regions as key members of the tanning process, targeting gene expression up-regulation of numerous pigmentation genes following UV-irradiation (2-3).

A combination of in vivo and in vitro experiments, including among others DNA-binding assays (ChIP, Band-shift) and gene expression experiments (Luc-assay, real-time PCR), using human keratinocytes (HaCaT), and a melanoma cell line (501mel) allowed us to identify a new USF-target. It is a member of the DNA-repair machinery that proved to be up-regulated following UV-radiation in a USF dependant manner.

Our data implicate for the first time the USF family in the DNA-repair process following UV-irradiation, giving new insights in understanding the complex function of USF in response to UV-stimulation.

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PF-4 causes down-regulation of PPAR gamma and increase formation of aggressive phenotype of MNU-treated breast cancer

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AIMS: To examine the effect of anti-angiogenic agent platelet factor-4 (PF-4) on the expressions of nitric oxide syntase (NOS), hypoxia-inducible factor-1alpha (HIF-1α) and peroxisome proliferator-activated receptor gamma (PPAR gamma) of methylnitrosourea (MNU)-treated rat mammary carcinoma. METHODS AND RESULTS: Breast carcinomas in Sprague-Dawley rats were induced by injecting intraperitoneally 70mg of MNU per body weight. The rats were divided into control group and PF-4 group where intratumoral injection of 10μg of PF-4 was given when the tumour size reached 1.2± 0.5cm. All the rats were sacrificed when the tumour in the control group reached 1.6 ± 0.5cm. Immunohistochemistry was performed to analyse the expression of NOS, HIF-1α and PPAR gamma in the tumour cells. Tumours injected with PF-4 showed a dramatic reduction in size compared to the control group. Histological study of the tumours in the control group showed cribriform (45%) and papillary (55%) type of breast carcinoma. In the PF-4 group, the phenotypes were cribriform (25%), papillary (63%) and diffuse infiltrating ductal carcinoma, no special type (12%). Necrosis is more prominent than in the control group. Positive expressions of NOS, HIF-1α and PPAR gamma in the control group were 100%, 100% and 91% respectively. In the PF-4 group, positive expressions of NOS, HIF-1α and PPAR gamma were 100%, 92% and 17% respectively. There was marked reduction of PPAR gamma expression in PF-4 treated group compared to the control group and this was statistically significant ($p < 0.001$). This trend was also observed in the intratumoural blood vessels. CONCLUSION: These results indicate the negative impact of PF-4 on the PPAR gamma and increase in the the number of aggressive type of breast carcinoma due to the anti-angiogenic activity of PF-4. It is possible that aggressive subclones developed from the suppression of blood vessels and PPAR gamma. Further study is needed to elucidate the mechanisms.

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BRAF-induced papillary thyroid carcinoma – validation of microarray data

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Background: Papillary thyroid carcinoma, constituting 80% of all types of thyroid carcinomas, in most cases is effectively treated with the thyreidectomy combined with the radiotherapy. However there are PTC cases with poor prognosis which do not exhibit radioiodine sensitivity and dedifferentiate to anaplastic carcinomas. The recent findings suggest correlation between the aggressiveness of the PTC and the presence of the BRAF mutation V600E and the study of Giordano et al (2005) indicated the significant differences in gene expression profile of between PTCs harboring different initiating mutations.

The purpose of the study was the analysis of differences in gene expression profile of BRAF-positive and RET/PTC-positive PTCs and validation of microarray data using the real time QPCR.

Methods: A meta-analysis of joint sets of 39 our papillary thyroid carcinomas and 51 PTC cases analyzed by Giordano et al. was performed. Two-class comparison (PTCs with RET/PTC rearrangements vs PTCs with BRAF mutation) was carried out and genes with univariate significance level lower than p=0.001 were selected. The verification of the selected genes was carried out on an independent group of 58 PTCs (among them 27 are BRAF-positive) by quantitative real-time PCR.

Results: 3383 probesets were differentially expressed between PTCs with RET/PTC rearrangements and BRAF mutation. Nine genes were selected to be validated: BRAF, IGF1, MAP2K1, MAPK14, MAPK1, PGF, PHLDA1, TM7SF4.

TM7SF4, with high significance in microarray data was strongly over-expressed in PTCs with V600E BRAF mutation ($p<0.001$). BRAF gene was up-regulated in BRAF(+) PTCs, but the dispersion of the results was higher ($p=0.0346$). Remaining three genes were down-regulated in BRAF-positive tumors: IGF1 ($p=0.000018$), PGF ($p=0.000257$), PHLDA1 ($p=0.0051$). For MAP2K1, MAPK14, MAPK1 genes we noted no significant difference ($p>0.06$).

Conclusions: There are distinct differences between BRAF-positive PTCs and BRAF-negative cases in gene expression profile. The function of selected genes is still to be investigated. The diminished expression of PHLDA1 may contribute to IGF-1 induced apoptosis while TM7SF4 may take part in antigen presentation by dendritic cells, thus, influence the immune response to PTC.

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Gene expression profile of follicular thyroid tumors

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Background: Morphological differences between thyroid benign lesions — follicular adenomas (FA) and malignant follicular carcinomas (FTC) are based only on the cellular invasion features. Genomic approaches have been undertaken to determine the genes relevant for differences in biology of these tumors, which may be also of utmost diagnostic importance. The aim of the study was to compare gene expression profiles of FTC and FA.

Material and Methods: We applied high density oligonucleotide microarrays (HG-U133A, Affymetrix). We included 22 follicular tumors from our own collection (10 malignant and 12 benign) and compared them both to the gene expression profile of other benign and malignant thyroid tumors, analyzed by us (in total approx. 100 specimens) as well as to published microarray study by Weber et al. (JCEM 2005).

We use bioinformatic techniques based both on unsupervised (SVD – Singular Value Decomposition) and supervised approach.

Results: When the genetic distance between the different types of thyroid tumors is evaluated by the number of genes with significantly changed expression, the difference between follicular adenomas and carcinoma is much smaller by each of the tests applied (290 significant genes, combined our and Weber's dataset) than the distance to other benign/malignant thyroid tumors. Some of the genes differentiating FA and FTC, obtained in our analysis were previously described, among them FOXO1A (forkhead box O1A, rhabdomyosarcoma) and LARP1 (La ribonucleoprotein domain family, member 1). Our attention was focused on sigificant changes within the genes related to MAP kinase regulation by dual specificity phosphatases, especially dipeptidylpeptidase 8, down-regulated at FDR 0.5% in FTC. Class prediction analysis allowed to properly classify 13 of 14 follicular tumors by 150 gene set (cross-validation approach).

Conclusion: Gene expression profiling reveals important differences between transcriptome of benign and malignant follicular thyroid tumors

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Capside proteins (L1 and L2) of human papillomavirus type 16 not increase the expression of costimulatory molecules and HLA-DR on dendritic cells

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Background: In order to evaluate the effect of Human Papillomavirus type 16 (HPV) capside proteins (L1 and L2) on the expression of costimulatory molecules, CD11c+ DR+ dendritic cells (DCs) were infected with lentiviral vectors expressing GFP-L1 or GFP-L2, and then CD80 + CD86 and