based case-control study population containing 1228 CRC case samples and 782 control samples, recruited in nine oncological departments and five gastroenterological departments in the Czech Republic, was genotyped using KASPar Assays®.
Results: The preliminary results indicated one SNP in ENPP1 (rs1033398) to be associated with the risk of CRC (p_{trend} 0.016).
Conclusion: The application of the ancestral-susceptibility model to intertwined complex common diseases may be a promising method to detect candidate genes for CRC.

60 Predisposing genes in hereditary breast and ovarian cancer in the Czech Republic

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Background: We screened patients at high risk of developing breast or ovarian cancer for mutations in two major predisposition genes, *BRCA1* and *BRCA2* and further we focused on the role of additional genes that also influence the risk of breast/ovarian cancer. In this study we analyzed the role of *CHEK2*, *ATM* and *p53* genes in tumourigenesis.
Materials and Methods: A series of 705 unrelated patients selected for genetic testing was first analyzed for the presence of mutations in *BRCA1/2* genes and those tested negative were subsequently screened for alterations in other susceptibility genes. Complete coding regions were analyzed in *BRCA1*/2, *ATM* and *p53* genes; the *CHEK2* gene was tested for the most common point mutation 1100delC and for the genomic deletion of 5395 bp that leads to the loss of exons 8 and 9 and occurs frequently in the Slavic population. All identified gene alterations were confirmed and characterized by direct DNA sequencing.
Results: Within 705 analyzed individuals, 125 (17.7%) carried a *BRCA1* mutation and 34 (4.8%) a *BRCA2* mutation. Large deletions or complex genomic rearrangements detected at the *BRCA1* locus accounted for 12% (15/125) out of all identified *BRCA1* mutations. No large deletions were detected in the *BRCA2* gene. Pathogenic mutations in other tested genes were less frequent. Of the 545 tested patients, 9 (1.7%) carried pathogenic mutations in *CHEK2*, 5 (0.9%) in *ATM* and 3 (0.6%) in *p53*.
Conclusions: Mutations in *BRCA1/2* genes included 90% (159/176) of all identified gene alterations. However, our results also indicated that analysis of locally prevalent recurrent mutations in other susceptibility genes may be of an important clinical relevance. The most relevant of the other tested genes was *CHEK2* and the two recurrent mutations in this gene, 1100delC and deletion of exons 8−9, identified in four and five patients respectively, belong to frequent gene alterations identified in breast/ovarian cancer families. On the other hand, families with mutations in *ATM* and *p53* gene were rare and the role of these genes in breast tumourigenesis is limited. Two mutations in the *p53* gene were detected in cases of breast cancer prior to age 28 years that were not from families with Li-Fraumeni features.
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61 Influence of polymorphism-modified gene expression on breast cancer survival

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There is substantial evidence of an inherited component in breast cancer susceptibility. Along with the previously characterized high-penetrance genes BRCA1 and BRCA2, also moderate-penetrance (e.g. ATM, BRIP, CHEK2, PALP) and low-penetrance genes (e.g. TGFB1, CASP8, loci identified in genome wide association studies (GWA)) have been discovered. However, also prognosis and survival in breast cancer are at least partly heritable. In this study, we applied the candidate gene approach. Candidate genes were chosen following a systematic analysis of literature about different gene expression profiles in different breast cancer survival groups. Therefore, we were not looking for non-synonymous single nucleotide polymorphisms (SNPs) but rather for SNPs in promoter, 5′ and 3′ untranslated region (UTR). We focused on genes directly involved in the regulation of the cell cycle, such as cyclins, cyclin-dependent kinases and cyclin-dependent kinase inhibitors and genes involved in the assembly of the pre-replicative complex for DNA replication. Genotyping was done in a Swedish population using KASPar assays. The genotyping data were correlated with risk, traditional prognostic markers, e.g. estrogen/progesterone receptor status, and survival in a population-based case-control cohort.
We found 6 SNPs in 4 genes to have an influence on the overall survival of breast cancer. Some of these mutations were also associated with traditional prognostic markers. In addition, we found 2 SNPs being associated with susceptibility to breast cancer.
Our findings support the finding of the gene-expression publications, which have always ranked cell cycle control genes as the ones most distinctly expressed in different survival groups.

62 Pre-diagnostic circulating parathyroid hormone concentration and colorectal cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort

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Background: Parathyroid hormone (PTH) has been proposed to play a promoting role in carcinogenesis. However, few epidemiologic studies have directly investigated its role in colorectal cancer (CRC).
Methods: A case-control study nested within the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort was conducted with 1,248 incident, sporadic CRC cases matched to 1,248 controls. Circulating pre-diagnostic PTH and 25-hydroxy vitamin D (25-(OH)-vitamin D) concentrations were measured by enzyme-linked immunosorbent assays. Detailed dietary and lifestyle data were collected from questionnaires. Multivariate conditional logistic regression was used to estimate the incidence rate ratio (RR) with 95% confidence intervals (95%CI) for the association between circulating PTH and CRC risk. Effect modification by various risk factors was examined.
Results: High levels of serum PTH ($\geqslant$65 ng/L) were associated with increased CRC risk (RR = 1.41, 95% CI: 1.03–1.93) compared with the serum PTH between 30 and 65 ng/L. In sub-group analyses by anatomical sub-site the risk for colon cancer was RR = 1.56, 95% CI: 1.03–2.34, and for rectal cancer RR = 1.20, 95% CI: 0.72–2.01 ($P_{heterogeneity}$ = 0.21). In interaction analyses, among participants who had a low intake of dietary calcium, the association between high PTH and CRC was the strongest (RR = 2.49, 95% CI: 1.38–4.50; $P_{interaction}$ = 0.64). Further stratified and joint analyses suggested potential differences in PTH-CRC effect estimates according to 25-(OH)-vitamin D and body mass index (BMI) categories, however, none of them was statistically significant.
Conclusions: The results of this study suggest that high serum PTH levels may be associated with incident, sporadic CRC in Western European populations, independently of dietary calcium and 25-(OH)-vitamin D.

63 What is the risk of venous thromboembolism in patients with cancer? – a systematic review and meta-analysis

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Background: The association between cancer and thrombosis was first observed 145 years ago, and remains a very clinically relevant research area. Several review articles exist on the topic, but most are narrative reviews, with no systematic review in the present literature detailing the absolute risk of venous thromboembolism in cancer patients. A systematic review and meta-analyses were therefore performed to determine the incidence rates of VTE in different cancer types in high risk and average (population-based) risk cancer patients.
Methods: The Medline database from 1950–October 2009 was searched, along with the reference lists of identified papers and reviews. Included studies assessed the risk of venous thromboembolism (VTE), manifesting as deep venous thrombosis (DVT) and pulmonary embolism (PE), in patients with a range of primary malignancy types over a specified follow-up period (measured in person-years). Cohort risk groups were assessed based on previous cancer treatment regimens and stage of disease, with patients receiving