with the development of peptic ulcer disease, atrophic gastritis, and gastric adenocarcinoma. Virulent Hp isolates harbor the cag (cytotoxin-associated genes) pathogenicity island (cagPAI), a 40 kb stretch of DNA that encodes components of a type IV secretion system (T4SS). This T4SS forms a pilus for the injection of virulence factors into host target cells, such as the CagA oncoprotein. In a previous study a very strong association between current infection with cagA-positive Hp strains and the severity of gastric precancerous lesions has been showed.
Material and Methods: We analyzed the genetic variability in CagA and other selected genes of the Hp PAI, using DNA extracted from frozen gastric biopsies or from cultured strains from patients with gastric preneoplastic or cancer lesions. Patients where from Venezuela, Mexico and Paraguay, areas with high prevalence of Hp infection and gastric cancer. Because of the high genetic variability of the Hp genome, the study required a thorough optimization of the experimental conditions. Thus, sequencing reactions were carried out by both, Sanger and next-generation pyrosequencing (454 Roche) methods.
Results: Sequence analysis showed high variability in most of the cagPAI genes we have tested. In particular, the *cagA* gene showed striking ethnic and individual variation in its C-terminal region, where repetitive phosphorylation (EPIYA) motifs are located. We found different combinations of these biologically important EPIYA types.
Conclusions: This first analysis confirms the presence of high variability in the Hp PAI genes, which warrants further investigations for the risk of neoplastic progression within CagA positive patients.

94 Withdrawn

95 Associations between functional EGFR polymorphisms and glioma risk

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Background: The epidermal growth factor receptor (EGFR) regulates important cellular processes and is frequently implicated in human tumours. Somatic alterations of this receptor tyrosine kinase influence several mechanisms of malignant transformation and are common in gliomas. In addition, germline *EGFR* functional polymorphisms may have implications in carcinogenesis. Two single nucleotide polymorphisms (SNPs) were found in the essential promoter region (−216G/T and −191C/A) of the *EGFR* gene. The −216G/T has functional consequences, with the T allele being associated with higher promoter activity, resulting in increased gene expression both *in vitro* and *in vivo*. Additionally, a highly polymorphic microsatellite sequence $(CA)_n$ repeat in intron 1 of *EGFR* has been shown to be functional, as the transcriptional levels of *EGFR* decline with increasing numbers of $(CA)_n$ repeats. In the present study, we aimed to elucidate the roles of these *EGFR* polymorphisms in glioma susceptibility and prognosis.
Material and Methods: We conducted a case-control study with 245 glioma patients and 412 cancer-free controls from Portugal. Genetic variants of *EGFR* were determined by PCR-RFLP analysis (for −216G/T and −191C/A) or by PCR followed by single capillary genetic analysis [for $(CA)_n$ repeat]. Univariate and unconditional multivariate logistic regression models were used to calculate odds ratio (OR) and 95% confidence intervals (95% CI). A Cox-regression model was used to evaluate patient survival.
Results: The allele frequencies of −216G/T, −191C/A, and $(CA)_n$ repeat polymorphisms in the cancer-free control group in our study are similar to those previously reported in American Caucasian populations. Associations between *EGFR* −216G/T and −191C/A variants and glioma risk were not statistically significant ($p > 0.05$). Furthermore, no associations were found when glioma patients were stratified by histological types (*e.g.*, astrocytoma and oligodendroglioma). In contrast, shorter variants of the intron 1 $(CA)_n$ repeat conferred higher risks for gliomas, glioblastomas, and oligodendrogliomas ($P < 0.05$). No associations were observed between *EGFR* polymorphisms and patient outcomes.
Conclusions: Our data do not implicate *EGFR* −216G/T and −191C/A polymorphisms as risk factors for gliomas, but suggest the length of *EGFR* $(CA)_n$ repeat in intron 1 as a susceptibility factor for development of gliomas. Future studies are warranted to investigate how these *EGFR* genetic variants may affect therapeutic responses, particularly to EGFR-targeted therapies currently tested in clinical trials for glioma patients.

96 Adiponectin functional polymorphisms and haplotype are associated with prostate cancer aggressiveness and to hormonal castration resistance

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Background: Adipokines have been proposed as mediators in the association between obesity and prostate cancer (PCa). Recent findings described that higher prediagnostic adiponectin levels predispose men to a lower risk of developing high-grade prostate cancer. Functional polymorphisms and haplotypes in *ADIPOQ* gene (*ADIPOQ+45T>G*, *ADIPOQ+276G>T* and haplotype +45/+276) seem to influence adipoQ circulating levels.
Material and Methods: We conducted a prospective study in biopsy-proven PCa patients (n = 944). Patients were appropriately followed in the clinical setting for a median time of 39.4 months (3.2 to 231.5 months). Polymorphisms were genotyped through PCR-RFLP and Real Time-PCR. Haplotypes were derived from *ADIPOQ+45* and *ADIPOQ+276* genotypes and analysed according to the adiponectin production genetic profile.
Results: Results presented evidence that *TT* carriers of *ADIPOQ+276* had increased risk for higher Gleason score (OR = 1.99; 1.2−3.3 $p = 0.004$). In the polymorphism at locus +45 an association was observed between higher levels of testosterone at diagnosis and carrying GG genotype ($p = 0.012$). Univariate Kaplan-Meier function plots analysis showed a shorter time to hormonal castration resistance in TT carriers of *ADIPOQ+276G>T* polymorphism, when compared with G carriers (54.4 and 93.2 months, respectively; $p = 0.006$). Combined haplotypic analysis showed an increased risk for Gleason $\geqslant 8$ with high/intermediate *ADIPOQ* expression genetic profile (OR = 1.92, 95%CI: 1.3−2.8; $p = 3.7 \times 10^{-4}$). This genetic profile was also associated with a higher body mass index (BMI) ($p = 0.022$). Kaplan–Meier function plots analysis showed shorter time to hormonal castration resistance in high/intermediate, when compared with Low adiponectin producers (54.4 and 96.7 months, respectively; $p = 3.6 \times 10^{-4}$). After multivariate Cox Regression analysis, using as covariants stage of disease, Gleason score and PSA at diagnosis, the high/intermediate adiponectin producers evidenced an increased risk for developing resistance to hormonal castration (HR = 1.8, 95% CI: 1.1−2.9; $p = 0.027$).
Conclusions: Functional *ADIPOQ* genotypes and haplotypes that correlate with circulating adiponectin levels might be associated with genetic susceptibility for PCa aggressiveness and shorter progression-free interval during hormonal castration treatment.

97 Non-synonym leptin receptor genetic variants, prostate cancer susceptibility and aggressiveness

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Background: Leptin is a hormone synthesized preferentially in adipose tissue. Circulating levels are well correlated with obesity status while its receptor (LEPR) was found to be overexpressed in prostate tumoural cells besides the central nervous system. We hypothesized that 3 non-synonymous *LEPR* polymorphisms (Gln223Arg, Lys656Asn and Lys109Arg) may be associated with prostate cancer (PCa) risk and aggressiveness.
Methods: This case-control study was conducted in histologically confirmed PCa (n = 1382) and benign disease patients (n = 471). We used Real-Time PCR and PCR-RFLP in order to investigate genotype distributions of the LEPR polymorphisms in these populations.
Results: Age- and BMI-adjusted binary logistic regression showed decreased PCa risk for LEPR Gln223Arg Arg carriers (aOR = 0.56; 95% CI = 0.38–0.83; $P = 0.003$). Cumulatively, we observed an association between *LEPR* Lys656Asn Asn carriers with higher Gleason score ($P = 0.008$). In PCa patients, multivariate Cox regression analysis evidenced that LEPR Lys109Arg Lys carriers had lower time-to-bone metastasis (HR = 0.37; 95% CI = 0.14–0.95; P = 0.039), after adjustment for Gleason score, stage of disease and PSA level.
Conclusions: Results from this large study using biopsy-proven absence of PCa in the control group, suggest that the non-synonymous polymorphism LEPR Gln223Arg is associated with PCa development and may be a potential molecular marker of susceptibility. Conversely, the polymorphism LEPR Lys109Arg might be linked with bone metastasis mechanisms, influencing the

time-to-onset of bone spread. LEPR Lys656Arg may be involved in tumour differentiation, thus influencing Gleason grade.

98 Association between primary brain tumours and specific IgE levels, measured in participants of the EPIC cohort study

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Background: Epidemiological studies investigating the association between allergic or atopic diseases, including asthma, hay fever or eczema (atopic eczema), and primary brain tumours (glioma, meningioma, schwannoma) showed nearly all an inverse association between glioma, with the less consistent results for meningioma. Only few cohort studies exist presenting with conflicting results. At the moment, no conclusive biological mechanism is known.
Our study investigates in frame of a large international cohort study based on specific IgE-levels the association between atopic condition and primary brain tumours.
Material and Methods:A nested case-control study has been conducted in frame of the EPIC (European Prospective Investigation into Cancer and Nutrition) brain tumour cohort. The serum samples were collected from the participants of this large international, multi-centric prospective cohort study, in general several years before the diagnosis of the brain tumour. 216 glioma, 137 meningioma and 39 schwannoma cases were available for testing. In total 595 controls sera were randomly selected from the cohort and matched to the cases according study centre, gender, data of birth, age, date and time of blood selection, and length of follow-up. ORs and their 95% CI were calculated using conditional logistic regression analyses. Adjustment has been done for educational level, smoking status, alcohol consumption, physical activity and hormone replacement therapy (for women only).
Results and Conclusion: In general the results of this cohort study confirm those of the case control studies. Using sera for testing specific IgE levels instead of questionnaire data from case-control participants avoid information and recall bias due to memory gaps and to missing symptoms although an atopic condition exists. Limitations and strength of the study design should be discussed, especially the issue of possible biological hypotheses.

99 Cycloxygenase-2 (COX2) expression in transitional cell carcinoma of the bladder does not confer independent prognostic properties

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Background: Cyclooxygenase-2 (COX2) is responsible for maintaining an acute inflammatory state in the body and its aberrant overexpression can trigger chronic inflammation and cancer. The link between inflammation and bladder cancer has provided the impetus for many studies to evaluate the prognostic significance of COX2 in this tissue with no clear consensus on independent prognostic potential having been made. Using, one of the largest cohorts of Transitional Cell Carcinomas (TCC), we attempted to further elucidate the independent prognostic potential of COX2 expression in bladder cancer.
Methods: Tissue microarrays containing 557 non-muscle invasive (NMIT) and 216 muscle invasive (MIT) bladder tumours collected as part of the Spanish Bladder Cancer study, were analyzed by immunohistochemistry using computerized quantitative image analysis technology. COX2 expression was assessed as a product of staining intensity and area, providing a continuous protein expression gradient. Univariate and multivariate Cox-proportional hazards statistics were then applied to determine whether COX2 expression was an independent prognostic marker for recurrence and progression in NMITs, and progression and disease-specific survival in MITs.
Results: COX2 protein expression was associated with tumour stage ($p < 0.0001$) and grade ($p < 0.0001$) in NMITs. Maintaining COX2 expression as a continuous variable in univariate analysis yielded an association with increased recurrence in NMITs (hazard ratio [HR] 1.019 [95% CI 1.000–1.038], $p = 0.048$), while a dichotomous expression score was associated with a decrease in progression of NMITs (HR 0.448 [0.252–0.795], $p = 0.01$). These associations did not maintain significance in the multivariate analysis.
Conclusions: To our knowledge, this study makes use of the largest cohort of TCCs to be analyzed for COX2 expression, and recapitulates the association of COX2 expression with other established cancer markers. However, there is lack of evidence to support that COX2 expression can be used as an accurate, independent prognostic marker in bladder cancer.

100 Cancer incidence in the Republic of Belarus: from 1970 to 2030

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Background: Cancer incidence rates grow dramatically in the world. 25.0 million new cancer cases are expected to be registered in 2030. This cancer burden is supposed in Belarus too. Thus we will need to prepare the medical service for new conditions and design new approaches in cancer prevention.
Methods: The data of obligatory cancer registration were studied for the past 39 years. Age Standardized Incidence Rates (ASR_{World} per 100,000) in males and females (urban and rural) were calculated. Absolute numbers of cancer incidence were analyzed and predicted up to 2030 in compliance with age-specific rates trends and demographic situation prognosis.
Results: In 1970 13,983 new cancer case were established in Belarus. This number has grown to 40,744 to 2008. This increase was caused partially by population ageing and by growth of age-specific rates due to cancerogenic factors affection. 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. Incidence rates for skin cancers in the both sexes, prostatic and renal cancer in males slowly increasing from the 1970s started growing rapidly in the middle of the 1990s. But considerable decrease was shown in ASR of males and females stomach cancer as in lip cancer in males. 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 1990s to be fixed at a certain level then. Thyroid cancer incidence jumped immediately after Chernobyl disaster from 0.45 in 1970 and 0.77 in 1986 to 3.1 in 2003 (males) and from 0.81 in 1970 and 1.71 in 1986 to 14.7 in 2003 (females). Since 2003 morbidity has been flatten out in males and started decreasing in females. Thyroid cancer incidence rates have returned to before-Chernobyl level in children age-groups but they continue increased in elder cohorts. It is expected that the population of Belarus will decrease by one million persons (10% from the 2008 level) but the proportion of 55 years old people will increase in 25% from 2008 to 2030. Most important cancers incidence rates grow rapidly exactly in people who are 55 years and elder. Both ageing of population and cancerogenic factors impact allow us to predict the 60,000 new registered cancer cases in 2030.
Conclusions: To ease the result of our expectancies we need to start realizing cancer screening programs, especially reinforcing prevention activity and expanding heath care and medical education systems in part of oncology.

101 Tumours of salivary glands from diagnosis to management

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Background: The three major salivary glands plus the hundreds of small minor salivary gland locates within the submucosa of the oral cavity and oropharynx are capable of giving rise to a wide range of neoplasms. The vast majority of salivary neoplasms are epithelial in origin. The ratio of benign to malignant salivary gland tumours is gland dependent. Epithelial salivary gland tumours are relatively uncommon and constitute a wide spectrum of variable morphologic and biologic entities. Among these cytological and morphological properties of salivary gland tumours, one of the most important criteria for measuring its biological behaviour and aggressiveness is cell proliferation. The cell proliferation/death balance is most important in the development of salivary gland tumours.
Material and Methods: Forty nine formalin fixed paraffin embedded tissue blocks of epithelial salivary gland tumours were used in this study. Haematoxylin and Eosin stain was used for reassessment of the histopathologic diagnosis. The cell proliferation activity was examined by proliferating cell nuclear antigen (PCNA) and Ki 67 immunohistochemistry and proapoptotic cell death Bax and Bcl-2 mRNA genes was analysed by in situ hybridization techniques.
Results: The parotid glands expressed a high frequency of affected site and about 25% demonstrated malignant behaviors while the minor salivary glands the frequency rate were account for 25% and have ability to demonstrated malignant behavior to 50%. Immunohistochemical analysis show high expression of PCNA and Ki 67 was noted in 8 of 12 pleomorphic adenoma cases (66.67%), 15 of 19 adenoid cystic carcinoma cases (78.95%), 6 of 7 mucoepidermoid carcinoma cases (85.71%), and 3 of 5 adenocarcinoma cases (60%). Significant difference was found between labeling index of benign and malignant salivary gland tumours, while no significant relationship was noted in labeling index between adenoid cystic carcinoma and mucoepidermoid carcinoma neither between mucoepidermoid carcinoma and adenocarcinoma.
In situ hybridization detection show low expression of Bax and was noted in pleomorphic adenoma cases (25%), in adenoid cystic carcinoma cases (52.63 %), however, mucoepidermoid carcinoma showed high expression of these markers than other salivary gland tumours, whereas adenocarcinoma show equal number of cases expressed both PCNA protein and Bax mRNA. No significant relationship was demonstrated between the immunostaining PCNA,