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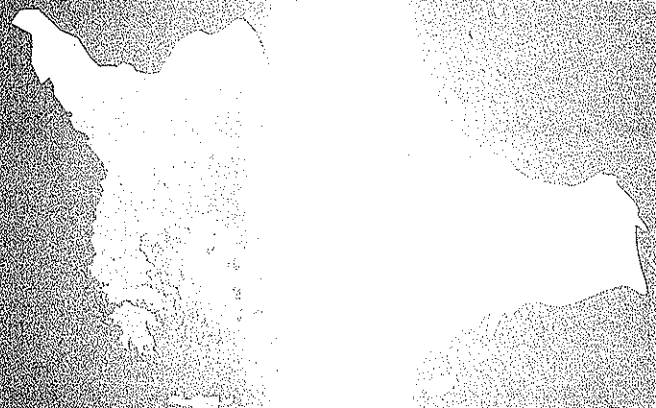

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## P 177

**P-GLYCOPROTEIN EXPRESSION IN COLORECTAL NORMAL MUCOSA, ADENOMA AND ADENOCARCINOMA**

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**Purpose:** P-glycoprotein (P-gp) mediates classic multidrug resistance by functioning as an energy-dependent efflux pump for chemotherapeutic drugs from cancer cells. P-gp is expressed in many different types of tumors and in certain normal organs including normal colon epithelium. The previous observations of P-gp expression in normal and malignant tissues of the colon prompted us to search additionally P-gp expression in colorectal adenomas and determine the clinical significance of P-gp expression in colorectal carcinomas.
**Material and methods:** Specimens of 30 colorectal adenomas and 30 colorectal adenocarcinomas were obtained from the archives of Akdeniz University Faculty of Medicine belongs to years of 1982 to 1991. Normal colon mucosa specimens were chosen from blocs of resection lines. Immunohistochemically, P-gp (JSB-1 monoclonal antibody) was applied in normal colon mucosa, colorectal adenoma and adenocarcinoma. Normal liver tissue was used as positive control. Chemotherapy regimens and clinical responses were evaluated in 15 cases.
**Results:** We found P-gp expression positivity in 6 normal colon mucosa, none of colorectal adenoma and 18 of 30 colorectal adenocarcinoma (%60). There was not any difference in chemotherapy response according to P-gp expression of 15 cases who received 5-Fluorouracil based adjuvant chemotherapy (p>0.05).
**Discussion:** Our findings related to P-gp immunostaining in colorecatal adenocarcinoma shows appropriateness with the literatue. We could not find any report related to P-gp immunostaining in colorectal adenoma in the literature. There was not P-gp immunostaining in the adenomas in our study. These findings indicates that multidrug resistance appear in the late period of colorectal tumourogenesis. In vitro studies had shown that mdr 1 cell lines are sensitive to 5-Fluorouracil. In spite of small number of cases, this study also showed us that response to 5-Fluorouracil should be independent of P-gp expression.

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SEROLOGIC/HISTOLOGIC CORRELATION FOR P53 OVEREXPRESSION IN PANCREATICOBILIARY CANCERS

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Mutations in the p53 tumor supressor gene and serum antibodies directed against p53 protein (p53-Ab) have been detected in various human cancer types. However potential associations between the presence of anti-p53 serum antibodies and immunohistostaining of p53 protein in pancreaticobiliary cancers have not been clearly determined yet.
In this study we investigated the potential correlation between the presence of anti-p53 antibody in the serum and overexpression of mutant p53 gene in the tumors of the pancreaticobiliary system whether this could be used for an early diagnostic modality
In the period between May 1997 and February 1998, 49 patients (31 male, 18 female) with malignant pancreaticobiliary tumors had undergone surgery at Atatürk Training and 9 Eylül University Hospitals in İzmir. Control group consisted of 81 patients with benign pancreaticobiliary diseases. Blood samples were obtained at the first presentation of the patients and centrifuged within 2 hours of collection and serums stored at -70°C. All tumor specimens (tissue samples in addition to fine needle aspirations, when available) were obtained during routine surgery.
The serum of these patients were analysed for the presence of circulating antibodies to the p53 protein by using Elisa system. p53 protein expression was immunohistochemically detected using monoclonal Do-1 antibodies staining by S-ABC technique in paraffin embedded tissues and FNA materials when available. Serum p53 values were evaluated using three different threshold levels. Immunohistochemical staining intensity was evaluated at a semi-quantitative basis as (+/++/+++). The potential correlation of these two values were investigated.

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THE VALUE OF Tc-99m (V) DMSA SCINTIGRAPHY IN THE DIAGNOSIS AND STAGING OF MALIGN NEOPLASMS

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In order to evaluate the value of Tc-99m (V) DMSA in the evaluation of various malignities 15 patients were undergone scintigraphy with Tc-99m (V) DMSA. 12 of the cases were primary and metastatic lung cancers (all male and mean age 59.3±7.4), 2 were renal cell cancers and 1 of them was gastric cancer. Total body imaging were done in all patients after 2 hours of radionuclitide administration and SPECT were performed in patients with lung lesions. The patients were also evaluated with bone scintigraphy, ultrasonography and computed tomography of the involved organ and the results were compared.

Lung lesions were demonstrated in 14 patients with computed tomography of the chest. 6 of the 7 lesions located peripherally were detected by Tc-99m (V) DMSA. Of the 7 lesions with central location only 1 of them was able to be detected by scintigraphy. In all of the 7 patients with bone metastases lesions were able to be visualised by Tc-99m (V) DMSA also. No intraabdominal metastases could be visualised by Tc-99m (V) DMSA.

As a result of this study, Tc-99m (V) DMSA seems to be a valuable method to visualise peripheral but not central lung lesions either metastatic or primary. This method has its own advantage of visualisation of bone metastases syncronously with the primary lesion which is a great advantage in staging of various tumors. Adding the capability to differantiate viable and non-vaible tissues of this technique, Tc-99m (V) DMSA scintigraphy can be regarded as a valuable method in staging and follow up of peripheral lung lesions either metastatic or primary. Being insensitive for mediastinal lesions because of blood pooling in this region and not being able to show intraabdominal organ metastases are disadvantages of this tehnique.

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THE ROLE OF *TP53*, *HA-RAS* MUTATIONS AND HUMAN PAPILLOMAVIRUS (HPV) DNA IN TRANSITIONAL CELL CARCINOMA (TCC) OF BLADDER

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Starting with the conflicting data on the role of *TP53*, *HA-RAS* mutations and presence of HPV in the development and progression of TCC in bladder, this study aimed at the investigation of the mutation frequency of *HA-RAS* and *TP53* as well as the presence of the HPV in primary and their recurrent superficial bladder cancers. Ninety-one archival tissues obtained from 20 patients with both primary and their (secondary) recurrent tumors were used. PCR was performed using *HA-RAS*, 1st exon, *TP53* 5-6th, 7th and 8th exons primers, and MY09/MY11 primers of HPV. To detect codon 12 point mutations of *HA-RAS* amplification products were digested with Hpa II enzyme. Single strand conformation polymorphism (SSCP) with silver staining was performed to detect mutations in the amplified products of *TP53*. We found HPV presence in 22 % of primary and 21% of secondary tumors. *HA-RAS* mutations were present in 17 % of primary and 21% of secondary tumors. For 5-6th exons of p53, 8% of primary, 10 % of secondary tumors were mutant, while for 8th exon of p53 60 % of secondary tumors were mutant. No mutation was found in the 7th exon of *TP53* gene. These data suggest that HPV may have a role as an etiologic agent for development of TCC. *HA-RAS* and 8th exon of *TP53* mutations might have been essential in the progression of superficial bladder cancer.