induced significant cell death in all 4 cell lines in vitro. Temozolomide, difluoromethylornithine and chloroquine (CQ) were then tested together with pegArg-I in U87 in vitro. We found that only CQ showed additive effect whereas pegArg-I did not. Temozolomide was associated with enhanced autophagy and necrosis as shown in transmission electron microscopy and autophagy markers’ expression by Western blotting. PegArg-I prolonged the survival of glioma mice, suggesting its possible additive effect. However, CQ+pegArg-I didn’t show further significant anti-cancer efficacy in vitro. CONCLUSION: PegArg-I may be useful in slowing the progression of glioma, but additional drug candidate which works synergistically with pegArg-I remains to be explored.

HHG-29. A CASE OF CIRCUMSCRIBED HIGH-GRADE ASTROCYTOMA WITH ATRX AND CDKN2A/B ALTERNATIONS WHO WAS INITIALLY DIAGNOSED AS GLOBLASTOMA AND HAS 20 YEARS SURVIVAL

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Pediatric high-grade gliomas are rare and often hard to classify, which grow locally and show longer survival than diffuse high-grade gliomas in adults. We report a case of circumscribed high-grade astrocytoma who was initially diagnosed as glioblastoma and has 20 years survival. A 7-year-old girl suffered from epileptic seizure due to a left occipital lobe tumor. The tumor was resected in another hospital and diagnosed as glioblastoma. The tumor disappeared after extended local irradiation and chemotherapy using nimustine hydrochloride (ACNU) and cisplatin (CDDP). Eighteen years after initial onset, first recurrence was confirmed as the intra-tumoral hemorrhage. The tumor was resected and diagnosed as anaplastic oligoastrocytoma. After 6 courses of temozolomide (TMZ), the tumor disappeared. Twenty years after initial onset and local recurrence was confirmed. Although Without a biopsy knife and TMZ was performed, the tumor did not disappear. The tumor was surgically resected. Histopathology showed localized growth with some infiltration and mitosis but lacked pseudopalisading and microvascular proliferative features. The patient was diagnosed as circumscribed high-grade astrocytoma. Immunostaining revealed ATRX nuclear loss and CDKN2A/B homozygous deletion. After 10 courses of TMZ, the third local recurrence was confirmed. The tumor was completely removed and has not occurred recurrence more than 20 years after surgery as the last operation. ATRX loss is expected to survive longer than invasive glioma. Pediatric gliomas should differ from adult gliomas in the genes of tumorigenesis. Care should be taken for its diagnosis and treatments. We also need a new classification based on histology and gene profile. HHG-30. ANALYSIS OF PEDIATRIC GLIOMAS IN OUR INSTITUTE

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PURPOSE: Recent advances in genetic interrogation of pediatric glioma increase the importance of single cell RNAsequencing using surgical specimen. However, surgical resection may be avoided to preserve quality of life, especially in brain stem glioma cases. We retrospectively examined diagnosis and treatment of pediatric gliomas in our hospital. METHODS: This study includes 14 consecutive glioma patients under the age of 18 who underwent initial treatment at our hospital from 2000 to 2019. Histopathological diagnosis, clinical course and molecular status such as IDH, H3F3A and BRAF were analyzed. RESULTS: 5 patients (1 pilocytic astrocytoma (PA), 3 diffuse astrocytomas, 1 oligodendroglioma) were treated only by surgical resection (group A). 7 patients (1 PA, 1 anaplastic oligodendroglioma, 2 diffuse midline gliomas and 3 glioblastomas (GBM)) received radiation and/or chemotherapy after surgical resection (group B). 2 diffuse intrinsic pontine gliomas (DIPG) received radiation and chemotherapy without surgical resection (group C). No IDH mutation was observed in all pathological specimen obtained cases. BRAF alteration was observed in all PA cases. 1 case of GBM had BRAF V600E mutation and the other had H3K27M mutation. During a median of 7.7 years of follow-up, group A patients have no recurrence. Group B includes various diagnosis and prognosis. 2 group C patients diagnosed DIPG by MRI showed different clinical courses. CONCLUSION: Pediatric gliomas include diverse biological subgroups and show broad range of clinical behaviors. Pediatric glioma has low incidence and wide variety of genetic mutations, multicenter study is important to improve the treatment of pediatric glioma.

HHG-31. UNIQUE BIOLOGICAL CHARACTERISTICS OF RADIATION-INDUCED GLIOMAS

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Radiation-induced gliomas (RIGs) are the most common secondary solid tumours with very unfavourable prognosis. We aimed to describe different clinical and molecular biological characteristic of RIGs from primary gliomas. We reviewed clinical data of ten patients with RIGs. In patients with available samples, we used the whole genome methylation array and performed targeted sequencing for specific mutations. Between 2000–2018, we diagnosed RIG in 10 patients (M/F 2/8) aged 5–12 years at primary diagnosis of different solid tumours and acute leukaemia. These patients developed RIG with a median 9.3 years (ranging 3–31) after primary diagnosis. Eighty-five percent of patients died within 1 year after diagnosis of RIG. In half of the patients from the group DMOs IDH wild-type, examined by methylation array, PDGFRA amplification was found. Our data shows that most RIGs are midline IDH-wild type glioblastomas with poor prognosis that are biologically different from primary DMGs. PDGFRA amplifications are potentially targetable by kinase inhibitors in order to order to prognosis of these patients.

HHG-32. UNCOVERING THERAPEUTIC VULNERABILITIES IN MISMATCH REPAIR-DEFICIENT GLIOMAS

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INTRODUCTION: We have observed that approximately 26% of recurrent glioma patients acquire hypermethylated, de novo methylated high-grade glioma (HGG) following TMZ. Intriguingly, 91% of these tumors harbor mutations in mismatch repair (MMR) genes. Strategies to target MMR-deficient gliomas thus stand to impact a large number of patients. METHODS: We ablated the MMR genes MSH2, MSH6, MLH1, and PMS2 using an all-in-one sgRNA-CRISPR/Cas9 expression vector to generate panels of isogenic MMR knockouts in patient-derived glioma cell lines. We have characterized the phenotype of these MMR-deficient glioma cells, and leveraged high-throughput drug screens to identify therapeutic vulnerabilities induced by loss of MMR. RESULTS: We demonstrate that loss of MSH2 or MLH1 confers differential dependencies to small molecule inhibitors. CONCLUSIONS: CRISPR/Cas9 knockout of individual MMR pathway members allows us to systemically study the response of MMR-deficient cells to alkylating agents in an isogenic context. MMR deficiencies in glioma confer dependencies to small molecule treatment, which may inform future therapies for MMR-deficient tumors.

HHG-34. DETECTION OF ONCOGENIC FUSION EVENTS IN SUPRATENTORIAL GLOBLASTOMAS OF YOUNG CHILDREN

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INTRODUCTION: Glioblastoma in infancy and early childhood is characterized by a more favorable outcome compared to older children, a stable genotype, and the occurrence of tyrosine kinase gene fusions that may represent therapeutic targets. METHODS: 50 glioblastomas (GBM) with supratentorial location occurring in children younger than four years were
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retrieved from the archives of the Brain Tumor Reference Center, Institute of Neuropathology, University of Bonn. DNA and RNA were extracted from FFPE tumor samples. Gene fusions were identified by FISH using break-apart probes for ALK, ROS1, NTRK1, -2, -3, RET, MET, and ROS1. 100% of cases were analyzed with the most sensitive method for analysis of FFPE samples, CNV.

CONCLUSIONS: Gene fusions involving the tyrosine kinase genes ALK, MET, ROS1 and NTRK1, -2, -3 occurred in 72% of glioblastomas of children younger than four years; the most frequent were ALK fusions occurring in infant GBM. DNA based MIP technology represented the most robust and sensitive assay.

HGG-35. PEDIATRIC PLEOMORPHIC XANTHOASTROCYTOMA WITH ANAPLASIA TREATED WITH SURGERY AND ADJUVANT CHEMOTHERAPY: A CASE SERIES OF 3 LONG-TERM SURVIVORS Rebecca Romsey1, Christopher Dunham1, Stephen Tp3, Juliette Hukin4, and Yip Wai21, 2, 3

OBJECTIVE: Pleomorphic xanthoastrocytoma (PXA) with anaplasia is a rare subtype of centrencephalic astrocytoma, generally treated as high grade gliomas. The optimal extent of therapy required is unknown. Here we report on 3 pediatric cases of PXA with anaplasia. We also describe molecular features and methylation profile in one of the two cases. METHODS: The database of the Department of Neurosurgery was searched for cases of PXA with anaplasia. Methods used included: subtyping, expression profiling, comparative genomic hybridization (CGH), immunohistochemistry, and next-generation sequencing. RESULTS: We present three pediatric cases of PXA with anaplasia. All tumors were WHO grade III. In two cases recurrent glioma in the surgical bed were encountered suggesting a radiation resistant clone. All patients received concurrent temozolomide with radiation followed by maintenance chemotherapy with temozolomide and lumostine for 6 cycles as per the Children’s Oncology Group Protocol ACNS04243. These two patients had a continued complete response. The third patient went on to recurrent disease following radiation and subsequently had recurrent disease at the end of treatment and went on to have a resection GTR and achieved complete response after 6 cycles of lumostine, vincristine and procarbazine. All are alive with no evidence of disease at more than 2 years post treatment (OS 23 months; 95% CI 1–467 months). CONCLUSIONS: This pediatric tumor is not well understood. The genetic landscape may be informative for optimizing treatment and prognosis.

HGG-36. HIF-2: A NEW DRUG TARGET IN PEDIATRIC HIGH-GRADE GLIOMA WITH PROMISING PRECLINICAL RESULTS Quentin Fuchs1, Marina Pierrevencl2, Christophe Papin2, Monique Dubertret3, and Natasha Ezri4,5,6,11,13

Pediatric high-grade gliomas (pHGGs) have a very dismal prognosis and need new innovative strategy for treatment. Despite the past discovery of histone H3 driver mutations, we are not able for instance to stop this in a minority (<15%) remaining wild-type only. Heterogenous G34-mutant gliomas displayed significantly higher K27M or G34R and K27M combined. We previously identified targets MYCN and NOTCH1 (both stabilised by FKB7, down-regulated by loss of chromosome 4q), as well as specific H3K36 lysine demethylases and splicing factors. Whole-genome CRISPR-Cas9 screening of patient-derived 3G34-R or 3G34-V/3G34-R/R cell lines identified the same as the K27M mutant pathways. We therefore analysed the pHGG dataset and showed these mutations are present in pHGG. In our study we will show that pHGG patients will have distinct mutation specific surfactome. We therefore analysed the cell surface proteomics of pHGG and DIPG, in order to identify novel targets for therapy.

HGG-37. PAEDIATIC GLOBLASTOMA CELLS SHOW CRITICAL DEPENDENCIES ON EPIGENOMIC AND EPITRANSCRIPTOMIC CONTROL OF GENE EXPRESSION BY H3.3G34R/V MUTATIONS Lynn Bekhe1, Alan Mackay1, Rebecca Rogers3, Yura Grigorescu1, Valeria Kizilkan1, Sante Tendler1, Kristina Cole2, Angela Watkins2, Angel Montero Carcaboso3, Maria Vinci1, and Chris Jones1, 1The Institute of Cancer Research, London, United Kingdom, 2Children’s Hospital of Philadelphia, Philadelphia, PA, USA, 3Ann & Robert H Lurie Children's Hospital of Chicago, IL, USA, 4'Hospital Sant Joan de Deu, Barcelona, Spain, 5The Bambino Gesù Children's Hospital, Rome, Italy

H3.3G34R/V mutations are restricted to glioblastomas of the cerebral hemispheres, and occur predominantly in adolescents and young adults. We have previously shown these mutations to result in a global re-organisation of the activating mark H3K36me3 and drive transcription of key developmental transcription factors and oncogenes such as MYCN, however the precise mechanisms were unclear. Using multiple H3G34V/R, parents and ChIP-seq, we wished to go further discovering new targetable proteins in pHGG. In our study we have at first isolated the cell membrane fractions in order to identify novel targets for therapy. We have at first isolated the cell membrane fractions in order to identify novel targets for therapy. We therefore performed to identify specific targetable factors, which can be then be used with antibodies specific to both wild-type and mutant histone H3.3, we show a high degree of incorporation of mutant histone into nucleosomes, with only a minority (<15%) remaining wild-type only. Heterogenous G34-mutant gliomas displayed significantly higher K27M or G34R and K27M combined. We previously identified targets MYCN and NOTCH1 (both stabilised by FKB7, down-regulated by loss of chromosome 4q), as well as specific H3K36 lysine demethylases and splicing factors. Whole-genome CRISPR-Cas9 screening of patient-derived 3G34-R or 3G34-V/3G34-R/R cell lines identified the same as the K27M mutant pathways. We therefore analysed the pHGG dataset and showed these mutations are present in pHGG. In our study we will show that pHGG patients will have distinct mutation specific surfactome. We therefore analysed the cell surface proteomics of pHGG and DIPG, in order to identify novel targets for therapy.

HGG-38. A COMPARATIVE PROTEOMIC ANALYSIS OF THE CELL MEMBRANE FRAGMENTS OF HISTONE 3 MUTATED BRAIN TUMOURS TO IDENTIFY NOVEL THERAPEUTICS Westrick, Ruman Rajan, Andrew Rayfield, and Farhana Haque1

In improvements in the treatments for childhood and adolescent brain tumours, high-grade gliomas (pHGG) and diffuse intrinsic pontine gliomas (DIPG), have not advanced much and they continue to carry a very poor prognosis. These brain tumours are now defined by mutations affecting histone 3 proteins, indeed 80% of DIPGs harbour histone H3.1 G34R/V mutations, relative to wildtype histone H3.1 and H3.3 G34R or G34V mutations. We hypothesized that the histone 3 mutant tumours will have distinct mutation specific surfacotm. We therefore analysed the cell surface proteomics of pHGG and DIPG, in order to identify novel targetable critical factors, which can be then be used for tumour specific precision-therapy. Results of these experiments will be presented.

HGG-39. CLINICAL CHARACTERISTICS AND OUTCOME OF PATIENTS WITH RADIATION-INDUCED GLIOMA Makoto Ohno1, Yasu Miyakita2, Masamichi Takahashi1, Takaki Ohtsuka1, Naruoko Satomi1, Yukie Tamura1, Yuko Matsushita1, Koschi Ichimura1, and Yoshitaka Narita1, 1National Cancer Center Hospital, Chuo-ku, Tokyo, Japan, 2National Cancer Center Research Institute, Chuo-ku, Tokyo, Japan

The development of gliomas subsequent to therapeutic cranial irradiation is a rare but serious complication. The purpose of this study is to understand the clinical characteristics and outcome of patients with radiation-induced glioma (RG). Between 2001 and 2018, we identified 10 patients with RG, which satisfied the criteria in our data base. There was no sex predominance (M: 5, F: 5), and the median age of the primary diseased was 13.5 years (range: 1–39). The primary diseases included 2 germinoma, 2 acute lymphoblastic lymphoma, 2 medulloblastoma, 1 diffuse astrocytoma, 1 pilocytic astrocytoma, 1 pituitary adenoma and 1 metastatic tumor from