12.0. Analysis was performed based on an unsupervised hierarchical clustering model and discriminatory microRNAs were validated by qRT-PCR.
Results: We identified a 9 microRNA signature that discriminated between ABC- and GC-like DLBCL. This included 3 newly identified microRNAs, not previously associated with DLBCL and predicted to target genes that are de-regulated in lymphoma. DLBCL was distinguished from FL by 4 microRNAs and a total of 18 microRNAs were identified that differentiated between all lymphoma and control populations. Most of the discriminatory microRNAs have been reported before to belong to known oncomiRs or act as tumour suppressors.
Conclusions: In conclusion, the present study identified a microRNA signature that correctly classified GC and ABC phenotypes in DLBCL cell lines. The numbers of microRNAs identified within each signature are manageable for potential use in a clinical setting. This signature has yet to be assessed for prediction in clinical samples. Such studies would be of great value in assessing the potential of microRNAs as biomarkers or therapeutic targets.

772 Nuclear factor kappa B expression and flowcytometric DNA analysis in Egyptian endometrial carcinoma and hyperplasia

A. Raafat[1], N. Asaad[2], A. Bahnassy[1], Z. Al Akabawy[2], M. Abdel Wahed[2]. [1]*National Cancer Institute, Pathology, Cairo, Egypt*, [2]*Faculty of Medicine, Pathology, Menoufia, Egypt*

Background: Endometrial carcinoma is an estrogen-related common tumour, developing most probably on top of atypical endometrial hyperplasia. Inhibition of apoptosis may be a cause of tumour development prolonging cellular life-span, thus allowing accumulation of other genetic alterations. NF-kappa B is a transcription factor that may inhibit apoptosis, thus may share in tumourigenesis. Quantitative evaluation of cellular DNA (ploidy) and cell cycle kinetics (S phase fraction) are also helpful prognostic factors in human neoplasms. DNA aneuploidy in endometrial cancer identifies high risk cases, and correlates with poor survival rate, which may have an impact on clinical management of these cases. This study aimed to evaluate the role of NF-kappa B expression in the development and progression of endometrial carcinoma. Also, it determined DNA ploidy and cell cycle kinetics by measuring SPF using flowcytometry (FCM).
Material and Methods: This study investigated 72 cases of endometrial biopsies, including normal cycling endometrium in the proliferative phase, hyperplastic and adenocarcinomatous endometrium. Immunostaining for NF-Kappa B expression was done using the streptavidin-biotin-peroxidase technique. Flowcytometric studies were done by a modified Hedley method, results presented as DNA distribution histograms.
Results: NF-kappa B nuclear expression was significantly different in malignant and non malignant tissues ($P = 0.048$), also cytoplasmic expression was significantly descending from malignant to proliferative endometrial tissues passing through hyperplasia ($P = 0.000$). There was a negative correlation between both nuclear ($p < 0.01$) and cytoplasmic staining of NF-kappa B and apoptotic index ($p < 0.001$). A significant positive relation was found between both nuclear ($p < 0.05$) and cytoplasmic stains ($p < 0.05$) and mitotic index. There was a statistically significant difference regarding ploidy satus between the 3 studied groups (neoplastic vs normal $p = 0.001$, neoplastic vs hyperplastic $p = 0.014$, hyperplastic vs normal endometrium $p = 0.043$). There was a significant correlation between increased expression of NF-kappa B and both aneuploidy and high SPF.
Conclusions: NF-kappaB plays an important antiapoptotic role in the endometrium and could play a role in tumour progression. Flowcytometric evaluation of DNA ploidy and SPF allow a more precise definition of high risk groups in endometrial cancer cases.

773 MicroRNA expression analysis in human lymphoma/leukemia cells

K. Nemes[1], A. Márk[2], M. Hajdu[2], T. Sticz[2], G. Csorba[2], L. Kopper[2], M. Csóka[3], A. Sebestyén[2]. [1]*Semmelweis University, 2nd Department of Paediatrics and 1st Department of Pathology and Experimental Cancer Research, Budapest, Hungary*, [2]*Semmelweis University, 1st Department of Pathology and Experimental Cancer Research, Budapest, Hungary,* [3]*Semmelweis University, 2nd Department of Paediatrics, Budapest, Hungary*

Background: MiRNAs are small non-coding RNAs that regulate post-transcriptional gene expression, probably by inhibiting protein translation. In recent years more and more studies have described changes of miRNA expression levels in different types of human neoplasia and their role in cancer development, and progression. The aim of our study was to determine the expression of miRNAs in human lymphomas and leukemias.
Materials and Methods: Human lymphoma/leukemia cell lines (BHD1, Nalm6, Mn60, KMH2, Jurkat, HL60, Raji, Ramos, BJAB, Daudi) were culture according to standard methods. Acute lymphoblastic leukemia (ALL) cells were isolated from the bone marrow of paediatric ALL patients by Ficoll gradient centrifugation. MiRNAs were isolated by miR Vana TM miRNA Isolation Kit, and cDNA was reverse transcribed with the TaqMan MicroRNA Reverse Transcription Kit. MiRNA expression was determined with real-time PCR using TaqMAn micro-RNA Assays (miR21, miR24, miR155, miR16, miR128b, miR142−3p, miR29b, miR223). Values were normalized to normal B- and T-cells.
Results: In the present study, the expression level of different miRNAs was analyzed in human lymphoma/leukemia cell lines, T- and B-cells, and in childhood ALL bone marrow cells. MiRNA 21 – known to be oncogenic (onco-miR) – was expressed in nearly all examined cell lines. The onco-miR 155 was overexpressed in 20% of lymphoma/leukemia cell lines. MiRNA 128b was overexpressed in all cell lines, but extremely high values were measured in Jurkat (T-ALL) and Nalm6 (B-ALL) cell lines.
Conclusions: In this study, the presence of several miRNAs was confirmed in human lymphoma/leukemia cell lines and in ALL cells. Our results suggest that different hematological malignancies have distinct miRNA expression profiles. Increasing knowledge of miRNA expression signatures may help characterize tumour subtypes, predict prognosis, and identify their regulatory role in cellular processes.
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774 WNT5A acts as an oncogene in EBV-associated nasopharyngeal carcinoma

L.F. Yap[1], A. Munirah[2], M.M. Zabidi[1], S.J. Chai[1], T.L. Chu[2], S.K. Tan[2], W. Wei[3], P.G. Murray[3], S.H. Teo[1], A.S.B. Khoo[2]. [1]*Cancer Research Initiatives Foundation, NPC Research Group, Subang Jaya, Malaysia,* [2]*Institute for Medical Research, Molecular Pathology Unit, Kuala Lumpur, Malaysia,* [3]*University of Birmingham, CRUK Institute for Cancer Studies, Birmingham, United Kingdom*

Nasopharyngeal carcinoma (NPC) is an Epstein–Barr Virus (EBV)-associated cancer which is particularly prevalent in Southern China and Southeast Asia. In Malaysia, NPC is the fifth most common cancer overall and third common in men. Over 70% of cases present with late stage disease and the 5-year survival rates are less than 50%. Novel therapeutic approaches to manage this disease are urgently required. Using expression microarrays, we identified the Wnt5a gene as being overexpressed in primary NPC tissue samples relative to cancer-free controls. Further, comparison with a published microarray study using 36 normal human organs revealed that the level of Wnt5a mRNA in NPC is significantly higher than in a wide range of normal organs. Wnt5a is one of the most highly studied Wnts which acts primarily through the non-canonical pathway. With respect to cancer biology, there is conflicting evidence whether Wnt5a has a tumour-promoting or -suppressing role, and its role in NPC has never been investigated. The upregulation of Wnt5a was validated in 12 NPC tissue samples by quantitative PCR, and its low expression level was confirmed in 16 normal human organs by RT-PCR. In NPC cell lines, however, the expression of Wnt5a was heterogenous. Nonetheless, a dramatic increase in the Wnt5a expression was shown in the only EBV-positive line, C666.1, suggesting a potential role of EBV in regulating the expression of Wnt5a. This data is also in accordance to our preliminary microarray data that in vitro infection of an EBV-negative NPC cell line with a recombinant EBV or individual EBV genes resulted in the upregulation of Wnt5a. In addition, we assessed the functional role of elevated Wnt5A on tumour cell behaviour in vitro. Ectopic expression of Wnt5a in NPC cell lines significantly promotes cell proliferation, migration and invasion. Taken together, Wnt5a appears to function as an oncogene in NPC, and its overexpression might be regulated by EBV. These data suggest that Wnt5a could be a useful therapeutic molecular target for NPC.

775 Plant phenols modulate JNK activity in mouse epidermis: the effect on transcription factors AP-1 and STAT

M. Cichocki[1], M. Dalek[1], W. Baer-Dubowska[1]. [1]*Poznan University of Medical Sciences, Pharmaceutical Biochemistry, Poznan, Poland*

The modulation of signaling pathways induced by tumour promoters is involved in early stage of cancer development. This includes the stimulation of protein kinases such as c-Jun N-terminal kinase (JNK). JNK is involved in activation of MAPK/AP-1 signaling pathway, responsible for regulation of inflammatory response, cell proliferation and death. Some data indicate that JNK may be also involved in activation of other transcription factors, such as STAT family (Signal Transducers and Activators of Transcription). AP-1, STAT, and JNK are considered as potential targets for chemoprevention and/or chemotherapy. Our previous study showed that both transcription factors are activated in mouse epidermis 2−4 hours after treatment with tumour promoter 12-*O*-tetradecanoylphorbol-13-acetate (TPA). In this study we assessed the effects of naturally occurring plant phenolic acids, protocatechuic (PCA), tannic (TAA), and chlorogenic acid (CHA) on TPA stimulated JNK activity in mouse epidermis, and the activation of AP-1 and STAT.
Animals were treated with a single dose (10 nmol/mice) of TPA or acetone (control group). Phenolic compounds (16 μmol/mice) were applied 15 min before TPA treatment. Mice were killed at selected time points and