induced significant cell death in all 4 cell lines *in vitro*. Temozolomide, difluoromethyornithine and chloroquine (CQ) were then tested together with pegArg-I in U87 *in vitro*. We found that only CQ showed additive effect with pegArg-I against glioma *in vitro*. Such additive cytotoxic effect may be 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 anti-glioma efficacy. However, CQ+pegArg-I didn't show further significant anti-cancer efficacy *in vivo*. 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.

HGG-29. A CASE OF CIRCUMSCRIBED HIGH-GRADE ASTROCYTOMA WITH ATRX AND CDKN2A/B ALTERNATIONS WHO WAS INITIALLY DIAGNOSED AS GLIOBLASTOMA 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, the second local recurrence was confirmed. Although gamma 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 pseudopallisading and microvascular proliferation. The tumor 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 3 months after the last operation. Circumscribed high-grade glioma 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. HGG-30, ANALYSIS OF PEDIATRIC GLIOMAS IN OUR INSTITUTE *Kaoru Tamura*, Mai Fujioka, Masae Kuroha, Motoki Inaji, Yoji Tanaka, Tadashi Nariai, and Taketoshi Maehara; Tokyo Medical and Dental University, Tokyo, Japan. PURPOSE: Recent advances in genetic interrogation of pediatric glioma increase the importance of molecular diagnosis 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 behavior. Since pediatric glioma has a low incidence and a wide variety of genetic mutations, multicenter study is important to improve the treatment of pediatric glioma.

HGG-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 9.5 years (ranging 3–31) after primary diagnosis. Eight patients died within 1 year after diagnosis of RIG and 2 patients are still alive more than 4 years from this diagnosis. According to Heidelberg DNA methylation-based classification, most RIGs belong to the IDH-wild type glioblastoma subclass midline which biologically corresponds to diffuse midline glioma (DMG). However, compared to primary DMGs they do not carry the characteristic H3K27M mutation. One patient developed anaplastic ganglioglioma with BRAF-V600E mutation and methylation profile identical to pleomorphic xanthoastrocytoma (alive for 4 years after diagnosis of RIG). In half of the patients from the group DMGs 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.

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

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INTRODUCTION: We have observed that approximately 26% of recurrent gliomas acquire hypermutation following treatment with temozolomide (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 sgRNA-CRISPR/Cas9 targeting of either *MSH2* or *MLH1* – the two obligatory components of the MutSα and MutLα complexes, respectively – also results in loss of protein expression of their respective binding partner MSH6 or PMS2. Moreover, we show that loss of each MMR component confers resistance to TMZ while maintaining sensitivity to the alkylating nitrosourea CCNU. Furthermore, we show that long-term TMZ treatment of *MSH2* and *MSH6* knockouts in an *MGMT*-methylated line induces hypermutation with enrichment of C > T mutations but not in MMR wild-type controls. Lastly, loss of MSH2 or MLH1 confers differential dependencies to small molecule inhibitors. CONCLUSIONS: CRISPR/Cas9 knockout of individual MMR pathway members allows us to systematically 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.

HGG-34. DETECTION OF ONCOGENIC FUSION EVENTS IN SUPRATENTORIAL GLIOBLASTOMAS 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 genome, 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