found. All affected workers were operators and had a long term direct professional contact with lubricating agent N80.

The aims: The purpose of this work was to estimate the possibility of determination of localization of carcinogenically dangerous production by data of Belorussian cancer registry.

Materials and methods: Skin cancer in two close settled cities Polotsk and Novopolotsk and whole Belorussian urban population was estimated by data of Belorussian Cancer Registry for 1990-2006. Standardized incidence ratios (SIRs) were calculated using the Belorussian urban population incidence rates to generate expected numbers. We have used in the study GIS methodology to make the Atlas of skin cancer SIR time (1978-2005) distribution by 117 regions of Belarus.

The results: We have designed some criteria for primary identification of occupational risk factors in small towns based on data of Population Cancer Registry. There are high numbers of cancer cases with specific localization and morphology, younger mean age of patients and plurality of tumors. Since 1990 to 2006 it was established 956 cases of skin cancer (C44) in Polotsk, 856 cases in Novopolotsk and 61586 in Belarus. According to Atlas of Skin cancer Standardized Incidence Ratios distribution Polotsk region seems to have high skin cancer risk in compare with other Belorussian areas. The proportions of C44.6 localization were 6,5% in Polotsk, 4,3% in Novopolotsk and 3,9% in Belarus. But in the same time among C44.6 cases the proportions of squamous cell carcinoma were 66% in Polotsk, 32% in Novopolotsk and 20% in Belarus. The next feature is the number of plural primary malignant tumors (10 double and 4 triple of metachronous tumors C44.6 in Polotsk against 1 of double tumors in Novopolotsk). The mean age of diseased of carcinoma C44.6 was 55,0 in Polotsk and 62,7 in Novopolotsk and 68,7 years in Belarus. SIR of C44.6 for Polotsk (SIR=2,18; 95%CI=1,67-2,82) and Novopolotsk (SIR=1,58; 95%CI=1,11-2,18) were significantly higher than in whole population. Thus we can conclude that presence of significant professional carcinogenic factor in small city could be discovered in population based descriptive epidemiological study.

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Mouse mammary tumor virus (MMTV)-related sequences in the juvenile acute myeloid leukemia patients

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Background: MMTV-homologous sequences were found earlier in DNA samples from tumor tissue and lymphoid cells of sporadic/familial breast cancer (BC) and Non-Hodgkin's lymphomas + BC patients. Two female BC patients in our cancer-register had child suffered with acute leukemia (AL). We have analyzed a primary patients with AL to verify this observation. Material and Methods: Peripheral blood and bone marrow DNA samples obtained from 11 primary patients with acute myeloid leukemia (AML) and 6 ones with acute lymphoblastic leukemia (ALL) were analyzed by PCR using specific primers for gp52-coding area of the env MMTV gene and Sag-coding area of 3'LTR MMTV. PCR products of 665 bp and 725 bp were cloned in pGEM-T vector and sequenced. RT PCR using primers for the env MMTV gene was performed to evaluate MMTV-homologous sequence expression. Results: 4 bone marrow DNA samples from 11 patients (3 boys of 9, 11,13 years old and 1 girl of 15 years old) were the env /LTR MMTV-positive, one boy has mother with BC and young healthy brother. While five ALL patients (3 - 11 years old) were MMTV-negative by PCR. Sequencing of the env MMTV and 3'LTR –related cloned PCR products has found 93-94% homology to the exogenous env MMTV gene (C3H starin and Mus musculus MMTV), and 92% homology to SAG protein gene of Mus musculus MMTV. The sequence transcripts were revealed by RT PCR. ORF finder has shown one Frame of 567 bp long in gp 52-coding area of the env MMTV sequence and one Frame of 563 bp long in Sag-coding sequence. BLAST analysis puts the sequences into tree clusters between endogenous MMTV RNA env gene / right LTR (Mtv 17) and Mus musculus mammary gland cDNA branches. Conclusions: MMTV-homologous sequences were firstly revealed in 4 from 11 juvenile patients with AML. It indicates that MMTV-related virus might involves both in lymphomas and in leukemia in human by infection of dendritic and/or pluripotent hemopoetic stem cells. A possible ways of MMTV infection in AML patients are under discussion.

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Glutathione-S-transferase T1, M1 and P1 polymorphisms as risk factors for early onset lung cancer

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Lung cancer (LC), the leading cause of cancer death worldwide, is considered the result of complex interactions between environmental - predominantly smoking - and genetic factors. It is supposed that a particularly strong genetic component exists in the group of individuals with early onset LC. Glutathione-S-transferases (GSTs) are among the central enzymes involved in cellular detoxification.

A case-control study was carried out to identify GST genetic polymorphisms that might modify the risk of developing early onset LC. 638 Caucasian patients under the age of 51 with confirmed primary LC and 1300 cancer free control individuals, matched by age and sex, were included in this analysis. Overall, 5 SNPs in the GSTP1 gene and deletion polymorphisms in GSTM1 and GSTT1 were analysed. Genotyping of the GSTP1 polymorphisms was carried out using MALDI-TOF (matrix assisted laser desorption/ionization time-of-flight) mass spectrometry. A new semi quantitative real-time multiplex PCR assay on the LightCycler 480 was established for genotyping GSTM1 and GSTT1 copy numbers.

Conditional logistic regression analysis adjusted by smoking was applied to assess polymorphism-associated ORs. The GSTP1 SNP rs1138272 homozygous variant genotype was associated with an increased risk of LC overall (OR 3.14; 95% CI 1.01-8.96, p=0.032). For GSTP1 SNP rs4891 an increased risk of LC associated with the homozygote variant genotype was observed in the group of heavy smokers (>21 packyears) (OR 1.76; 95% CI 1.05-2.84, p=0.032). Interestingly, for GSTT1 an effect was only observed in the group of heavy smoking women, where carriers of at least one null allele showed an increased risk of LC (OR 2.33; 95% CI 1.31-4.14, p=0.004). However, all these findings were not significant after Bonferroni correction for multiple testing. An effect of GSTP1 SNP rs1695 was detected only among individuals with GSTT1 null genotype (OR 3.36; 95% CI 1.36-8.32 p=0.009), however, gene-gene interaction was not significant (p=0.07).

Our results do not support a main effect of GSTP1, GSTM1 and GSTT1 genotypes with regard to LC. However, further studies, including gene-gene interaction analysis, will be necessary. To the authors' knowledge the current study is the first investigation of GSTT1 and GSTM1 deletion polymorphisms as risk factors for early-onset LC, employing a method that distinguishes between homozygous wild-type and heterozygous individuals.

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Melanocortin receptor 1 variants and melanoma risk - a study on two European populations

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The G-protein coupled Melanocortin receptor 1 (MC1R) is a pivotal component of melanin synthesis in melanocytes. The gene encoding MC1R is highly polymorphic and many variants are associated with an increased risk of melanoma. At least five variants are strongly associated with high risk phenotypes of red hair and fair skin (RHC alleles; D84E, R142H, R151C, R160W and D294H) in Caucasians.

We investigated two European populations, German and Spanish, for the effect of MC1R variants on risk of malignant melanoma and on disease outcome. 1298 melanoma cases (595 German and 703 Spanish cases) and 1582 healthy controls (1038 German and 544 Spanish controls) were genotyped by direct sequencing. The risk of any variant in the German population (odds ratio OR 1.59, 95% confidence interval CI 1.24-2.05) was comparable to the risk observed in the Spanish population (OR 1.84, 95% CI 1.42-2.40). Carriers of two variants were at twice the risk than carriers of only one polymorphism indicating a gene dosage effect of this risk factor.

Despite similarities in the risk associated with MC1R variants, we also observed subtle differences in the two populations. RHC variants were more frequent in German than in Spanish population. However, an association between RHC variants and increased risk of melanoma was found in both populations (German: OR 2.40, 95% CI 1.81-3.19, Spanish:

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