this issue by directly looking at the relationship between APOE and HNC, as well as the interaction with potential effect modifiers.
**Materials and Methods:** Four hundred seventeen HNC cases and 436 hospital controls were genotyped for *apoE* polymorphism. The relationship between HNC and putative risk factors was measured using the adjusted odds ratios (ORs) and their 95% confidence intervals (CIs) derived from logistic regression analysis. Finally a gene-environment interaction analyses were performed.
**Results:** A nearly significant 40% decreased HNC risk (OR = 0.58, 95% CI: 0.31–1.05) was observed for individuals carrying at least one apoE ε2 allele while no effect was shown for those with one ε4 allele. A statistically significant interaction resulted between alcohol drinking and the ε4 allele (p-value for interaction = 0.044) with alcohol drinkers carrying at least one ε4 allele having a 2-fold HNC increased risk respect to non drinkers with ε3/ε3 genotype.
**Conclusions:** Our study provides for the first time evidence of a possible protective effect of the ε2 allele against HNC, thus suggesting a direct relationship between cholesterol levels and HNC risk. Larger studies are needed to confirm these findings to further investigate the role of *apoE* genotype in HNC etiology and give insight into the causal role of cholesterol on carcinogenesis as well.

### 68 Examination of GST and CCR5 gene polymorphisms in children with acute lymphoid leukemia in Hungarian population

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The glutation-S-transferase (GST) genes are involved in the metabolism of carcinogens and chemotherapy drugs, while the C-C chemokine receptor type 5 (CCR5) gene is a member of the beta chemokine receptor family of integral membrane proteins, which plays an important role in the tissue infiltration of lymphoblasts. These genes are polymorphic in humans and may affect the risk of acute lymphoid leukemia (ALL) and the outcome of the antileukemia treatment. The GSTT1 and GSTM1 genes have frequent inactive (null) variants and the CCR5D32 is a deletion mutation which makes the CCR5 receptor unfunctional.
Previous studies showed inconsistent results about the role of GST and CCR5 variants in childhood leukemia. To investigate the putative role of the inactive variants of these genes in the risk of ALL, we performed an analysis on 455 ALL children (diagnosed 1980–2005) and 359 controls using polymerase chain reaction (PCR) and gel electrophoresis.
Based on our data, we found that the homozygous frequencies of GSTM1 null genotype in the control group and in patients with ALL, did not show significant difference (51.6% vs. 54.6%; p = 0.399; OR = 1.13 (95% CI (0.85–1.49)). Comparison of deletion allele frequencies of the *CCR5*D32 in control patient and ALL cases (8.8% vs. 8.8%; p = 0.996; OR = 1.00 (0.70–1.42)) showed neither significant difference. The frequencies of patients homozygous for the inactive GSTT1 variant differed significantly between ALL children and controls (18.6% vs. 25.0%; p = 0.035; OR = 0.70 (0.50–0.98)), indicating that children without GSTT1 had a reduced risk against developing ALL in Hungarian children. GSTM1 or CCR5 deletions or deletion both in GSTT1 and GSTM1, or in GSTM1 and CCR5 genes, were not associated with ALL.
Our data suggest that the absence of GSTT1 gene may decrease the risk of developing ALL in the Hungarian population, however the inactive variants of the GSTM1 or CCR5 genes or deletions in both GSTT1 and GSTM1, or in CCR5 and GSTM1 do not affect of the risk of childhood ALL.

### 69 Post-GWAS pancreatic cancer susceptibility loci and their importance in survival

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**Background:** Pancreatic cancer is one of the neoplasms with the worst mortality rate (5-year survival: 4.3%). Relatively little is known about etiology (tobacco smoking, obesity, diabetes, chronic pancreatitis, family history are the only established risk factors, and pancreatic cancer is part of some genetic cancer syndromes). There is no effective screening test for the malignancy and metastatic disease is commonly present at initial diagnosis. In 2009 the PanScan project, a genome-wide association study, identified various loci affecting susceptibility to pancreatic cancer. The aims of this study are: to replicate the association between loci identified by PanScan and pancreatic cancer risk, and to evaluate the possible associations between the inter-individual variation and overall survival time of pancreatic cancer patients.
**Material and Methods:** Fifteen SNPs mapping to six regions identified by PanScan were typed in a population of 700 patients and 2200 healthy controls recruited from Heidelberg and Liverpool. Genotyping was performed using the TaqMan real time PCR assay. Association between SNPs and pancreatic cancer risk was performed with logistic regression; survival analysis was performed with Cox regression models.
**Results:** Most of the PanScan SNPs were significantly associated with pancreatic cancer risk in our population. In addition, we found that a SNP in chromosome 15 may also play an important role in overall survival of pancreatic cancer patients.
**Conclusions:** The majority of the associations found in PanScan were replicated in this population and one SNP was found to be associated with a different survival time of the patients.

### 70 Genetic polymorphisms and risk of familial non-medullary thyroid cancer

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**Background:** Thyroid cancer is the most common endocrine malignancy. Non-medullary thyroid cancer (NMTC), with its main subtypes papillary and follicular thyroid cancer, represents about 90% of all cases. Epidemiological data show that risk of NMTC in the ?rst-degree relatives of affected cases is elevated five- to ninefold. Familial NMTC (FNMTC) accounts for about 3−7% of all thyroid tumours and is a clinical entity characterized by a more aggressive phenotype than its sporadic counterparts. Characterization of genetic susceptibility to FNMTC was attempted a decade ago with microsatellite genotyping and linkage analysis methods, and led to the mapping of a few susceptibility genes, but identification of specific variants was not possible at that time. The advent of high-throughput SNP genotyping recently led to the identification of polymorphisms affecting NMTC risk in its sporadic and familial forms. In particular, a genome-wide association study (GWAS) identified common SNPs at 9q22.33 and 14q13.3, which increase the risk of sporadic NMTC. We have investigated if these newly identified genetic risk factors for NMTC are relevant for FNMTC as well.
**Material and Methods:** We genotyped 13 SNPs from recent studies, reported to affect the risk of NMTC, in 805 subjects belonging to 133 pedigrees with at least two observed cases of NMTC. Genotyping was performed with amplification refractory mutation system (KASPar) technology. Data were analyzed for both linkage and association. Single-SNP analysis of the candidate loci was performed either on the nuclear families (N = 239) using Family-Based Association Tests (FBAT), or on the whole set of pedigrees (N = 133) using Modified Quasi-Likelihood Score (MQLS).
**Results:** SNPs on chromosomes 9q22.33 and 14q13.3 showed convincing evidence of association with NMTC risk in these families using both methods, whereas the other tested markers resulted negative. Haplotype analyses for the loci where more than one SNP was tested confirmed the results of the single SNP analyses.
**Conclusions:** Consistent with findings from a recent GWAS, SNPs on chromosomes 9q22.33 and 14q13.3 appear to be associated with the familial form of NMTC as well as the sporadic form. We will perform further genotyping in the familial samples of SNPs located in *FOXE1* (9q22.33) and *NKX2* (14q13.3), as well as additional SNPs reported to be associated with risk of NMTC.