risk and clinical tumor characteristics. Survival probabilities were compared between different subgroups.

As a novel finding several SNPs seemed to associate with the hormone receptor status. The strongest association was observed between the variant allele of the SNP in the ITGB4 gene and estrogen receptor negative (ER-) tumors (OR 2.09, 95% CI 1.19-3.67). Moreover, the ITGB4 SNP was associated with survival. The variant allele carriers had a worse survival compared to the wild type genotype carriers (hazard ratio [HR] 2.11 95% CI 1.21-3.68). The poor survival was significantly associated with the aggressive tumor characteristics: high grade, lymph node metastasis and high stage. Since the variant allele of the investigated SNP in the ITGB4 gene may cause a loss of the binding site for the miRNA miR-34a, the SNP may increase the expression of the ITGB4 gene and enhance the ability of integrin β4 to promote tumor cell growth, survival and invasion, and thus partly explain the observed bad survival of the carriers of the variant allele.

As the ITGB4 SNP seems to influence tumor aggressiveness and survival, it may also have prognostic value in the clinic. Since integrin-associated proteins are involved in all major signal transduction pathways regarding proliferation and survival they are likely candidates for targeted therapies. The observed genetic variation may also cause inter-individual variation in the response to integrin targeted therapy.

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Loss of expression of Claspin in tumour cells may be involved in breast carcinogenesis

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Breast cancer is the most common cancer among women. Familial forms may be associated with germ-line mutations in BRCA1/2. However, these mutations have incomplete penetrance, suggesting involvement of other genetic/environmental factors. As BRCA1/2 interact with other cellular proteins in a common DNA damage repair pathway, it is likely that alterations in genes that encode these proteins may modify the risk of breast cancer development in BRCA1/2 mutation carriers or in familial cases in which BRCA1/2 mutations are not identifiable. Claspin is a recently described protein that participates in DNA replication and DNA damage response, being an important checkpoint mediator essential for ATR-dependent activation of Chk1. It may also interact with BRCA1. We have thus investigated whether alterations in Claspin could be associated with increased breast cancer risk. DNA from 32 familial (characterized for BRCA1/2 mutations) and 36 sporadic breast cancer cases (all patients being followed at IPO Coimbra FG, EPE), and 60 healthy controls was screened for germline mutations in Claspin coding sequence and splice junctions using PCR-SSCP and DNA sequencing. We have detected two single nucleotide polymorphisms (Asn525Ser and IVS10+16), which co-segregated in most cases, two novel mutations (on 5'UTR-68 and codon 744) and one novel polymorphism (codon 6). The 5'UTR-68 and codon 744 mutations were found in only two of the 153 individuals analysed, one with familial and the other with (apparently) sporadic breast cancer. The Gly6Asp variant was over-represented in sporadic breast cancer patients. These findings suggest the association of this variant with an increased risk for the development of breast cancer. Preliminary data have shown that co-segregating polymorphisms were associated with loss of expression of Claspin in breast tumour cells, while expression was retained in normal cells. These data suggest a role for Claspin as a tumour suppressor, which may be related to its function in the control of DNA replication and triggering of cell cycle checkpoint responses, namely through activation of Chk1.

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Combined effects of p53 and p73 polymorphisms on head and neck cancer risk and progression - an Italian case-control study

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Background. The purpose of this study is to analyze the effects of selected p53 and p73 polymorphisms, their combination and the interaction with lifestyle habits, in association with head and neck cancer (HNC) risk and progression in an Italian population.

Methods. Two hundred and eighty-three cases and 295 hospital controls were genotyped for p53 polymorphisms on exon4 (Arg72Pro), intron 3 and 6, and p73 G4C14-to-A4T14. Modification of the effect measures on HNC by age, gender, alcohol, smoking and familiarity for cancer was tested through homogeneity tests across strata estimates from logistic regression analysis.

Results. We showed a statistically significant association between p73 variant allele and cancer of the oral cavity [Odds Ratio (OR) = 2.51; 95% CI: 1.19 – 5.35]. An effect modification of p73 variant allele by age was observed [OR= 12.85 (95% CI: 2.10 – 78.74) among those aged less or equal to 45 years at diagnosis, versus an OR of 1.19 (95% CI: 0.72 – 1.96) among those >45; p-value for homogeneity among strata estimates = 0.013]. Also, an OR of 3.60 (95% CI: 1.30 – 9.92) among current smokers carrying p73 variant allele was observed, versus an OR of 1.32 (95% CI: 0.80 – 2.19) among ex- and never-smokers with the identical genotype (p value of heterogeneity among strata estimates= 0.10).

From the gene-gene interaction analysis, it was observed that in all of the combinations individuals carrying two risk genotypes had not an additional risk compared to those with only one risk genotype, except those carrying both p53 intron and p73 mutant alleles, showing an OR of 2.22 (95% CI: 1.08-4.56). A poorer survival resulted among carriers of p53 intron 6 variant allele (Hazard Ratio = 0.49, 95% CI: 0.21 – 1.09).

Conclusion: This study shows that p73 G4C14-to-A4T14 polymorphism might be a risk factor for HNC, especially among young subjects. For the first time our study shows that individuals carrying the unfavourable variant of both p53 intron 3 and p73 exon 2 have an additional risk to develop HNC. Larger studies are required to confirm our results.

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Solid cancer incidence in the Republic of Belarus (1970-2007) - 16 years before and 22 years after Chernobyl accident

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Background: Despite of many studies of the relation between huge radiation contamination by different radioactive elements and changes of cancer incidence rates in Belarus, the question on the consequences of this disaster has not still lost its actuality.

Methods: The data of obligatory cancer registration were studied for the past 38-years. Age Standardized Incidence Rates (ASRWorld per 100 000) in males and females (urban and rural) were calculated.

Results: From 1970th to 2007th 969 714 new cancer cases (485797 (50,1%) - in males and 483917 (49,9%) - in females) have been established in Belarus. In the analysis five main types of time-related ASR trends were distinguished. (1) Considerable decrease was shown in ASR of males and females stomach cancer as in lip cancer in males. (2) No considerable changes in ASR were detected for liver, pancreas, esophagus, larynx, lung and bladder female cancers. (3) Constant growth of ASR was noted for colon cancer and melanoma of skin in both males and females and for breast, corpus uteri and renal female cancers. (4) ASR for female and male recto-sigmoidal cancer and male cancers of oesophagus, larynx, lung and bladder had been increasing till the middle of the 90s to be fixed at a certain level then. Thyroid cancer incidence jumped immediately after disaster from 0,45 in 1970th and 0,77 in 1986th to 3,1 in 2003d (males) and from 0,81 in 1970th and 1,71 in 1986th to 14,7 in 2003d (females). Since 2003d morbidity has been flatten out in males and started decreasing in females (12,3 in 2007th). The highest level of thyroid cancer incidence is noted in Gomel, Mogilev and Brest regions (most radiation contaminated). (5) Incidence rates for skin cancers in the both sexes, prostatic and renal cancer in males slowly increasing from the 70s started growing rapidly in the middle of the 90s.

Conclusions: Despite of differences in structure and dynamics of cancer incidences in males and females the total number of new cancer cases was equal in both sexes. The above-mentioned ASR trends may be indicative of the impact of some environmental factors at certain periods of time which are modifying cancer incidence trends. Now we are working at cancer mapping through 118 administrative areas of Belarus to study mentioned above tendencies in details and propose some possible carcinogens to provide a basis for further analytical epidemiological studies.

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Capacity of Belorussian population cancer registry to identify occupational skin cancer in Polotsk-city

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Background: In the end of 80th 25 cases of carcinoma of skin of the arm (C44.6) in workers of Polotsk Glass Fiber Enterprise were occasionally