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94 Withdrawn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

B.M. Costa[1], M. Viana-Pereira[1], S. Costa[1], J. Lima[2], P. Soares[2], J. Amorim[3], P. Linhares[4], C. Pinheiro[5], P. Oliveira[6], R.M. Reis[1]. *[1]University of Minho, Life and Health Sciences Research Institute (ICVS) School of Health Sciences, Braga, Portugal, [2]IPATIMUP, Institute of Molecular Pathology and Immunology, University of Porto, Porto, Portugal, [3]Hospital S. Marcos, Department of Oncology, Braga, Portugal, [4]Hospital S. João, Department of Neurosurgery, Porto, Portugal, [5]Hospital Santo António, Department of Neurosurgery, Porto, Portugal, [6]University of Minho, Department of Production and Systems Engineering, Braga, Portugal*

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

V. Cunha[1], R. Ribeiro[1], A. Azevedo[1], C. Monteiro[1], F. Pina[2], A. Fraga[3], F. Calais da Silva[4], F. Lobo[5], R. Medeiros[6]. *[1]Oncology Portuguese Institute, Molecular Oncology, Oporto, Portugal, [2]Hospital S. João, Urology Department, Oporto, Portugal, [3]Porto hospital Centre, Urology Department, Oporto, Portugal, [4]Central Lisbon Hospital Centre, Urology Department, Lisbon, Portugal, [5]Portuguese Institute of Oncology, Urology Department, Oporto, Portugal, [6]Portuguese Institute of Oncology, Molecular Oncology, Oporto, Portugal*

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

C. Monteiro[1], R. Ribeiro[1], A. Azevedo[1], V. Cunha[1], A. Fraga[2], F. Pina[3], F. Calais da Silva[4], F. Lobo[5], R. Medeiros[1]. *[1]Portuguese Institute of Oncology, Molecular Oncology, Porto, Portugal, [2]Porto Hospital Centre, Urology Department, Porto, Portugal, [3]Hospital S. João, Urology Department, Porto, Portugal, [4]Central Lisbon Hospital Centre, Urology Department, Lisbon, Portugal, [5]Portuguese Institute of Oncology, Urology Department, Porto, Portugal*

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