vs 30 controls and (iii) 18 pathologists/anatomists exposed to formaldehyde vs 18 controls. Centromere-negative micronucleus (C-MN), centromere-positive micronucleus (C+MN), micronucleus containing only one centromere (C1+MN) and micronucleus containing more than one centromere (Cx+MN) were scored.

Results: In untreated cancer patients, (i) about 70% of the MN were C+MN, (ii) about 50% of the MN were Cx+MN, and (iii) about 66% of the C+MN were Cx+MN. In welders, (i) about 50% of the MN were C+MN, (ii) about 25% of the MN were Cx+MN, and (iii) about 50% of the C+MN were Cx+MN. In pathologists/anatomists (i) about 78% of the MN were C+MN, (ii) about 50% of the MN were Cx+MN and (iii) about 66% of the C+MN were C1+MN.

Conclusions: Most of the MN were centromere positive whatever the population was. In untreated cancer patients, one-half of the MN and two-thirds of the C+MN were Cx+MN suggesting that most of the aneugenic events leading to micronucleus formation involve several chromosomes per micronucleus. In welders, aneugenicity was partly responsible for the higher MN frequency in exposed subjects than in controls and the groups did not differ in MN content. In contrast, formaldehyde exposure leads to an increase in the C1+MN only, suggesting that aneugen mechanisms involve only one chromosome per micronucleus. Our results suggest that aneugenic events leading to centromeric micronuclei in cancer patients and workers occupationally exposed to mutagens/carcinogens arise from different pathways of C+MN formation.

P32

Bone mass density and subsequent risk of prostate cancer

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To test the hypothesis that high bone mass density, a potential marker for cumulative exposure to androgens, insulin growth factors, calcium and vitamin D intake, is associated with a higher risk of prostate cancer. 558 men older then 60 years were followed through record-linkage of cancer registry, after a measure of bone mass density by densitometry in four different sites (lumbar spine L2-L4, Ward's triangle, trochanter, femoral neck). All incident cases of prostate cancers were confirmed histologically. Overall 18 cases of prostate cancer were observed cf 14.5 expected (standardized incidence ratio (SIR) = 1.24, 95 percent confidence interval (CI=0.74-1.65). The SIR increased with increasing bone mass density showing a significantly risk of 42% (Ward's triangle) to 66% (lumbar spine, trochanter, femoral neck) for men who were at the higher bone mass density, comparatively to men who were at the lowest bone mass density.

Our results are consistent with the hypothesis that men with high bone mass may be at an increased risk of prostate cancer. Although the biological mechanisms underlying this relation are not understood, cumulative exposure to high levels of androgens, IGF-I or calcium and vitamin D intake may be involved.

P33

Preoperative predictability of ovarian malignancy using risk of malignancy index

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Topic: Preoperative predictability of ovarian cancer using risk of malignancy index. Aims: To determine the sensitivity, specificity and the predictive powers of using risk of malignancy index in the prediction of ovarian cancer in women with adnexa masses before surgical operation.

Method: This is a case-controlled study involving all women with suspected adnexa masses at the Friedrich-Alexander University Frauenklinik, Erlangen, Germany from January 2002 to September 2005. Their case rocords were retrieved from the medical records and information were extracted and entered directly into SPSS software. The data were validated and computed using the same software to determine the sensitivity, specificity and the positive and negative predictive values of risk of malignancy index in determining which of the adnexal masses was malignant before surgery.

Results: This will follow as soon as we have been able to complete our analysis.

Chemoprevention (experimental and clinical)

P34

Natural cloudy apple juice and polyphenol-enriched apple juice extract prevent intestinal adenoma formation in the APCMin/+ model for colon cancer prevention

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Apples and apple juice are known to contain a variety of phenolic compounds with potential cancer preventive potential. The aim of the present study was to investigate cancer preventive efficacy of cloudy apple juice (CAJ) in comparison with a polyphenol-enriched apple extract (PAE) in the C57BL/6-ApcMin (ApcMin) mouse strain commonly used in cancer chemoprevention studies. Groups of seven-week-old male mice (n=12 each) received either CAJ (containing 90 mg/L polyphenols), PAE (0.2% in drinking water, containing 600 mg/L polyphenols) or water ad libitum for 10 weeks. Average daily CAJ intake was significantly higher than water or PAE intake (average (avg) in mL/animal/day; control: 2.7, CAJ: 3.6, PAE: 2.8), concomitant with a slight decrease in daily food intake in both intervention groups (avg in g/animal/day control: 3.7, CAJ: 3.3, PAE: 3.5), but there was no difference in average body weights (bw avg in g after 10 weeks of intervention; control: 25.1, CAJ: 25.4; PAE: 25.5). Importantly, CAJ and

PAE treatment significantly lowered the number of adenomas in the small intestine by 38% and 40% (avg ± standard error of the mean (SE) control: 64.7. ± 7.2 vs. CAJ: 40.3 ± 5.0, P = 0.011, and PAE: 38.9 ± 2.9, P = 0.007), whereas tumor numbers in the colon were not affected (avg ± SE control: 1.3 ± 0.3, CAJ: 1.8 ± 0.4, PAE: 0.9 ± 0.2). Adenomas were stronger decreased in the middle and the distal part of the SI than in the proximal part. Further, particularly numbers of medium and large adenomas were significantly reduced by both interventions compared to control. Intestinal cell proliferation, determined by immuno-histochemical staining of proliferating cell nuclear antigen, was not influenced by either intervention. Hematocrit values as an indication of intestinal bleeding were negatively correlated with total tumor numbers in both intervention groups (r = -0.82), whereas a positive correlation was observed between spleen weights and adenoma numbers (r = 0.91). Both parameters were slightly ameliorated by the treatments, with significant effects observed with PAE intervention. Overall, our study suggests that CAJ and PAE should be further investigated as part of a prevention strategy for hereditary and sporadic colorectal cancer.

P35

Cancer chemopreventive and anti-angiogenic activities of xanthohumol from hop (Humulus lupulus L.)

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Hop (Humulus lupulus L.) is a good source of phenolic constituents in beer. We investigated a hop extract in a series of test systems indicative of cancer chemopreventive potential and isolated the chalcone xanthohumol (XN) as a most interesting lead structures with high chemopreventive potential at the initiation, promotion and progression stage of carcinogenesis. Although hop is commonly linked with phytoestrogenic effects, we identified XN as a pure estrogen antagonist. Interestingly, XN also affected the generation of estrogens by inhibition of the enzymatic activity of aromatase, which converts testosterone into estrogen. In an uterotrophy assay with prepubertal rats, XN treatment (100 mg/kg bw/day) lowered unstimulated as well as ethinylestradiol-induced uterine weights by about 30%. XN did not cause any adverse effect on female reproduction and on the development of offspring when given either for four weeks prior to or during mating, gestation and nursing. Treatment of male rats prior to mating however significantly (p = 0.027) increased the sex ratio of male to female offspring. Inhibition of angiogenesis represents an innovative approach to cancer chemoprevention. We investigated the angiostatic potential of XN in a human in vitro anti-angiogenic assay premised on the principle of wound healing. We observed dose-dependent reduction of newly formed capillary growth in a concentration range of 0.5 to 10μM. Further mechanistic investigations were performed with HMEC-1, an immortalized human microvascular endothelial cell line. XN effectively inhibited migration of HMEC-1 cells after wounding in a wound closure assay (half-maximal inhibitory concentration IC50=0.03μM). Also, XN effectively inhibited tube-formation on basement membrane matrix at 1, 5 and 10μM, respectively, whereas at 0.1μM, some tubes started to form within the incubation period of 6 h. These effects were only partly due to inhibition of HMEC-1 proliferation, as XN inhibited cell growth with an IC50 of 6.4μM. Xanthohumol also inhibited the transcription of hypoxia-inducible genes under hypoxic conditions. Subcutaneous application of XN (1mg/g body weight) for 14 days to SCID mice bearing human MX-1 breast tumor xenografts significantly reduced the tumor size in treated animals by 82%. Concomitantly, we observed a 30% reduction of tumor-induced neovascularization.

Based on these results, chemopreventive and therapeutic activities of XN will be further investigated.

P36

HMG CoA reductase inhibitors decrease the risk of pancreatic cancer in US veterans: longer use translated to higher protection

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Background: HMG CoA reductase inhibitors (Statins) are commonly used cholesterol-lowering agents that are noted to suppress tumor growth in cell cultures and several animal models. The anti-tumor effects of statins are exerted by its antiproliferative, proapoptotic, anti-invasive and radio sensitizing properties. Statins induced apoptosis is predominantly mediated through depletion of geranylgeranylated proteins. Anti invasive effects are mediated by RhoA inactivation.

Methods: US Veterans Health Administration (VHA) is organized into 21 administrative regions called Veterans Integrated Service Networks (VISN). VISN 16 or the South Central (US) VA Health Care Network provides health care treatment to >1.4 million veterans in an eight state region. The network, an integrated health care system, includes ten medical centers, 33 community-based outpatient clinics, seven nursing homes, and two domiciliary. The data was queried from Oct 1998 to June 2004, using a retrospective case control design. Statistical analysis was performed using SAS software version 9.0 (Chicago, IL). Multiple logistic regression analysis was used with calculation of odds ratios and 95% confidence intervals. The data was adjusted for age, race, gender, BMI, smoking, alcohol use and diabetes. Patients were placed in the Statin user group if they were using statin prior to the diagnosis of pancreatic cancer.

Results: Of the 483,733 patients in the study, 163,662 (33.8%) were on statins and 475 (0.1%) patients had a primary diagnosis of pancreatic cancer. Statin use of more than 6 months was associated with a risk reduction of pancreatic cancer of 67% (adjusted OR, 0.33; 95% CI, 0.26 to 0.41; p value <0.01). A dose response relationship was noted between statin use duration and pancreatic cancer with 80% risk reduction (adjusted OR, 0.20; 95% CI, 0.33 to 0.71; p value, <0.01) with use of statin for more than 4 years. Furthermore, the protective effect of statin was seen across different age and racial groups, and was irrespective of the presence of diabetes or alcohol use. The protective benefit was not seen in smokers.