damage and execute cell cycle arrest through inhibiting the activity of cell cycle regulators.

PATIENTS AND METHODS: In order to detect the gene expression patterns we analyzed three sample types for each of our 30 patients: specimens from diverse sites of healthy gut, adenomatous polyps and malignant tissue. In order to asses the RNA quality we analysed the 18S and 28S ribosomal RNA bands integrity by electrophoresis on a denaturing agarose gel. For every sample 3.0 μg of total RNA were available at a concentration greater than 0.33 mg/ml. We used a Human DNA Damage Signaling Pathway Microarray that includes 113 genes associated with the ATR/ATM signaling network and transcriptional targets of DNA damage response. Genes related to cell cycle arrest, apoptosis, and the stabilization and repair of the cellular genome as a result of DNA damage signaling were represented as well. To complete our data analysis we used a specially designed web-based and a completely integrated Array Expression Analysis Suite.

RESULTS: We successfully performed focused microarray analysis showing that a dysfunction in DNA damage response contributes to genomic instability in colon samples. In 10 of our malignant samples we detected a significantly reduced expression of six DNA repair genes (ANKRD17, EXO1, MLH1, MLH3, MSH2, MSH3) than in normal colon specimens. Our obtained data were validated by quantitative RT-PCR.

CONCLUSION: Determination of gene expression profiles by using low density DNA microarrays is an ideal tool to improve our knowledge of CRC molecular pathways. However, defined gene signatures are highly variable among studies, none of the identified expressional patterns or molecular markers has been successfully validated as a diagnostic or prognostic tool applicable to routine clinical practice.

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The first pilot study on characteristics and practice patterns of Kuwaiti breast cancer patients

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Background: Non-genetic breast cancer risk factors have never been evaluated in Kuwait. Accordingly, we aimed at examining these factors as well as the immune profile of the patients.

Materials and methods: Fifty-stage I-breast cancer patients and fifty age group-matched normal controls were assessed for the level of their peripheral blood lymphocyte subsets, and for risk factors associated with their demographic and reproductive characteristics, and with diet.

Results: The percentages of CD4+ T lymphocytes, CD4+:CD8+ ratio, and CD19+ B lymphocytes were significantly higher in the patients as compared to controls, while the percentages of CD8+ T lymphocytes and natural killer (CD56+) cells were significantly reduced. Risk factors associated with the disease included higher BMI, lack of regular exercise and physical activity in the past five years, early age at menarche, late age at first pregnancy, lack of previous information about breast cancer, hormonal therapy, and presence in Kuwait during the invasion/ liberation. Other parameters included significantly more frequent consumption of carbohydrate, sweets, animal fat, and vegetable oil (margarine), and less frequent consumption of fresh vegetables and olive oil.

Conclusions: This is the first study to highlight the environmental risk factors associated with breast cancer among the Kuwaiti women. We recommend introducing a nation-wide campaign to further investigate these factors, and addressing them accordingly.

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Death receptors and p53 dependent impairment of UV-induced apoptosis in FADD knockouts cells

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Ultraviolet (UV) irradiation is the cause of many adverse biological effects including development of cancer and aging. UV light targets both membrane receptors and nuclear DNA, thus evoking signals triggering apoptosis. In UV mediated apoptosis different molecular pathways are involved including DNA damage, activation of tumor suppressor gene p53, triggering of cell death receptors either directly or by autocrine release of death ligants, mitochondrial damage and cytochrome C release. Detailed knowledge about the interplay between these pathways will increase our understanding of photo-carcinogenesis.

To investigate comparatively the role of death receptors apoptotic signaling pathway and participation of the p53 mutation in the signaling cascade of UV induced apoptosis we used mouse embryonic cell lines from knockout mice deficient for death-domain-containing adaptor molecules FADD (Fas-associated protein with death domain). FADD is responsible for downstream signal transduction of death receptors belonging to the tumor necrosis factor (TNF) superfamily. Survival, apoptosis, and p53 mutations studies revealed that exposure of two cell lines, knockout and wild type, to UV-C radiation and TNF. As expected, FADD knockout cells were protected completely from death induced by TNF. The results indicate that apoptosis induced by UV-C light does not require FADD protein. The knockout cells were more sensitive than wild-type cells with respect to cell death. Allele-specific PCR detection of p53 in genomic DNA from UV-C irradiated knockout and wild type cells were analyzed by gel electrophoresis. The results show that UV-C induced apoptosis is independent of functional p53 for which the FADD knockout cells showed to be mutated. We challenge the hypothesis that UV carcinogenesis in wild type cells includes a loss of FADD function and generation of p53 mutations.

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Bile reflux induced mutagenesis on esophageal epithelium in an animal model and the effect of low dose Aspirin

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Background: Barrett's esophagus and adenocarcinoma of the esophagus are related to long-standing duodeno-gastroesophageal reflux. The development of an animal model in which Barrett's esophagus and/or carcinoma is induced by duodeno-(gastro-)esophageal reflux could provide better understanding of the pathogenesis of the metaplasia-dysplasia-carcinoma sequence and would create the possibility of investigating new treatment strategies for this aggressive disease.

Aim: This study examines the incidence of bile reflux induced oesophageal metaplasia carcinoma sequence in an attempt to develop an animal model for Barett's esophagus & adenocarcinoma. We have also done the caspase 3 activity

Materials and Methods: Thirty Wistar rats weighing a minimum of 150 gms with an average age of 6 weeks were included in the study [Gp1 18 and Gp II 14]. Of these, 60% of the animals were subjected to side to side and 40 % were end to side oesophago-duodenostomy under intra peritoneal thiopentone sodium. Rats in group II received dissolvable aspirin at the dose of 15mg/Kg of the rats and from the third day till the day of sacrifice. Along with histopathology Caspase 3 activity was measured as an index of apoptosis.

Results. Mortality was higher in the end to side procedure. 18 rats without aspirin(Gp I)and 14(Gp II) with aspirin survived through one year. 8(45%)developed nodular lower esophagus[0.8x0.5cm on gross] and group2 none[$p<0.001$,with Fisher's exact]. GpII had 30 % small intestinal mocosa where Gp II did not have. basal cell hyperplasia, Epithelial hyperplasia, pappillamatosis were siginificantly in Gp II [$p<0.003$]. There was no difference in dysplasia rate Three rats did not show any changes as the side to side anastamosis was stenosed.. Carcinoma was present in one in Gp 1. The histopathologic evaluation was more suggestive of a reactive mucous producing lesion fitting the diagnosis of "esophagitis cystica profunda in Gp I and the incidence of carcinoma and dyspasia is not as high as that is been reported in the literature. However, no change in caspase 3 activity was evident under these conditions.

Conclusion: End to side oesophago-duodenostomy is the best animal bile reflux model and perioperative mortality is around 40%. Contrary to many studies reporting bile reflux induced carcinoma, Gp 1 developed "esophagitis cystica profunda." And one carcinoma. Low dose aspirin does have a role in reducing the incidence of bile induced changes in the oesophagus. This findings can be extrapolated in humans with barrettes and other reflux induced changes in esophagus

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Implication of the upstream stimulating factor family in the DNA-repair process - identification of a new target in response to UV

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The upstream stimulating factor –1 and -2 (USF1, USF2) are two distinct members of the evolutionary conserved basic-Helix-Loop-Helix Leucine Zipper transcription factor family (bHLH-LZ) that interact with high affinity to cognate E-Box regulatory elements (CANNTG) (1). USF genes are ubiquitously expressed, with their respective protein regulating a wide number of gene networks. We have previously implicated USF-1 transcription factor and specific E-Box elements located within promoter