reduces *WWOX* expression both in hetero and homozygous cases. There was a positive correlation between expression level of *WWOX* and marker of proliferation *Ki67* ($R_s = 0.5440$; $p < 0.0001$), antiapoptotic gene *Bcl2* ($R_s = 0.7092$; $p < 0.0001$) and *JM-a* isoform of *ErbB4* mRNA level ($R_s = 0.7102$; $p < 0.0001$).
Conclusions: Our results suggest that loss of heterozygosity (relatively frequent in GBM) along with promoter methylation may decrease the *WWOX* tumour suppressor expression. We also confirmed that *WWOX* is correlated with *ErbB4* signalling pathway as well as with proliferation and apoptosis in glioblastoma multiforme.

739 Altered expression of miR-205 affects cell proliferation in human cervical cancer

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Background: Cervical cancer is the second most common malignancy of women worldwide. Recently, aberrant miRNA expression has been demonstrated in human cervical cancer, however the functional role of miRNAs in cervical cancer remains unclear. We previously observed a significant over-expression of *miR-205* in human cervical cancer tissues as compared to their matched normal cervical tissues in a sequencing-based miRNA profiling analysis. In this study, we further explore the role of *miR-205* in cervical cancer.
Materials and Methods: We evaluated the expression of *miR-205* in 29 matched pairs of human cervical cancer and normal tissues, as well as eight cervical cancer cell lines using quantitative PCR analysis. To investigate the functional consequences of altered *miR-205* expression in cervical cancer cells, we determined the effect of *miR-205* on cell proliferation in cervical cancer cell lines using a *miR-205* specific mimic or inhibitor. Cell proliferation was measured by WST-1 (water-soluble tetrazolium salt) assay.
Results: We observed significant over-expression of *miR-205* in cervical cancer samples ($p = 0.0052$), as compared to their matched normal counterparts. Over-expressing of *miR-205* in HeLa and SW756 cells, the two cell lines with no detectable or low level of endogenous *miR-205* expression, resulted in significant increase in cell proliferation in both cell lines as compared to the negative control (treated with a non-targeting sequence pre-miR molecule). As a complement to the over-expression experiments, we suppressed endogenous *miR-205* expression in CaSki cells using a miRNA inhibitor, which cell line has a high-level of endogenous *miR-205* expression; which resulted in inhibition of cell proliferaion.
Conclusions: Over-expression of *miR-205* is frequently observed in human cervical cancer, and its dysregulation can alter cell proliferation in cervical cancer cell lines. Our findings provide new insight into the role of *miR-205* in cervical cancer, which may have potential value for clinical diagnosis and therapeutics.

740 Role of the tumour suppressor FOXO3a and its regulation by β-catenin in the pathogenesis of non-Hodgkin's Lymphomas

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Background: Non-Hodgkin's Lymphomas (NHL) are a heterogeneous group of aggressive haematological malignancies with high incidence. This group of tumours is characterized by molecular alterations in cellular processes such as cell cycle regulation and apoptosis in which FOXO3a is involved. The aims of this study are: 1) to evaluate the role of FOXO3a and its regulation by β-catenin in the pathogenesis of NHL; 2) to study its role as a functional target of therapeutic agents.
Materials and Methods: A panel of NHL cell lines was used. Cells were treated with different inhibitors of the PI3K/AKT/FOXO3a pathway (LY294002, Rapamycin, Triciribine and Psammaplysene) and the Wnt/APC/β-catenin pathway (Quercetin) for further analysis. Conventional drugs such as Doxorubicin were also used. Cell viability (Cell Titer-Glo Luminiscent assay kit) and cell cycle analysis (FACS) were performed. Expression and cellular localization of different proteins were studied by means of Western Blot, quantitative PCR and immunocytochemistry.
Results: The role of FOXO3a in a panel of non-Hodgkin's lymphomas has been evaluated. Cells lacking FOXO3a expression are resistant to inhibition of the PI3K/AKT pathway. On the contrary, cells expressing FOXO3a are capable of inducing cell death and apoptosis after PI3K/AKT inhibition, suggesting that FOXO3a inactivation has a role in lymphomagenesis. Moreover, β-catenin, a well known oncogene, is constitutively activated in these cells and interacts with FOXO3a.
Conclusions: The reactivation of FOXO3a and the suppression of β-catenin activity represent a potential therapy for NHL that could enhance the effects of conventional drugs.

741 microRNA-34 expression and the status of TP53 in the primary ovarian cancer

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Background: Changes in TP53 and TP53-dependent pathways are critically important for the pathogenesis of ovarian cancer and seem to determine treatment response. TP53 is known to directly transactivate a set of microRNAs (miRNAs), including miRNA-34 family. The role of TP53-regulated miRNAs in ovarian cancer biology has not been characterised. We aimed to reveal the impact of *TP53* status on the expression of a family of miRNA-34 in ovarian cancer tumours.
Material and Methods: Post-surgical tumour samples from ovarian cancer patients were characterised histopathologically and with regard to the *TP53* status, including differentiation between missense and nonsense mutation as well as to TP53 protein accumulation. Samples were divided into the following groups: low grade carcinomas with the wild-type *TP53* ($n = 7$), high grade carcinomas with wild-type *TP53* ($n = 13$) and carcinomas with the determined types of *TP53* alterations ($n = 23$). Samples containing a minimum of 75% of cancer cells were subjected to miRNA-34a/b/c expression analyses, with the use of TaqMan MicroRNA Assays. Small nuclear RNA, RNU6B (Applied Biosystems) was used to normalise data.
Results: In all series of the samples, a considerable number of ovarian cancer samples showed elevated levels of expression of miRNA-34 family members. Samples with *TP53* mutations presented higher levels of microRNA-34b expression than those with wild-type *TP53*.
Conclusions: (1) Elevated levels of miRNA-34 family members in some ovarian cancer tumours suggest that these TP53-regulated microRNAs may present other roles than tumour suppressors, contradictory to some other cancers, where miRNA-34, has been reported to be downregulated. The miRNA-34 functions apparently depend on the molecular context, tissue type and/or clinical characteristics of a disease. (2) An increase in the miRNA-34b expression in ovarian cancer cells with mutated *TP53* suggests that there are TP53-independent mechanisms of miR-34 regulation.

742 MicroRNAs in the differential diagnosis of aggressive B-cell lymphomas

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Background: Fast and reliable differentiation of Burkitt's lymphoma (BL) *vs* diffuse large B-cell lymphoma (DLBCL) is of major importance for therapeutic decisions, as BL and DLBCL patients need to be treated differently, and in BL, once the diagnosis is established, treatment should be initiated promptly. However, a clear-cut diagnosis between the two malignancies is difficult as some aggressive B-cell lymphomas do not meet the criteria of BL or DLBCL. We aimed to investigate miR-155, miR-21 and miR-26a, as potential biomarkers for the differential diagnosis of BL *vs* DLBCL.
Material and Methods: Fresh ($n = 44$), fine-needle tumour biopsies and formalin fixed paraffin-embedded (FFPE) tumour samples ($n = 5$) from patients with adult BL, DLBCL and intermediate BL/DLBCL were examined. Samples were characterised according to the recent WHO recommendations (2008). miRNAs were measured using TaqMan microRNA assays (Applied Biosystems), with RNU6B as a reference gene. Normal peripheral blood mononuclear cells were used as a calibrator sample. Ten patients' sera were assessed for miR-155 and miR-26a. Expression of the miR-155 precursor, *BIC*, was estimated in 22 samples.
Results: In adult DLBCL miR-155 was significantly higher than in BL and intermediate BL/DLBCL, where it was either absent or very low. In BL and BL/DLBCL also *BIC* expression was very low. So far, we showed no differences in miR-26a expression between DLBCL and BL and a bit higher miR-21 expression level in DLBCL than in BL. FFPE samples were shown to be acceptable as a material to assess microRNA expression.
Conclusions: (1) The expression level of miR-155 differentiates BL from DLBCL, but not BL from intermediate BL/DLBCL. miR-155 assessment may be an additional method of choice for routine differential diagnosis of BL *vs* DLBCL. (2) Low levels of miR-155 expression in BL seem to relate to low/absent transcription of *BIC*, the miR-155 precursor, and not to the alterations in the miRNA-155 biogenesis. (3) The value of miR-21 as a biomarker deserves further studies; miR-26a seems to have no diagnostic value. (4) Supplementing immunophenotype and cytogenetic data in aggressive B-cell lymphomas by microRNA measurements may provide new insights in the pathogenesis of these diseases.