients. Very high levels of acute phase proteins could be a sign of metastasis in cancer patients. However, measurement of serum levels of quantitative CRP cannot discriminate secondary infections in cancer patients, that may superimpose in any immunosuppressed patients.

**252** PUBLICATION

**Relationship between genes expression, proteins induction, polymorphisms and radiotherapy complications in Saudi cancer patients**

G. Alsbeih[1], M. El-Sebaie[2], N. Al-Harbi[1], M. Al-Buhairi[1], M. Al-Hamed[3], M. Torres[1], N. Al-Rajhi[2]. [1]*King Faisal Specialist Hospital & Research Centre (KFSHRC), Biomedical Physics, Riyadh, Saudi Arabia;* [2]*KFSHRC, Radiation Oncology, Riyadh, Saudi Arabia;* [3]*KFSHRC, Aragene Project, Riyadh, Saudi Arabia*

**Background:** Patient-to-patient variations in the sensitivity of normal tissues are well recognized in clinical radiotherapy practice. Studies in exquisitely sensitive patients have identified mutations in cell cycle and DNA repair genes and suggested that polymorphic variations in multiple genes could be associated with radiation sensitivity (RS). In this study we sought to: 1. Affirm these variations in our radiotherapy patients; 2. Identify some of the genes and proteins involved; 3. Explore the association with certain single nucleotide polymorphisms (SNPs) in susceptible genes.
**Materials and methods:** Fibroblasts were established from 53 Head and Neck cancer patients treated with radiotherapy. The *in vitro* RS was measured using the clonogenic assay. Genes and proteins expression were studied in representative cell strains using 1.2 cDNA macroarrays and Western blotting, respectively. Basal genes and protein levels and induction 3 hours after a dose of 5 Gy were evaluated. SNPs were studied by heteroduplex analysis (MDE gel) and/or sequencing.
**Results:** Survival curves showed a wide range of RS. The surviving fraction at 2 Gy (SF2) ranged between 0.16 and 0.56 (mean, 0.36). There was a statistically significant difference in SF2 between the group of patients having minimal late complications (Grade 0–1 fibrosis) and the group who suffered more severe fibrosis (Grade 2–3) ($p = 0.001$). Genes' expression profile was distinct in cell strains studied and was associated with RS. Basal protein levels varied but no correlation was observed with RS. In control cells, CDKN1A, TP53 and MDM2 proteins were induced $\geqslant$1.5 fold after irradiation, and to a lesser extent DNA LIG IV, MRE11 and NBS1, but not ATM, DNA-PKcs, Ku70, Ku80, XRCC4, RAD50, BRCA1, CDKN1B and RB. MDM2, CDKN1A, and TP53 proteins induction showed tendency toward a correlation with both the *in vivo* grade of fibrosis and the *in vitro* SF2. Preliminary results with SNPs in TP53 codon 72, CDKN1A codon 31 and XRCC3 codon 241 showed no association with RS. Other SNPs in XRCC1, MDM2, ATM, LIG IV and TGFb1 are being studied.
**Conclusions:** These results suggest that our patients vary significantly in RS and potentially can benefit from a predictive test. The RS is associated with distinctive genes expression profile and with the level of induction of TP53, CDKN1A and MDM2 proteins; however, this was not associated with the SNPs studied in TP53, CDKN1A or XRCC3. Supported by KFSHRC grants 2000 031 and 2040 025.

**253** PUBLICATION

**Factor V Leiden and PT G20210A mutations in cancer patients with and without thrombosis**

A. Eroglu[1], A. Ulu[2], C. Kurtman[3], N. Akar[2]. [1]*Numune State Hospital, Surgery, Konya, Turkey;* [2]*Ankara University Medical School, Molecular Genetic, Ankara, Turkey;* [3]*Ankara University Medical School, Radiation Oncology, Ankara, Turkey*

**Background:** Cancer patients have an increased risk for thromboembolism (TE). Factor V Leiden (FVL) has been identified as the most common inherited risk factor for TE. The aim of the study was to determine the prevalence of FVL and PT G20210A mutations in cancer patients who developed TE during treatment, e.g. surgery, radiotherapy and chemotherapy as compared to those who did not.
**Material and Methods:** The study consisted of 35 cancer patients who developed TE during treatment (group I), 50 cancer patients without TE (group II), 50 patients with TE without malignancy (group III), and 60 healthy controls (group IV). FVL and PT G20210A mutations were measured by the method of polymerase chain reaction-based DNA analysis.
**Results:** The prevalence of FVL was significantly greater in cancer patients with TE (10 of 35, 28.6% compared with the other groups: 2 of 50 (4%) in group II, 2 of 50 (4%) in group III, and 4 of 60 (6.7%) in group IV ($p = 0.003$). There was no significant difference in the prevalence of PT G20210A between the groups ($p > 0.05$).