Thursday Poster Abstracts

2x10^6 cells were cultured in Liquid Media RPMI 1640 for 8 weeks, and compare to 4 cell lines (NGP, IMR5, LAN-5, SKNSH) and non NBL mobilized PBHSC at which time the same characterization performed at day 0. Results: On day 0 there was no gene expression of TH or MYCN in-patient samples compare to 1.8 x 100 and 1.4 x10-1 in negative controls vs. 2.9x106 and 9.x102 for TH and MYCN respectively in the cell lines. At week 8 there was a 6.5x 103 fold increase in TH and 1.6x103 fold increase in MYCN gene expression in patient samples while the negative controls show no increase expression and the cell lines show similar gene expression. In Table 1 we show the comparison results of the flow cytometry. Conclusion: These data suggests the presence of NBL TICs in collected HPBSC because of the appearance of NBL specific markers (increase GD2, CD56, CD9 cell surface expression and increase in gene expression of TH and MYCN)

Poster Board Number: 2105

KRUPPEL-LIKE FACTOR 4 SUPPRESSES NEUROBLASTOMA GROWTH BY PROMOTING SMOOTH-MUSCLE DIFFERENTIATION

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Neuroblastoma (NB) is an embryonic tumor and possesses a unique propensity to exhibit either a spontaneous regression or an unrestrained growth. Growing evidence suggests that NB comprises heterogeneous populations of improperly differentiated neural crest cells and a small subset of NB cells behaves as stem cells. Commitment of NB stem cells to the fibromuscular lineage may give a favorable outcome, while to the neuronal lineage results in a malignant tumor progression. Krüppel like factor 4 (KLF4) is one of the key reprogramming factors. Intriguingly, it also possesses paradoxical functions in cancers, either as an oncogene or tumor suppressor dependent of cell context. In this study, we elucidated the roles of KLF4 in the lineage determination of NB stem cells and tumor progression. Quantitative RT-PCR showed that loss of KLF4 expression was frequently found in the high-stage NB (Stages III and IV). In particular with the high-risk factors such as age of patient >1 year, N-myc amplification and low TrkA expression, the decreased expression of KLF4 was significantly associated with an unfavorable NB outcome. Subsequent targeted down-regulation studies using a NB cell line (SK-N-SH and Be(2)-C) directly demonstrated that reduced KLF4 expression favors the growth of NB cells and tumorigenesis. In concordance with this, overexpression of KLF4 profoundly suppressed proliferation and induced apoptosis of NB cells (SH-SY-5Y). At the molecular level, KLF4 directly up-regulated the cell-cycle inhibitor protein p21CIP and induced cell cycle arrest and cell death. In addition, KLF4 overexpressing cells have lost their neuroblastic phenotypes, they were epithelial-like, strongly substrate-adherent, expressing smooth muscle marker and became non-tumorigenic. Moreover, KLF4 knockdown clones were not able to committed to fibromuscular lineage, suggesting that KLF4 expression is crucial for lineage determination of NB stem cells. Collectively our work showed that decreased KLF4 expression is associated with poor disease outcome and KLF4 can directly mediate the growth and lineage determination of NB cells.

Poster Withdrawn

Poster Withdrawn

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THE PROGNOSTIC ROLE OF HUMAN ADULT CANCER STEM CELL MARKER PROFILES IN AGGRESSIVE METASTATIC COLORECTAL CANCER

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Background: Despite advances in screening and treatment, metastatic colorectal cancer (CRC) remains the third-leading cause of cancer-related death in the United States. CRC most commonly metastasizes to the liver, and once this occurs, survival rates are tremendously impacted. A small subset of patients may achieve long-term survival with metastasectomy. However, the majority of patients develop a disease recurrence within 2 years, and only one-third achieve 5-year survival. Several studies have proposed that cancer stem cells (CSC) may be the functional effectors of tumor metastasis, treatment resistance and recurrence. However, no one to date has examined whether the differential expression of CSC markers can be used as prognostic indicators of recurrence and overall survival in metastatic CRC. Methods: Formalin-fixed, paraffin-embedded metastatic CRC tissue samples were obtained from 96 patients treated with metastasectomy for liver disease. Using standard immunohistochemical techniques, tissue samples were stained with antibodies to previously characterized CSC markers CD166, CD44, CD26, and Aldehyde Dehydrogenase 1. Cellular expression patterns for solitary and multiple CSC markers were captured with confocal microscopy and analyzed using an automated open source image quantification program (CellProfiler 2.0). Expression profiles were then correlated to patient outcomes (disease recurrence and overall survival). Results: Variable expression of CSC markers was seen between long- and short-term survival as well as rate of recurrence. Patients with an overall survival of greater than 2 years showed a higher level of CD166 expression. A loss of CD44 expression correlated to an increased disease-free survival of greater than 2 years. Conclusion: In this study, we identify a subset of CSC markers that correlates to disease behavior and tumor biology in metastatic CRC. Further delineation of CSC profiles may give valuable clues to therapeutic resistance as well as offer new therapeutic targets in the treatment of this disease.