Results: Both malignancies showed high HDAC1 expression ranging from 38.7% in DLBCL to 59.2% in CTCL (P = 0.10). Almost all samples (97%) showed moderate or high level of HDAC2 expression. High HDAC2 expression ranged from 31.2% in CTCL to 60.6% in DLBCL (P < 0.0001). In total, 21 CTCL showed high HDAC2 expression. These included 12 of 17 cases with aggressive histology or phenotype. HDAC6 showed low to moderate level of expression in both lymphomas. Low level of HDAC6 was observed in 29.4% of DLBCL and 30.7% of CTCL (P = 0.89). High level of acetylated H4 was more common in DLBCL (35.3%) compared to CTCL (14.3%) (P = 0.02). Furthermore, high H4 acetylation seemed to be more common in DLBCL belonging to the activated B-cell like (ABC) category (42.1%, 8 of 19) than in the less aggressive germinal center B-cell (GCB) type (10%, 1 of 10) (P = 0.12).
Conclusion: The prevalence of HDAC2 expression in both malignancies, and particularly in the more aggressive phenotypes of CTCL, suggest a possible involvement of HDAC2 in the development of malignant lymphomas. The low level of H4 acetylation in CTCL might be encouraging as a possible biomarker for HDACi response. These observations should however be validated in prospective studies.

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Hypermethylation induced SPARC, TIMP-3 and PENK down-regulation in endometrial cancer

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Background: Endometrial cancer remains the leading cause of gynecological cancer. This study was to investigate the genes down-regulated in the endometrial cancer.
Methods: Initially, we performed a genome-wide analysis of gene expression in a set of 55 sporadic endometrioid endometrial adenocarcinomas and compare this to 29 normal endometrium controls using microdissection and high density oligonucleotide microarray. To identify signaling pathways that are associated with cervical tumorigenesis, microarray expression data were imported into a PathwayAssist software. We further measured methylation of the three genes using methylation-specific polymerase chain reaction (MSP-PCR) in a total of 76 endometrioid endometrial cancers
Results: We obtained a dominant signaling pathway in which 25 genes were coordinately regulated in endometrial cancer. These genes encode for proteins that are part of a signaling pathway associated with cell cycle progression and invasion. Of the 25 genes, SPARC (5q31.3−q32), TIMP-3 (22q12.1−12.3) and PENK (8q23−q24) were down-regulated in cancer for 2.9-fold, 3.48-fold and 3.12-fold, respectively, when compared to normal. The results showed hypermethylation of SPARC, TIMP-3 and PENK in 99%, 25% and 95% of these cancers, respectively. Furthermore, we found the hypermethylation of TIMP-3 was correlated to clinical stage of the tumors and total survival of the patients.
Conclusions: The results obtained from this study indicate that hypermethylation induced down-regulation of SPARC, TIMP-3 and PENK might be related to the development and progression of endometrioid endometrial cancer. Demethylation and reactivation of the three genes may be as an adjunct therapy for the endometrial cancer.
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Secreted frizzled-related protein 4 inhibits proliferation and metastatic potential in prostate cancer

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Background: Activation of the Wnt signaling pathway is implicated in aberrant cellular proliferation in a variety of cancers. In prostate cancer, Wnt 3A signaling promotes cell growth through an androgen-dependent interaction with downstream beta-catenin signaling. Secreted Frizzled-Related Protein 4 (sFRP4) inhibits Wnt signaling by binding and sequestering the Wnt ligand. Our group has already demonstrated that increased expression of membranous sFRP4 predicts for a good prognosis in localized prostate cancer. Thus the aim of this project was to investigate the phenotype of sFRP4 overexpression in androgen-dependent and androgen-independent prostate cancer models.
Material and Methods: sFRP4-overexpressing androgen-dependent (LNCaP) and androgen-independent (PC3) prostate cancer models were established *in vitro*. Changes in proliferation and metastatic potential were assessed using Cell Titer 96® system, soft agar assays and matrigel invasion chambers. Immunofluorescence and immunohistochemistry were used to identify changes in adhesion molecules *in vitro* and *in vivo* respectively.
Results: sFRP4 overexpression in both cell line models results in a morphologic change to a more epithelioid cell type with increased membranous beta-catenin and cadherins (E-cadherin in LNCaP, N-cadherin in PC3) resulting in more adhesions between cells. Functionally, sFRP4 overexpression is associated with a decreased rate of proliferation (p = 0.0002) and decreased anchorage-independent growth in both systems (p < 0.0001) and decreased invasiveness of PC3 cells (p < 0.0001). Furthermore, in human localized prostate cancer (n = 224) increased membranous sFRP4 expression is associated with increased membranous beta-catenin expression (p = 0.02).
Conclusions: These data suggest that sFRP4 is an inhibitor of prostate cancer growth and metastasis independent of hormonal status with correlative evidence in human disease. Consequently, sFRP4 is a potential new therapeutic target for androgen-independent prostate cancer.

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The significance of Pyk2 in hepatocellular carcinoma invasiveness

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Background and Objective: Our previous study showed that proline rich tyrosine kinase (Pyk2) is over-expressed in tumor tissues as compared to their adjacent non-tumor tissue. Statistical analysis suggests that this over-expression is significantly correlated with tumor growth and venous invasion. Over-expression of Pyk2 is also significantly correlated with shorter overall and disease-free survival. However, the precise mechanism of Pyk2 on tumor invasiveness is still unclear due to the limited reports. In the current study, we aim to investigate the role of Pyk2 on the invasiveness of hepatocellular carcinoma cells by both *in vitro* functional study and *in vivo* animal models.
Materials and Methods: In the *in vitro* study, plasmids containing the full length or dominant negative form of Pyk2 was transfected into HCC cell line (PLC). After selection with antibiotics (G418), stable clones with the expression of full length or dominant negative form of Pyk2 was isolated. The invasiveness was compared according to their ability to adhere to the extracellular matrix, colony formation assay and wound healing assay. The mechanism of the Pyk2 signaling was investigated by western blotting and immunoprecipipation assay.
In vivo tumor models were done in athymic nude mice. Tumors produced from the different transfectants were implantanted into the liver of the mice. After 48 days the mice were sacrificed and tissue samples were collected. Tumor growth pattern including invasiveness was examined by H&E staining. Tumor cell proliferation (Ki67) and apoptosis (TUNEL) were compared among the groups of mice with liver tumor from different transfectants.
Results: The full length Pyk2 transfectant possessed the highest cell motility as compared to the vector control and C-terminal transfectants by wound healing assay. Pyk2 full length transfectant also presented significantly stronger adhesiveness towards collagen I, fibronectin and laminin by adhesion assay. It promoted the anchorage-independent growth as well as the anchorage dependent growth by the soft agar assay and colony formation assay. Western blotting and co-precipipation assays indicated that Pyk2 forms a signaling complex with c-Src. Phosphorylation of c-Src, MEK and ERK 1/2 were up-regulated in full length Pyk2 transfectants as compared to the vector control and C-terminal transfectants.
The tumors from the full length Pyk2 transfectants got the highest incidence of Ki67 positive staining tumor cells and least apoptotic cells as compared to empty vector control and C-terminal transfectants.
Conclusion: Over-expression of Pyk2 may contribute to an invasive phenotype of HCC.

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Peroxiredoxin II protects cancer cells in a way of proteasome inhibition

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Background: Peroxiredoxin II, a cytosolic isotype of human 2-Cys peroxiredoxin(Prx), can behave either as a peroxidase or as a molecular