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

P. Pohlreich[1], J. Stribrna[1], I. Ticha[1], J. Soukupova[1], Z. Kleibl[1], M. Zikan[1], M. Zimovjanova[2], J. Kotlas[3], A. Panczak[3]. [1]*Charles University in Prague First Faculty of Medicine, Institute of Biochemistry and Experimental Oncology, Prague, Czech Republic,* [2]*Charles University in Prague and General University Hospital in Prague First Faculty of Medicine, Department of Oncology, Prague, Czech Republic,* [3]*Charles University in Prague and General University Hospital in Prague First Faculty of Medicine, Institute of Biology and Medical Genetics, Prague, Czech Republic*

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

J.K. Eckert[1], A. Brandt[1], R. Johansson[2], K. Enquist[3], R. Henriksson[2], K. Hemminki[1], P. Lenner[2], A. Försti[1]. [1]*German Cancer Research Center, Division of Molecular Genetic Epidemiology, Heidelberg, Germany*, [2]*Norrlands University Hospital, Department of Oncology, Umeå, Sweden,* [3]*Umeå University, Department of Public Health and Clinical Medicine/Nutritional Research, Umeå, Sweden*

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

V. Fedirko[1], E. Riboli[2], S. Rinaldi[3], T. Norat[2], H.B. Bueno-de-Mesquita[4], F.J.B. van Duijnhoven[5], T. Pischon[6], E.H.J.M. Jansen[7], M. Jenab[8], on behalf of the EPIC Group International Agency for Research on Cancer, NME/DEX, Lyon, France. [1]*International Agency for Research on Cancer, ENV/LCA, Lyon, France,* [2]*Public Health and Primary Care Faculty of Medicine Imperial College, Division of Epidemiology, London, United Kingdom,* [3]*International Agency for Research on Cancer, NME/DEX, Lyon, France,* [4]*National Institute for Public Health and the Environment (RIVM), Department of Gastroenterology and Hepatology University Medical Centre Utrecht (UMCU), Utrecht, The Netherlands,* [5]*National Institute for Public Health and the Environment (RIVM), Julius Centre for Health Sciences and Primary Care University Medical Centre, Utrecht, The Netherlands,* [6]*German Institute of Human Nutrition Potsdam-Rehbruecke, Nuthetal, Germany,* [7]*National Institute for Public Health and the Environment (RIVM), Bilthoven, The Netherlands*

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

F. Horsted[1], M. Grainge[2], J. West[2]. [1]*University of Nottingham, Medicine, School of Community Health Sciences-Epidemiology and Public Health, Nottingham, United Kingdom,* [2]*University of Nottingham, School of Community Health Sciences-Epidemiology and Public Health, Nottingham, United Kingdom*

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

chemotherapy, surgery, radiotherapy, or with metastatic cancer constituting a 'high risk' group. All others were considered 'average risk'.
Results: 16 studies, published in 20 papers, were identified for inclusion. The data from the included studies consistently reported annual VTE incidence rates of between 2−10%, depending on the populations studied. The highest incidence cancer types for average risk patients were bone (75.47/1000; 95% CI: 33.91, 167.99) and brain malignancy (64.27/1000; 95% CI: 45.92, 89.95), and for high risk patients were pancreatic cancer (100.74/1000; 95% CI: 66.95, 151.60) and brain malignancy (96.93/1000; 95% CI: 36.28, 258.96).
Conclusions: Venous thromboembolism is common among cancer patients, and there is considerable variation in risk by cancer type and in those with additional risk factors for VTE. Venous thromboembolism is a devastating complication which, with adequate treatment, may be prevented from occurring to a reasonable degree. This review highlights patient groups at particular risk who may well benefit from targeted strategies to deliver antithrombotic interventions.

64 Subtype-specific risk of testicular germ-cell tumours among immigrants and their descendants in Sweden, 1960–2007

O. Beiki[1], F. Granath[2], P. Allebeck[3], O. Akre[2], T. Moradi[1]. [1]*Karolinska Institutet, Institute of Environmental Medicine, Stockholm, Sweden,* [2]*Karolinska Institutet, Department of Medicine, Stockholm, Sweden,* [3]*Karolinska Institutet, Department of Public Health Sciences, Stockholm, Sweden*

Background: Testicular cancer is the most common cancer among young male adults in many populations and there has been an unexplained dramatic increase in its occurrence in several populations over the past decades. To elucidate the importance of genetic and environmental factors in testicular cancer etiology and to gain insight into the potential timing of exposures; we compared histo-pathological subtype-specific risk of testicular cancer among migrants and their descendants to that of Swedish-born men.
Material and Methods: A nation-wide cohort of 3.6 million men aged 15−54 years was followed between 1960 and 2007 through the linkage between Swedish National Registers including Total Population Register, Cancer Register, Cause of Death, and Multi-Generation Register. Incidence rate ratio (IRR) adjusted for age and calendar period of follow-up with 95% confidence intervals (CIs) was estimated using Poisson regression models.
Results: 5,801 cases of testicular cancer occurred during 80 million person-years of follow-up. First-generation immigrants had a lower risk compared with Swedish-born men (IRR = 0. 66; 95% CI = 0.60–0.72). The risk among first-generation immigrants varied remarkably by birthplace, reflecting the risk in their countries of birth. The risk of testicular seminomas was statistically significantly modified by age at immigration and duration of residence among immigrants born in high-risk areas ($P_{homogeneity}$ = 0.004 and 0.05, respectively). We observed a statistically significantly convergence of risk among second-generation immigrants toward the risk in Sweden (RR = 1.02; 95% CI = 0.93–1.12). This convergence was regardless of the risk level (high or low) in the parental country of birth. The risk among second-generation immigrants was not affected by duration of stay of their mothers in Sweden before pregnancy.
Conclusions: Our study provides evidence that interaction between exposures in uterus and after birth might be important in the development of testicular cancer.

65 A noble melanoma discrimination index based on hyperspectral data

H. Okutani[1], T. Nagaoka[2], A. Nakamura[2], Y. Kiyohara[3], T. Sota[1]. [1]*Waseda University, Department of Electrical Engineering and Bioscience, Tokyo, Japan,* [2]*Waseda University, Waseda Research Institute For Science and Engineering, Tokyo, Japan,* [3]*Shizuoka Cancer Center Hospital, Dermatology Division, Shizuoka, Japan*

Backgrounds: It is well known that noninvasive and untouchable diagnosis of malignant melanoma at an early-stage is very important to reduce melanoma-related mortality rate. Therefore a lot of automated melanoma screening systems have been studied. Objective of this study is to develop a melanoma discrimination index based on hyperspcetral data (HSD), which consist of both spatial and spectral information.
Material and Methods: 157 HSD (52 HSD from 5 melanoma patients, 95 HSD from 11 seborrheic keratosis (SK) patients and 10 HSD from 4 volunteers with nevus: The patients and volunteers were all Japanese) were measured using a newly designed hyperspectral imager. A spectrum of each pixel was considered as a multi-dimensional vector, and a spectral angle between the vector and a reference vector was calculated. Here the reference vector was defined by an average spectrum of typical normal skin. An entropy index was calculated every HSD using the probability of finding a spectral angle and regarded as a melanoma discrimination index. Statistical tests were performed to verify the effectiveness of the proposed index. Statistical significance was set to be 5%. Receiver operating characteristic (ROC) analysis was also made. The present study was approved from the Institutional review board at Shizuoka Cancer Center.
Results: Mann–Whitney U test revealed that the present index was useful to discriminate melanomas from SK and nevus. An area under the ROC curve was 0.93 with the present index, while it was 0.77 with the pseudo-fractal dimension based index which we had proposed previously. A linear discrimination analysis gave an accuracy of 91.1%, a sensitivity of 92.3% (95% CI: 85.0–99.6%), and a specificity of 90.5%(95% CI: 84.9–96.1%).
Conclusions: We have proposed a noble melanoma discrimination index derived from spectra which vary from site to site. Although the sample size is still small, the index has been considered to be useful for discriminating melanomas from SK and nevus. The present result suggests that disordered nature of pigment skin lesions may be important in melanoma screening system.

66 Publish or perish in cancer – but where?

R.W. Glynn[1], J.Z. Chin[1], N. Miller[1], M.J. Kerin[1], K.J. Sweeney[1]. [1]*Clinical Sciences Institute, Department of Surgery, Galway, Ireland*

Background: Bibliometric analysis has previously been employed as a method of correlating research productivity in oncology with geographic variation in output and funding, and the development of translational research. Investigation of output across a range of disciplines within oncology has not been undertaken previously. The aims of this study are to measure the proportion, quality and relevance of articles relating to common malignancies in the medical press.
Materials and Methods: Both PubMed and the WoS databases were consulted for the reference period 01/01/2007 to 31/12/2007. Publications were retrieved by searching for each malignancy using its medical subject heading (MeSH) term in PubMed. The subheadings encompassed by each MeSH term were then employed to perform an equivalent search in the WoS database. The 26 malignancies with the highest incidence as defined by the Surveillance, Epidemiology, and End Results (SEER) database of the National Cancer Institute (NCI) in 2006 were included in the study. The top twenty journals by impact factor (IF) and eigenfactor (EF) in general medicine and oncology journals, and the presence of each malignancy within these titles was then analysed. The journals publishing most prolifically on each neoplasm were also identified and their impact assessed.
Results: The two databases generated 63260 (PubMed) and 126845 (WoS) entries, respectively. The 26 neoplasms accounted for 25% of total output from the top medical publications. 5 malignancies dominated the first quartile of output in the top oncology journals; breast, prostate, lung, and intestinal cancer, and leukaemia. Journals publishing most frequently on these neoplasms are associated with much higher IFs and EFs, though these measures are not equivalent across all sub-specialties. The EF and IF correlated strongly in the general medical ($r = 0.854$, $p = 0.000$) but not in the oncology literature ($r = 0.289$, $p = 0.217$).
Conclusions: Oncology enjoys a disproportionately large representation in what are traditionally regarded as the more prestigious medical journals. 5 malignancies receive the majority of this attention however, and there is a need to delineate between proxy measures of quality and the relevance of output when assessing its relative merit. Our results also suggest that the most relevant information for those working in many of the oncologic sub-specialties is not necessarily to be found in the most prestigious journals as delineated by proxy indicators of quality. These findings raise significant questions regarding the best method of assessment of research and scientific output in the field of oncology.

67 A case-control study on the effect of ApoE genotypes on head and neck cancer risk

E. De Feo[1], G. Cadoni[2], J. Rowell[1], N. Nicolotti[1], M. Volante[2], G. Paludetti[2], D. Arzani[1], R. Amore[1], G. Ricciardi[1], S. Boccia[1]. [1]*Catholic University of the Sacred Heart, Institute of Hygiene, Rome, Italy*, [2]*Catholic University of the Sacred Heart, Institute of Otorhinolaryngology, Rome, Italy*

Background: The Apolipoprotein E gene (19q13.2) which is involved in the clearance of lipoproteins from plasma has three major isoforms encoded by ε2, ε3 and ε4 alleles with different receptor-binding abilities. Since a nearly linear relationship between A*poE* genotypes and levels of total and low-density lipoprotein serum cholesterol (LDL-C) has been reported, the ε4 allele is associated with hypercholesterolemia whereas the ε2 allele relates with the reverse effect if compared to the reference ε3 allele. An inverse relationship between serum cholesterol and head and neck cancer has been previously suggested but the role of *apoE* genotypes on HNC etiology has never been investigated. Since the question on the role of hypocholesterolemia as a predisposing factor, or result of the preclinical stage of HNC itself, remains still under debate, our hospital-based case-control study aimed to overcome