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European Organisation for Research and Treatment of Cancer

ECCO
European CanCer Organisation

EACR
European Association for Cancer Research

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European Society of Breast Cancer Specialists

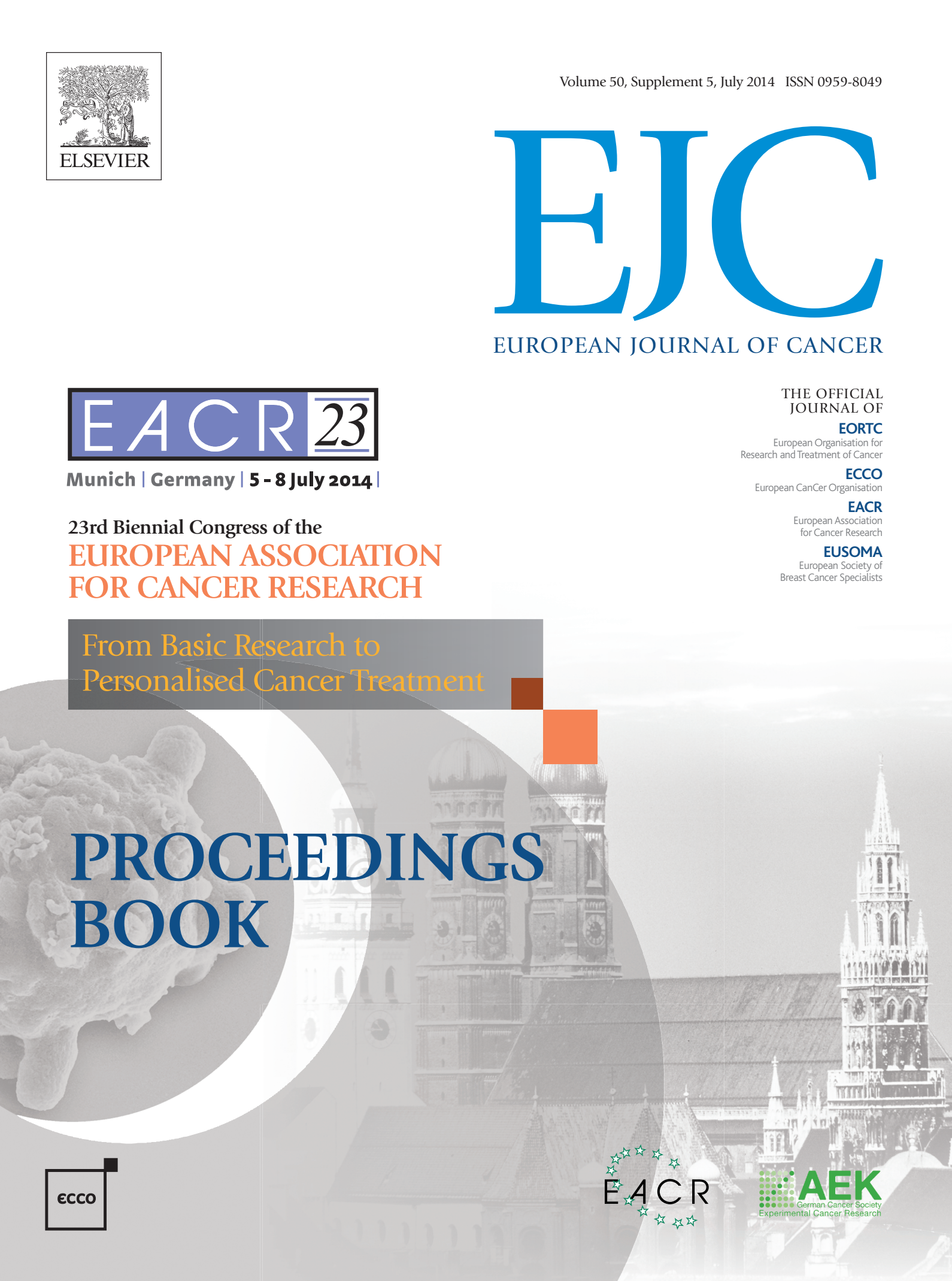
EACR 23

Munich | Germany | 5 - 8 July 2014 |

23rd Biennial Congress of the
EUROPEAN ASSOCIATION FOR CANCER RESEARCH

From Basic Research to Personalised Cancer Treatment

PROCEEDINGS BOOK



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AEK German Cancer Society Experimental Cancer Research

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Letter of Welcome

On behalf of the Executive Scientific Committee, we are pleased to welcome you to Munich for the 23rd Biennial EACR Congress.

We are very pleased that the EACR-23 Congress is actively supported by the German Cancer Society, Experimental Cancer Research (AEK).

EACR congresses are well known for providing a rich and diverse programme. During the next four days EACR-23 will provide a unique opportunity for participants to learn from and meet with leaders in the field of basic and translational research, apply new data to inform practice and ultimately improve patient outcomes.

The Congress will focus on the latest developments in basic and discovery driven translational research, through to personalised precision cancer treatment. Keynote and Award Lectures are complemented with focussed symposia across eighteen topics. The programme will offer exceptional Plenary Lectures, Plenary Symposia with ample time for discussions, Scientific Symposia, Workshops and Oral and Poster presentations.

We are also pleased that the Congress will be held in one of Europe's most lively cities; a city with a leading position in oncology and a remarkable reputation for cancer research and cancer care.

We trust that you will return from the Congress inspired by colleagues from around the world and that you will have made new friends and scientific contacts that will support you in your essential work.

We are delighted to be welcoming you at what promises to be another highly educational, collaborative and successful EACR Congress.

Kind regards,

Professor Moshe Oren
Congress & Scientific Chair

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with TET1 siRNA showed reduction of these mucin mRNAs expression. Thus, it is suggested that the TET1 plays a key role in DNA demethylation to regulate the expression of MUC1 and MUC4.
Conclusion: This is the first report that the TET1 was an important factor for DNA demethylation to regulate the expression of MUC1 and MUC4 in lung cancer. The analysis of the epigenetic changes of *MUC1* and *MUC4* may be useful for diagnosing the carcinogenic risk and predicting outcome of patients.
No conflict of interest.

414 Epigenetic modifications of androgen receptor signaling in castration resistant prostate cancer (CRPC)

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Introduction: Prostate cancer is one of the most common forms of cancer in Turkish and European men. For those patients with late-stage prostate cancer, androgen depletion therapy is current standard treatment. While initially successful, almost all patients eventually develop resistance against this treatment. Once the cancer reaches this advanced, progressive form, it is termed castration resistant prostate cancer (CRPC). Whereas the progression mechanisms of CRPC are poorly understood, it has been shown that in CRPC patients, the androgen receptor (AR) is still active despite undetectable androgen levels. Since AR signaling is important in the progression and growth of prostate cancer, understanding how AR mediated signaling occurs in CRPC is critical to more efficient treatment of this recurrent disease.
Material and Methods: There are several possible causes for this conversion from androgen-sensitive to androgen-independent prostate cancer. Previous work has demonstrated that epigenetic modifiers such as EZH2 and LSD1 can mediate the sensitization of androgen receptor in CRPC. However, only a small subset of epigenetic modifiers has been characterized. To better understand the role of histone modification on CRPC, we conducted a large scale shRNA screen of epigenetic modifying enzymes to identify those genes that prevent androgen-independent growth.
Results and Discussion: From this screen several hit genes have been found that cause a reversion of androgen-independent to androgen-dependent prostate cancer. The shRNA knock-down of these hit genes was confirmed by western blot and qRT-PCR. We are currently characterizing how these epigenetic modifiers affect androgen-receptor mediated signalling.
Conclusion: These results will offer new insight into the role of epigenetic modifiers in nuclear receptor signalling.
No conflict of interest.

415 Telomerase reverse transcriptase promoter mutations in primary cutaneous melanoma

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Introduction: We previously reported a disease segregating causal germline mutation in a melanoma family and recurrent somatic mutations in metastasized tumours from unrelated patients in the core promoter region of the telomerase reverse transcriptase (*TERT*) gene. Here we screen 287 primary cutaneous melanomas to validate the presence of mutations in primary melanoma and to find association, if any, with phenotypic, epidemiologic and clinical features.
Material and Methods: Primary tumours from 287 melanoma patients diagnosed between 2000 and 2012 were retrieved from the biobank of the Instituto Valenciano de Oncologia, Spain. The database contains systematically collected information from patients treated at the institution. Ethical approval for the study and written informed consent from all study patients were obtained. Mutational status of the *TERT* core promoter region (position −27 to −286 from ATG start site), p.600 of *BRAF*, p.61 of *NRAS* and *CDKN2A* was determined by PCR and Sanger sequencing. Further alterations at *CDKN2A* were investigated by Methylation-sensitive multiplex ligation-dependent probe amplification (MS-MLPA). *TERT* expression levels were determined by quantitative real-time PCR using Syber Green and a housekeeping gene as internal standard.
Results and Discussion: Mutations in the *TERT* promoter region were detected in 109 of 287 (37.9%) melanomas, which is higher than the frequency of mutations found in *BRAF* (36.2%). We show that *TERT* promoter mutations associate with increased patient age (>65 years), increased Breslow thickness and tumour ulceration. The mutations are more prevalent at both intermittently and chronically sun-exposed sites than non-exposed sites and tend to co-occur with *BRAF* and *CDKN2A* alterations. *TERT* promoter mutations cause a statistically significant increase in TERT mRNA expression levels. Tumour thickness and ulceration in melanoma have persistently been shown to be markers of poor survival and increased risk of death. The association with parameters generally connected with poor outcome of the disease, coupled with high recurrence and mechanistic relevance, raises the possibility of the eventual use of *TERT* promoter mutations in the disease management.
Conclusion: The *TERT* promoter mutations represent novel genetic alterations with a role in cancer development through alteration of gene expression. Further research will determine usefulness of the *TERT* promoter mutations in the context of melanoma treatment.
No conflict of interest.

416 DNA methylation profiles in invasive breast tumours associate with methylation in lymph node metastases and not in plasma samples

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Background: More than 25% of breast cancer patients develop metastatic disease and its incidence has not decreased over the last 20 years. The regional lymph node metastases presence correlate with the risk of subsequent recurrence at distant sites; therefore, the molecular analysis of metastatic lesions is gradually increasing our understanding of the processes of invasivity and distant spread of breast cancer cells from primary cancers. In the present study DNA methylation changes from primary cancers to metastatic lesions were analysed aiming to metastatic potential evaluation by epigenetic markers.
Material and Method: In our study paraffin embedded tumour tissues and positive lymph nodes, plasma and blood cell samples from 48 patients with invasive breast carcinomas were analysed. The study group consists of 39 patients with ductal and 9 patients with lobular invasive breast cancer in TNM stages from I to IV. DNA methylation levels were quantitatively evaluated in promoters of 11 genes (*APC, ADAM23, CXCL12, ESR1, PGR B, CDH1, RASSF1A, SYK, TIMP3, BRMS1* and *SOCS1)* using bisulfite pyrosequencing. Statistical analyses were performed by SPSS 15.0 software.
Results: Positive correlations between DNA methylation levels of primary tumours and lymph node cancer cells were found in *APC* ($p = 0.000$), *ADAM23* ($p = 0.008$), *CXCL12* ($p = 0.039$), *PGR B* ($p = 0.039$), *RASSF1A* ($p = 0.026$) and *SOCS1* ($p = 0.018$) promoter sequences; however, without higher prevalence in lymph nodes in comparing with primary tumours. No correlations were observed between plasma samples and primary tumours. Moreover, the cumulative methylation profiles of primary tumours and lymph node metastases are very similar in contrast to plasma samples. These cell-free DNAs manifest intermediate spectrum of methylated genes as was shown in genomic and tumour DNA of patients. Methylation levels in tumours and lymph nodes were statistically different between ductal and lobular invasive cancers in *APC*, *CXCL12* and *ADAM23* genes and according to tumour size in *ADAM23* gene.
Conclusions: In present study, we evaluated the DNA methylation status in lymph node metastases and found that methylation profiles which already accumulated in primary cancers could continue in metastatic tumours. The results from plasma samples indicate the simultaneous presence of methylation profiles from tumour and genomic DNA originated from physiological degradation processes that could decline the tumour specificity of analyses.
This study was supported by the Slovak Research and Development Agency under the contract No. APVV-0076−10, Research and Development Operational Programme (ERDF), contract No. 26240220058, Scientific Grant Agency, contracts No. 2/0120/13 and No. 2/0169/14 and RFL2010 programme founded by the Slovak Cancer Research Foundation.
No conflict of interest.

417 Visualization of tumor formation in the WAP-TGFa/FGFR4Arg385 KI breast cancer mouse model

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Introduction: The FGFR4 (fibroblast growth factor receptor 4) gene occurs with a single nucleotide polymorphism (SNP) (50% of the kaukasian population) that converts a Glycine to an Arginine at codon 388 (murine 385). The FGFR4Arg388 allele is an 'oncogene enhancer' of breast cancer *in vivo* and is further correlated with the enhanced progression of other cancer types in humans.