this strategy, we intend to enhance the efficiency of cancer therapies, and cover up possible resistance to individual treatments. Studies are in progress to assess the in vitro efficacy of these combined treatments. In parallel, we perform preclinical trials to investigate the importance of these mechanisms for tumor formation and metastasis in vivo. The efficacy of these treatments is first investigated in chicken metastasis assays. Besides, we have generated transgenic mice over-expressing Met in a temporally and spatially regulated manner. Met-overexpressing cells also express the luciferase, for non-invasive monitoring of primary tumours and metastasis. These mice are precious tools to better understand Met-triggered tumorigenesis and validate the efficiency of combined treatment to un-favour cell survival in Met-triggered cancers.

Altogether, by targetting Met activity and its downstream survival signals, we will elucidate the efficacy of novel combined anticancer therapies.

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A standardized approach to animal study data collection, analysis and management practices expands possibilities for the sharing of results

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The lack of data digitization and a standardized approach to data collection, analysis, content, format and storage conventions makes animal study (AS) data access and cross-study comparisons impractical within and across research organizations. Current methods of AS data collection, analysis and management for animal studies in oncology are highly variable and primarily manually-based, using combinations of paper notebooks and electronic spreadsheets. As a consequence, data cannot be accessed and shared effectively because: 1) data recorded in lab notebooks remain un-indexed and inaccessible once collected; 2) spreadsheets often contain only primary measurement data and are stored in data silos, 3) AS conditions, methods and model details are recorded inconsistently, in insufficient detail, and reside in multiple locations and formats. The unintended consequence is a systematic, unintentional, and yet preventable waste of data, information, organizational knowledge, time and resources. Continued improvements in in vivo modeling result in an ever-increasing amount of information which is becoming increasingly difficult to manage. A growing number of scientists are finding that commercial AS management software applications provide a standardized approach to managing this information which reflects industry-wide best practices. These software systems also improve process efficiency, data integrity and security, and data accessibility as well as increase the transparency of study data and processes, facilitate personnel oversight, IACUC compliance, and inter-study comparability. Standardization of data into a single, digital form would enable the creation of a centralized, web-based study repository for the voluntary sharing and pooling of AS data from many labs, which would give investigators, journals, and institutions the opportunity to publish their both negative and positive non-proprietary results. By having the details on historical studies available, researchers could obviate needless repetition of studies, reduce the number of animals used, expedite model implementation projects, refine current animal models and build on existing work. The net result would be a significant improvement in information sharing, much more efficient use of limited research resources and ultimately a decreased time to identify, develop and market new therapeutics for cancer.

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ZNF23 induces apoptosis in human ovarian cancer cells

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The Krupple-associated box-containing zinc finger proteins (KRAB-ZFPs) constitute one of the largest families of transcription factors. Some members of this family play critical roles in regulation of development, cell proliferation and apoptosis. Many KRAB-ZFPs are implicated in malignancies. Previously, we cloned and characterized ZNF23, which was a member of this family. Its gene localized to the 16q22, a chromosomal region frequently altered in solid tumors. ZNF23 expression was reduced in human cancers and ectopic expression of ZNF23 inhibited cell growth by inducing cell cycle arrest. Here we showed that in ovarian cancer cells, ZNF23 expression also induced apoptosis. The protein level of ZNF23 was greatly down-regulated in 20 samples of ovarian tumors compared with that in 13 samples of normal ovarian tissues. In ovarian cancer cell line SKOV-3, restoration of ZNF23 expression led to apoptosis as demonstrated by activation of caspase-3, nuclear condensation and formation of a sub-G1 peak. This apoptotic process was accompanied by loss of mitochondrial membrane potential, cytochrome c release and caspase-9 activation. Furthermore, ZNF23-induced apoptosis was partially through down-regulation of Bcl-XL. Thus, our study suggested that ZNF23 also played an important role in the induction of apoptotic cell death, and pointed to the possibility that its down-regulation might render ovarian cancers to an increased survival capacity.

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Endothelial cell KIT expression in pediatric brain tumors

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Background: Receptor tyrosine kinases expressed in vascular endothelial cells are potential targets for therapy with tyrosine kinase inhibitors. KIT (receptor of the stem cell factor, SCF) has recently been found in tumor vessel endothelial cells of glioblastomas. It is not known whether KIT is expressed in endothelial cells of pediatric brain tumors, and its role in tumor angiogenesis is unknown.

Methods: We evaluated KIT, phosphorylated (p-KIT), SCF, and VEGFR-2 (vascular endothelial growth receptor factor-2) expression in a series of 69 pediatric brain tumors (35 pilocytic astrocytomas, 12 medulloblastomas, 11 ependymomas, 7 dysembryoblastic neuroepithelial tumors (DNTs), and 4 gangliogliomas) using immunohistochemistry. The median age at the time of the diagnosis was 9 yrs (range, from 0 to 20). PDGFRA (platelet derived growth factor receptor alpha), KIT, VEGFR2, and EGFR (epidermal growth factor receptor) gene copy numbers were determined using chromogenic in situ hybridization.

Results: Marked endothelial cell KIT expression was found in 13 (37%) of 35 pilocytic astrocytomas, 6 (55%) ependymomas, and 1 (8%) medulloblastoma, whereas none of the DNTs or gangliogliomas showed marked expression. Twelve (60%) of the 20 tumors with marked expression expressed also markedly p-KIT as compared to only 7 (14%) of the 49 tumors that lacked marked KIT expression (P =.0001, chi-square test). Endothelial cell KIT expression was associated with age at diagnosis in the largest histological subset (pilocytic astrocytoma), where 11 (69%) of the patents aged 8 or less had marked endothelial cell expression as compared to only 2 (11%) of those older than 8 (P =.0004). In the entire series 16 (53%) of patients < 8 at diagnosis had marked KIT expression in tumor endothelial vessels as compared to 4 (10%) among those > 8 (P <.0001). No KIT, PDGFRA, VEGFR2, or EGFR gene amplifications were detected in the endothelial cells of any of the tumors.

Conclusions: Endothelial cells of pediatric brain tumors often express KIT that is activated (phosphorylated), whereas marked VEGFR-2 expression is rare. Patients diagnosed with pilocytic astrocytoma at a young age often have a tumor with a marked endothelial cell expression of KIT, whereas such ex-pression is usually not found in tumor vessels of pilocytic astrocytomas detected at an older age. These findings suggests that angiogenesis of pilocytic astrocytomas of young children may differ from that of older ones.

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Heterocyclic thiosemicarbazones and their Zinc(II) complexes inhibited proliferation of four different neoplastic cell lines

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Background: It has been reported that thiosemicarbazones (TSCs) are potent antitumor agents. This class of compounds can suppress tumor growth by inhibiting the bioactivity of ribonucleotide reductase (RNR). RNR is the rate-limiting enzyme in DNA synthesis due to its low abundance in normal cells. In comparison with several other key enzymes, RNR shows the greatest increase in activity in tumor cells and, therefore, RNR is considered an important intracellular target for inhibiting cellular proliferation. The aim of this work was to asses the antiproliferative action of some newly synthesized heterocyclic thiosemicarbazones and their zinc (II) complexes, on four human neoplastic cell lines: human cervix carcinoma (HeLa), chronic myelogenous leukemia (K562), and breast carcinoma (MDA-MB-453, and MDA-MB-361).

Methods: A new series of thiosemicarbazones (TSCs) and Zinc(II) complexes were synthesized. The structures of all the compounds were determined by analytical and spectral (1H-NMR,13C-NMR, IR, MS and