Risk factors of HCC (Poster P173)

| | Case/Control | Total | Case/Control | No virus |
|---|---|---|---|---|
| Risk factors | 347/1075 | AOR (95% CI) | 190/1039 | AOR (95% CI) |
| Family history of any cancer | 236/728 | 1.4 (1.1-1.9) | 138/700 | 1.7 (1.1-2.5) |
| First degree history of any cancer | 191/587 | 1.2 (.9-1.6) | 111/564 | 1.3 (.9-1.9) |
| First degree history of liver cancer | 21/9 | 3.9 (1.4-11.5) | 8/8 | 4.1 (1.3-12.9) |
| Diabetes mellitus | 120/112 | 4.4 (3-6.3) | 79/107 | 4.9 (3.3-7.1) |
| Alcohol consumption (> 60 ml eth/day) | 73/64 | 3.1 (1.8-5.2) | 34/59 | 3.5 (2-6.3) |
| Cigarette smoking (> 20pack/year) | 137/259 | 2 (1.4-2.9) | 72/250 | 1.8 (1.2-2.7) |
| Virus infection (HCV/HBV) | 157/36 | 21.7 (14.3-32.9) | _____ | _____ |

OR 2.67, 95% CI 1.86-3.83). Interestingly, non-RHC variants were associated with statistically significant increased risk only in the Spanish population (OR 1.54, 95% CI 1.19-2.09). In the German population the variants D84E, R142H, R151C and R160W and in the Spanish population the variants V60L, R160W and D294H were associated with increased risk of melanoma. Interestingly, the V60L variant showed a tendency towards a protective effect in the German population.

The differences between the two populations were also reflected in inferred haplotypes. While five haplotypes were common to both populations, two were unique in German and one was unique in Spanish population. Out of the common haplotypes, the one with the V92M and T314T variant alleles, while associated with increased risk in the Spanish population (OR 1.55 95% CI 1.08-2.23) was protective in Germans (OR 0.74, 95% CI 0.55-0.99).

A combined analysis of the outcome of the disease showed that the presence of two MC1R variants was associated with decreased metastasis free survival (median 10 months compared to 18 months in non-carriers). The associated hazard ratio HR was 1.70 (95% CI 1.18-2.44). The presence of any RHC variant was also associated with decreased metastasis free survival (HR 1.47, 95% CI 1.06-2.03).

In one of the largest studies so far on melanoma risk and MC1R variants we observed that the presence of MC1R variants is associated with an increased risk of melanoma. However, the variants conferring risk differ in populations. Further, in a first observation of its kind, we found an association between MC1R variants and metastasis free survival.

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**Interleukin-6 functional polymorphism influences susceptibility and has a predictive factor in prostate cancer patients receiving androgen blockade therapy**

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Background: The tumor growth independent of the presence of androgens is a main challenge in prostate cancer (PCa) treatment. Interleukin-6 (IL-6), a pleiotropic cytokine with critical roles in inflammation and immune responses, also acts as a growth factor for PCa cells and is associated to the androgen-independent (AI) phenotype.

To further investigate the possible role of genetic susceptibility of IL-6, we examined the IL6 -174 G>C genetic polymorphism, which has been found to directly affect the IL-6 transcription rate in vitro and IL-6 levels in vivo, in relation to PCa and AIPCa.

Materials and Methods: This study was conducted in histologically diagnosed PCa patients (n=328) and normal men recruited from the Institute´s Blood Donors Bank (n=344). Genotyping of IL6 -174 G>C was performed through polymerase chain reaction – restriction fragment length polymorphism (PCR-RFLP).

Results: Logistic regression analysis in genotypes stratified according to recessive model revealed an increased age-adjusted risk for PCa development in C homozygous carriers (OR=2.22, CI=1.13-4.36, P=0.021). When compared to the control group, CC genotype frequencies were significantly increased in the group of patients who developed androgen-independent disease (OR=2.51, CI=1.02-6.04, P=0.024), in those diagnosed at stage III and IV (OR=2.05, CI=1.06-3.93, P=0.019) and in patients with a PSA level at diagnosis above 20 ng.mL-1 (OR=2.27, CI=1.07-4.75, P=0.017). The time free of AI in patients submitted to androgen blockade therapy (n=233), was analysed through Kaplan Meier function plots with Breslow test and Cox logistic regression. Univariate analysis showed an association of C homozygous genotype to an earlier AI relapse (P=0.027). Furthermore, multivariate model analysis including as covariates age, prostatectomy, stage, metastases and PSA level, showed a significantly increased risk for AI (HR=2.87, CI=1.18-6.99, P=0.020).

Conclusions: Prostate cancer development and AI emergence may share common pathways. Our results support a role for the IL-6 pathway in PCa and AIPCa development. The IL6 functional polymorphism might be a useful molecular marker for PCa susceptibility and as a predictive factor for AI relapse.

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**Familial tendency of hepatocellular carcinoma in USA**

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The connection between a family history of liver cancer and hepatocellular carcinoma (HCC) development has not been well explored in the United States. In an ongoing case-control study at The University of Texas M. D. Anderson Cancer Center, we studied 347 patients with pathologically confirmed HCC and 1,075 healthy controls. All subjects were interviewed to determine their family history of cancer, including the number of relatives with cancer, the type of cancer, the subjects' relationship with the relative, the age at which the relative was diagnosed, and whether the relative was alive or deceased. We used unconditional logistic regression models to estimate the odds ratios (AOR) and 95% confidence intervals (CI), adjusting for possible confounding risk factors. Independent of chronic HBV/HCV, a history of any cancer (OR 1.7 [95% CI, 1.1-2.5]) and liver cancer specifically (OR 4.1 [95% CI, 1.3-12.9]) in a first-degree relative were significantly associated with HCC development. Multiple relatives with liver cancer were only observed among HCC patients with chronic HBV/HCV infection. Affected siblings with liver cancer is significantly associated with HCC development with and without HBV/HCV infection; (OR 5.7 [95%CI, 1.2-27.3]) and (4.3 [95%CI 1.1-20.9]) respectively. Individuals with HBV/HCV and a family history of liver cancer were at higher risk for HCC (OR 61.0 [95%CI, 6.5-579.7]). However, a history of cancers at other sites in first-degree relatives was not significantly related to HCC development. Our study demonstrated that a family history of liver cancer is associated with HCC development. Further research exploring the genetic–environment interactions associated with risk of HCC is warranted.

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**Intake of protein, fat, carbohydrate and fiber and risk of renal cell carcinoma in Canada**

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Introduction: Over the past few decades, several studies have been conducted to explore the role of diet and nutrition in kidney cancer etiology, but no specific component of diet has been clearly implicated in the risk of renal cell carcinoma (RCC). A diet high in protein and fat has been related to RCC risk but the issue is still undefined. The study was intended to further explore the role of intake of protein, fat, cholesterol, carbohydrate and fiber on RCC.

Methods: Between 1994 and 1997, mailed questionnaires were completed by 1138 incident, histologically confirmed cases of RCC and 5039 population controls. Measurement included information on socio-economic status, lifestyle habits and diet. A 69-item food frequency questionnaire provided data on eating habits two years before data collection. For each food item, cases and controls were asked to describe how often (per day, per week, per month), on average, they ate the serving size specified of the item. Estimates of total weekly nutrient intake were