reveal any drop metastases. The patient initiated therapy per ACNS0331 with craniospinal irradiation posterior fossa boost. He also received weekly vincristine. After completion of radiation therapy, the family declined further chemotherapy despite medical advice. He had no evidence of relapse most recently at 51 months from completion of therapy. Next generation sequencing and methylation testing are currently pending. CONCLUSION: Current efforts aim at optimizing therapy based on molecular subgrouping, to minimize long-term adverse events associated with current therapies. We report a unique case of an adolescent male with an standard-risk medulloblastoma, who achieved remission with only radiotherapy. Further molecular tumor analysis may elucidate the response of the tumor.

MEDB-55. SINGLE-CELL TRANSCRIPTOMICS REVEALS PROGENITOR CELLS EXPRESSING A PHOTORECEPTOR PROGRAM AS PUTATIVE CELLS ORIGIN OF MYC-DRIVEN GROUP 3 MEDULLOBLASTOMA

Miao Zhao[1], Oliver Mainwaring[1], Gabriela Rosén[1], Ramy Elgendy[1], Milena Doroszko[1], Sanne Rijpkema[1], Anders Sundstrom[1], Sven Nelander[1], Holger Weishaupt[1], Takahisa Furukawa[2], Fredrik J. Swartling[1]; [1]Uppsala University, Uppsala, Sweden. [2]Osaka University, Osaka, Japan

Brain tumors are the leading cause of childhood cancer-related death. Medulloblastoma is the most common malignant pediatric brain tumor with about 70% survival. Medulloblastoma comprises four distinct subgroups respective of genomic and molecular drivers influencing tumorigenesis. It has been established that despite being considered a single disease entity, each subgroup arises from a distinct population of cells found within unique compartments of the developing brain. The cell of origin of Group 3 medulloblastoma, the most malignant medulloblastoma subgroups, is currently unknown and remains controversial. Transcriptional profiling has revealed that Group 3 medulloblastomas are characterized by elevated expression of a photoreceptor program, which has not been described in the normal cerebellar development but is well characterized in the developing pineal gland and retinal. By investigating and comparing brain and tumor development between our previously developed medulloblastoma mice model (GMYC), where mice spontaneously develop Group 3 medulloblastoma after 4-6 months of age, and their control counterparts, we found that tumor cells emerged from progenitor cells where MYC overexpression drove the transformation of immature progenitor cells expressing a photoreceptor program. Our data suggest that MYC-driven Group 3 medulloblastoma originates from progenitor cells expressing a photoreceptor program, which has implications for future research and the development of novel treatments targeting this devastating childhood malignancy.

MEDB-56. POX NPS MEDIATED DELIVERY OF (TLR7/8) AGONIST RESIQUIMOD IMPROVES TREATMENT OUTCOMES IN SHH MEDULLOBLASTOMA BY TARGETING TUMOR ASSOCIATED MACROPHAGES

Duhyeong Hwang[1], Coral del Mar Alicea[1], Chaemin Lim[1], Christopher Park[2], Timothy Gershon[1], Marina Sokolsky-Papkov[1]; [1]UNC-Chapel Hill, Chapel Hill, NC, USA. [2]UNC Chapel Hill, Chapel Hill, NC, USA

Cancer immunotherapy, the utilization of the patients' own immune system to treat cancer, has emerged as a powerful new strategy in cancer treatment. Recent clinical data has demonstrated immunotherapy to be effective in a wide range of cancers, including lung, bladder, renal cell, colorectal, gastro-esophageal, and head and neck cancers5-11. However, clinical reports of immune-based treatments for medulloblastomas are scarce and preliminary. Therefore, there is a need in developing strategies to improve medulloblastoma immunotherapy. Our recent studies have confirmed that SHH medulloblastomas are enriched in Tumor Associated Macrophages (TAMs) and unlike other tumors, TAMs are associated with positive outcomes and play a positive role by impairing tumor growth. Overall, analysis of TME in medulloblastomas reveals TAMs as a potential therapeutic target. Resiquimod is a synthetic small molecule agonist of Toll-like receptors 7 and 8 (TLR7/8) that modulates innate immune cells. We have loaded resiquimod into ultra-high-capacity polyoxazoline (POx) block copolymers forming small, homogeneous nanoparticles (POx-resiquimod). Our recent study shows that loading into POx nanoparticles improves drug delivery to tumors and treatment with 3 injections of POx-res as the single-agent treatment results in a profound anti-tumor effect G-Smo mice while treatment with free drug shows no therapeutic benefit. Our data also shows that that the tumors of G-Smo mice are enriched with the mixed populations of anti-inflammatory and pro-inflammatory macrophages and the treatment with POx-resiquimod have enhanced infiltration of macrophages into the tumors, enhanced the repolarization of macrophages to M1 subtype and decreased tumor cells viability. These studies show for the first time that targeting the medulloblastoma TME with POx-resiquimod can produce a significant anti-tumor effect. Furthermore, combination of POx-resiquimod with radiation resulted in long term survivals, showing potential therapeutic combination. The expression of TLR7/8 on TAMs in patient-derived medulloblastoma samples suggests that resiquimod may produce similar anti-medulloblastoma effects in humans.

MEDB-57. *GNAS* INACTIVATION AS A DRIVER FOR SONIC HEDGEHOG-ACTIVATED MEDULLOBLASTOMA

Erin Goode[1], Liliana Montoya[1], Eric Graham[1], Brianna Pruniski[1], Curtis Simmons[1], Alexander Ngwube[1], Lindsey M Hoffman[1], Nishant Tiwari[1], Kenneth Aldape[2], Harper N Price[1], Vera Paulson[3], Ross Mangum[1]; [1]Phoenix Children's Hospital, Phoenix, AZ, USA. [2]National Cancer Institute, Bethesda, Maryland, USA. [3]University of Washington, Seattle, WA, USA

INTRODUCTION: Sonic hedgehog (SHH)-activated medulloblastoma is one of the four consensus molecular subgroups of medulloblastoma and is typically associated with PTCH1, SUFU, and/or SMO mutations. GNAS inactivating mutations are a less commonly recognized tumorigenic driver for SHH pathway activation. CASE PRESENTATION: We report the case of an 11-month-old male who presented with a large posterior fossa mass, cerebellar tonsillar herniation, and obstructive hydrocephalus. Following a successful gross total resection, pathology was consistent with desmoplastic/nodular medulloblastoma. Tumor molecular profiling using a DNA-based, next-generation sequencing platform detected a pathogenic frameshift mutation in the GNAS gene (p.D189Mfs*14, NM_000516.4:c.565_568del) at a variant allele frequency of 81%, suggestive of biallelic GNAS inactivation. The same mutation was detected from a buccal swab sample, confirming germline GNAS inactivation. Whole genome methylation profiling was consistent with medulloblastoma subclass SHH B (infant). Concurrent with this brain tumor evaluation, a skin biopsy was performed of scattered subcutaneous, plate-like nodules distributed over the patient's back and extremities. This revealed metaplastic-appearing cancellous bone within the dermis and subcutaneous tissue consistent with plate-like osteoma cutis. He was treated with high-dose chemotherapy followed by autologous stem cell rescue and remains disease-free 15 months from diagnosis. DISCUSSION: There have been scattered case reports describing germline loss-of-function GNAS mutations acting as tumorigenic drivers of SHH medulloblastoma. However, GNAS alterations are not covered by most standard diagnostic molecular sequencing panels for medulloblastoma. Other phenotypic manifestations of germline inactivating GNAS mutations include pseudohypoparathyroidism, pseudopseudohypoparathyroidism, progressive osseous heteroplasia, and osteoma cutis. CONCLUSION: Knowledge of the possible association between germline GNAS inactivating mutations and the development of childhood SHH-activated medulloblastoma is essential for prompt diagnosis and treatment initiation. As such, consideration should be given for inclusion of GNAS alterations in diagnostic medulloblastoma sequencing panels, especially in the setting of osteoma cutis or other endocrinopathies.

MEDB-58. RISK FACTORS AND RISK PREDICTION MODELS FOR MEDULLOBLASTOMA RECURRENCE

Juan Li, Mingyao Lai, Linbo Cai; Guangdong Sanjiu Brain Hospital, Guangzhou, Guangdong, China

BACKGROUND: There is a clear need for systematic appraisal of models/factors predicting medulloblastoma recurrence because clinical decisions about adjuvant treatment are taken on the basis of such variables. METHODS : A total of 273 patients diagnosed with medulloblastoma were retrospectively analyzed. The pre-rediotherapy neutrophile-lymphocyte ratio (NLR) was calculated, and other clinical characteristics were collected such as genetic type , whether with dissemination, degree with excision. The Kaplan-Meier method was used for survival analysis. Cox regression models was used to identify independent prognostic factors. R software was used to develop a nomogram with all the independent prognostic factors included. The prognostic predictive ability of the nomogram was evaluated by Concordance-index (C-index), area under the curve (AUC), and calibration curve. RESULTS: The median median progression-free survival time was 63.8 months in overall cohort. Univariate and multivariate cox hazards regression analysis identified independent prognostic factors associated with the PFS of patients with medulloblastoma to include age, residual tumor volume > 1.5cm3 after excision, NLR > 4.5, whether with dissemination before RT, and whether the genetic type is group 3,which were integrated to establish a nomogram. The C-indexes of nomogram were 0.696 and 0.676 in the training and validation cohort, respectively. The AUC of predicting 3-years PFS showed satisfactory accuracy as well (Training cohort: AUC=0.696; Validation cohort: AUC=0.676). The calibration curve showed agreement between the ideal and predicted values. Kaplan-Meier curves based on the PFS showed significant differences between nomogram predictive low-, and high groups (P < 0.001). CONCLU-