Background: B7-H3 positive tumors, including osteosarcoma, neuroblastoma, and high grade glioma, cause significant morbidity and mortality in pediatric patients despite aggressive management with multimodality therapy. Current B7-H3-targeted immune-therapies take advantage of the monoclonal antibody (MAb) 8H9, which is actively being evaluated in Phase I clinical trials. We now propose to develop a T-cell therapy approach targeting B7-H3 using Engager (ENG) T cells. ENG T cells, which secrete bispecific engager molecules consisting of single chain variable fragments (scFvS) specific for CD5 and a tumor antigen, are a new class of antigen-specific T cells, with the unique ability to redirect bystander T cells to tumor cells, amplifying antitumor effects.

Objectives: To generate B7-H3-specific Engager (B7-H3-ENG) T cells, and pre-clinically evaluate their effector function in vitro and in vivo.

Design/Method: B7-H3-ENG T cells were created by synthesizing a mini gene consisting of a leader sequence and a B7-H3-specific scFv derived from MAb 8H9. The mini gene was cloned into a SFG retroviral vector containing a CD3-specific scFv and mOrange separated by an internal ribosomal entry site. RD114- pseudo tretinoid retrowiral vectors were used to transduce CD3D82-activated human T cells. The effector function of B7-H3-ENG T cells was evaluated in vitro by performing coculture and cytotoxicity assays with B7-H3-positive osteosarcoma (LM7), neuroblastoma (CHLA255), and glioma (U373) cell lines, and a B7-H3-negative lung cancer (HTB-119) cell line.

Results: Post transduction 30-60% of T cells were genetically modified as judged by mOrange expression. In coculture assay B7-H3-ENG T cells recognized B7-H3-positive target cells (LM7, CHLA255, U373) as judged by IFNγ production and cytotoxicity assays. In contrast, B7-H3-negative cells (HTB-119) T cells secreting an engager molecule specific for an irrelevant antigen (CD19) did not recognize or kill any of the target cells.

Conclusion: We have successfully generated B7-H3-ENG T cells and shown that these cells recognize and kill B7-H3-positive tumor cells in an antigen-dependent manner. In the future, we plan to extend our in vitro studies, and also evaluate antitumor activity in relevant preclinical animal models of pediatric solid tumors.
cases were irresectable. Cases with stage I and II had no adjuvant chemotherapy, while stage III and IV received Doxorubicin, Etoposide, Cisplatinum and Mitotane with no treatment related mortality. Stage I and II are alive in CR, while stage III and IV died due to progressive disease. Overall survival 47.6% (median survival time 31 months). Progression free survival 42.9% (Median follow up 29 months).

Conclusion: Adrenocortical carcinoma in children is a very rare disease. Patients with ACC suffer not only from the malignant mass itself but also from the consequences of excess hormones. The prognosis is essentially dependent on complete resection of the tumor and thus on the initial tumor stage. The adrenotoxic mitotane and various chemotherapy protocols may only control tumor growth in the advanced stages for only short periods.

POSTER # 1105

IMPACT OF 1p AND 16q LOH ON THE OUTCOME OF FAVORABLE HISTOLOGY WILMS TUMOR

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Background: Wilms tumor (WT) represents 6.5% of childhood cancers accounting for 87% of pediatric renal tumors. According to the fifth National Wilms Tumor Study (NWTS-5), tumor-specific loss of heterozygosity (LOH) for chromosomes 1p and 16q identifies a subset of WT patients with favorable histology (FH) who have a significantly increased risk of relapse and death.

Objectives: The aim of this study was to find out if 1p and 16q LOH frequencies in FH-WT patients as well as its correlation to survival outcome, epidemiologic and clinical characteristics.

Design/Method: The data of FH-WT patients presented to the National Cancer Institute, Egypt (NCI) during the period from January 2005 to December 2009 was retrospectively analyzed. Clinical and demographic data were reviewed and paraffin blocks were tested for 1p and 16q LOH using polymorphic loci that span the minimal regions of 1p and 16q as described in earlier studies.

Results: The study included 100 patients with a median age of 5 years (8 months-15 years) and male to female ratio was 10:75. 39/100 patients showed LOH at 1p (n = 14), 16q (n = 13), or both (n = 12). LOH was most frequently encountered in patients above 10 years of age (55%), advanced stages disease (80% of stage V and 50% of each stage IV and III patients). All patients with progressive disease during chemotherapy (n = 5) were positive for LOH. The 3 years OS and EFS were significantly lower in patients with double LOH (56% & 50%) followed by 1q 59% (59% & 55%) in comparison to 1p (93% each) and negative LOH cases (98% each) respectively (P = 0.001).

Conclusion: Combined LOH (1p + 16q) followed by 16q LOH alone are predictive of poor outcome and are associated with lower OS and EFS in FH-WT. Our data indicated a higher risk disease that would suggest the need for a different approach of therapy in aforementioned patients.

POSTER # 1106

MOLECULAR PROFILING OF ADULT PATIENTS WITH PEDIATRIC-TYPE MALIGNANCIES IDENTIFIES NOVEL SOMATIC ABERRATIONS

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Background: Many common pediatric oncologic diseases such as medulloblastoma, Wilms tumor and Ewing sarcoma, are infrequently found in the adult population. Pediatric malignancies in adults are clinically aggressive, with higher risk of relapse, and more resistance to chemotherapeutics. Thus, they are very challenging to manage. Molecular profiling has recently become available for more detailed molecular analysis of these entities. These may provide insights into the aggressive biology of the disease.

Objectives: To describe molecular/genomic abnormalities present in adult patients diagnosed with cancers that are more frequently encountered in pediatric patients.

Design/Method: We conducted a retrospective chart review of adult patients diagnosed with pediatric malignancies referred to The Center for Targeted Therapy and/or Department of Pediatrics at MD Anderson Cancer Center. The archival tumors were analyzed using the CLIA certified exome next-generation sequencing at Foundation Medicine, Boston, MA, or MD Anderson Cancer Center, Houston, TX.

Results: Five patients had genomic profiling for review. Median age at presentation was 28.8 years (23–38 years). All of the encountered malignancies were solid tumors. The genetic aberrations identified in the two patients with history of medulloblastoma were BRCA1 (splice site c.498T>G), PTCH-1 (N978I) and K1636C-N6. One case of Wilms tumor in a 36-year old male showed CTNNB1, IGFR1, FAM123B and SPEN Q1122 alterations in the absence of WT1 and WTX mutations whereas another patient with Wilms tumor harbored WT1 mutation. One patient with Ewing sarcoma harbored CDKN2A/BR, and BCL2L2 and c17orf19 amplification.

Conclusion: Identification of somatic aberrations in adult patients with pediatric type malignancies using CLIA certified clinical next generation sequencing is feasible. Although it is unfeasible to perform clinical trials in this population, establishment of a rare disease registry is warranted. In addition further larger analysis of these types of patients along with clinical correlation is needed.

POSTER # 1107

PERIVASCULAR LEUKOCYTE AGGREGATES FORM IN TUMORS AFTER CHEMOTHERAPY

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Background: Evidence is mounting to support the hypothesis that immune processes play a critical role in tumor clearance after standard treatment such as chemotherapy. In spite of this, anti-tumor immunity is often less robust than expected. One of the major problems with immunologic therapy for tumors is that immune cells fail to traffic to the tumor and often cannot cross the vascular endothelium to enter the tumor parenchyma.

Objectives: To test the hypothesis that standard chemotherapy treatment leads to immune activation.

Design/Method: We used syngeneic murine tumor models of glioblastoma (intracranial orthotopic GL261 implantation) and melanoma (subcutaneous B16F10 implantation) to study the effect of chemotherapy (temozolomide or dacarbazine) on immune cell infiltrates in earlier studies.

Results: In both glioblastoma and melanoma, leukocytes aggregated in perivascular locations after chemotherapy. These perivascular immune cell “cuffs” became more prominent and frequent over time, but were confined to the tumor and peritumoral tissue. Despite the proximity to intratumoral vascular structures, analysis of endothelial integrin expression showed no upregulation of cell-surface ICAM or VCAM after chemotherapy. Immunohistochemical analysis showed a preponderance of macrophage lineage cells with a less prominent CD4 T cell component, and very few CD8 T cells. Only a very small number of T cells were in cell cycle by Ki67 staining, and a high proportion of the CD4 T cells were found to be regulatory T cells. When tumor-specific CD8 T cells were transferred into tumor-bearing mice, they did not traffic to the tumors. Finally, perivascular cuffs failed to form in Rag1-deficient host mice that lack T cells.

Conclusion: Our data demonstrate that chemotherapy treatment results in large immune cell aggregates around tumor vessels which are composed primarily of macrophage-lineage cells. Despite these prominent perivascular leukocyte cuffs, the vascular endothelium failed to demonstrate an activated phenotype. Interestingly, T cells were mechanistically critical for cuff formation, even though they were less frequent in the cuff architecture. Based on the histiocytic nature of the perivascular cuffs, we speculate that they are made up of tumor-associated macrophages/microglia that sense tumor tissue damage and migrate to perivascular locations, where they can protect the tumor from immune attack.

POSTER # 1108

CENTRAL LINE-ASSOCIATED BLOODSTREAM INFECTION RATES IN HOSPITALIZED AND AMBULATORY PEDIATRIC HEMATOLOGY/ONCOLOGY PATIENTS BY CENTRAL LINE TYPE

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Background: Central line-associated bloodstream infections (CLABSI) are a significant cause of morbidity and mortality in the pediatric hematology/oncology (PHO) population and it has been suggested in prior small studies that the CLABSI risk varies by line type. Three types of permanent central venous catheters (CVC) are commonly inserted in children for easy vascular access: totally implantable catheters (porto), single or multi-lumen tunneled externalized catheters (STL, TE or MLTEC), and peripherally-inserted central catheters (PICC).

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