survival of <1 year. The critical location in the brainstem and the often in-
tact blood-brain barrier (BBB) pose significant challenges in the treat-
ment of DIPG. The objective of this study was to demonstrate the potential for focused ultrasound (FUS)-induced BBB disruption (FUS-BBBD) to improve DIPG
treatment by enhancing the safe and efficient delivery of drugs. A genetically
engineered mouse model of DIPG was generated using the RCAS (replication-
competent avian sarcoma-leukosis virus long-terminal repeat with splice
acceptor) system. A modeling system to enhance microenvironment (FEU) was
constructed, with FUS (MRgFUS) system was used to induce BBB disruption in these mice with the FUS targeted at the center of the tumor. Two radiolabeled agents with different sizes were used to evaluate the delivery efficiency of the FUS-
BBBD mice: a small molecular radioisotope of DOTATATE (DOTA-
ECL1), and a radiolabeled nanoparticle. 4Cu-labeled copper nanoparticles
(4Cu-CuNCs, 5 nm in diameter), 64Ga-DOTA-ECL1i (half-life -1 h) and
4Cu-CuNCs (half-life ~13 h) were intravenously injected into the mice after FUS sonication, and microPET/CT imaging was performed at 1 h and 24 h, respectively, to evaluate the spatial-temporal distribution of these two agents
in the brain and quantify the delivery outcome. FUS treatment increased the uptake of 64Ga-DOTA-ECL1i and 4Cu-CuNCs to the DIPG tumor by 3.25
folds and 4.07 folds on average, respectively. These findings demonstrated, for the first time, that FUS can increase BBB permeability in a murine model of DIPG and significantly enhance the delivery of agents of different sizes into the DIPG tumor.

HGG-19. 5-AMINOLEVULINIC ACID (5-ALA)-GUIDED RESECTION OF PEDIATRIC BRAIN TUMORS
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Between tumor and normal brain, allowing a higher degree of resec-
tion, and improved patient outcomes. In recent years, several reports have emerged regarding the use of 5-ALA in other brain tumor entities, including pediatric brain tumors. Since gross total resection (GTR) of many brain tumors in children is crucial, the role of 5-ALA-guided resection requires elucidation.

Methods: A systematic literature review of EMBASE and MEDLINE/PubMed databases revealed 20 eligible publications encompassing 186 5-ALA-guided operations on pediatric brain tumors. To reduce bias, pub-
lications were reviewed independently by two authors. Results: 5-ALA-guided resection enabled the surgeons to identify the tumor more easily and was considered helpful mainly in cases of glioblastoma (GBM, 21/27, 78%), anaplastic astrocytoma WHO grade III (10/14, 71%), and medulloblastoma 5-ALA-guided surgery did not show consistent fluorescence signals and 5-ALA was considered helpful only in 12% and 22% of cases, respectively. Accumulation of fluorescent porphyrins seems to be related to WHO tumor grading. In cases of high fluorescence signal we con-
sidered helpful, it was associated with a greater degree of resection. One study showed an association between visible fluorescence signal and concen-
tration of protoporphyrin IX (PPIX) concentration. A threshold of 4µg/ml was required in order to visualize the fluorescence signal. The rate of ad-
verse events related to 5-ALA was negligible, especially new postoperative sequelae. Conclusion: 5-ALA could play a role in resection of malignant, contrast enhancing, supratentorial pediatric brain tumors. At present, we are conducting a prospective phase II multicenter clinical trial to evaluate side effects and feasibility of 5-ALA guided surgery.

HGG-21. MALIGNANT SYNAPTIC PLASTICITY IN PEDIATRIC HIGH-GRADE GLIOMAS
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Pediatric high-grade glioma (pHGG) is a devastating group of diseases that urgently require novel therapeutic approaches. We have previously demon-
strated that pHGGs express the BDNF-TrkB signaling pathway on glioma cell depolarization, mediated by calcium-permeable AMPA channels, promotes their proliferation. The regulatory mechanisms governing these post synaptic connections are unknown. Here, we investigated the role of BDNF-TrkB signaling in modulating the plasticity of the malignant synapse. BDNF ligand activation of its canonical receptor, TrkB (which is encoded for by the gene NTRK2), has been shown to be one important modulator of synaptic regul-
at ion in the normal setting. Electrophysiological recordings of glioma cell membranes, in response to acute twitch stimulation, demonstrate in an inward current resembling AMPA receptor (AMPA)-mediated excitatory neurotransmission. Extracellular BDNF increases the amplitude of this glutamate-induced tumor cell depolarization and this ef-
fect is abrogated in NTRK2 knockout glioma cells. Upon examining tumor cell excitability using in situ calcium imaging, we found that BDNF increases the intensity of glutamate-evoked calcium transients in GCaMP6s expressing glioma cells. Western blot analysis indicates the tumors AMPA properties are altered downstream of BDNF induced TrkB activation in glioma. We find that BDNF-TrkB signaling promotes neuron-glioma synaptic plasticity as measured by high-resolution confocal and electron microscopy in culture and tumor xenografts. Our analysis of published pHGG transcriptomic datasets, together with brain slice conditioned medium experiments in culture, indicate that BDNF-TrkB signaling regulates the spatial-temporal dynamics of the BDNF-TrkB pathway in patient-derived orthotopic glioma xenograft models, both genetically and pharmacologically, results in an increased overall survival and reduced tumor proliferation rate. These findings suggest that gliomas leverage mechanisms of plasticity to modulate the excitatory chan-
nels involved in synaptic neurotransmission and they reveal the potential to target the regulatory components of glioma circuit dynamics as a therapeutic strategy for these lethal cancers.

HGG-22. EVALUATING THE REGULATION OF BLOOD-BRAIN BARRIER INTEGRITY IN DIPG MOUSE MODELS
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Diffuse intrinsic pontine gliomas (DIPGs) are considered to maintain a fairly intact blood-brain barrier (BBB) based on patient imaging and neuropathological characteristics. In contrast, recent development of mouse models, DIPG mouse models, we identified differences in BBB function and increased Angiopointi1 (Angpt1) in H3 K27M DIPG mouse models. We hypothesize that H3 K27M mutations promote the maintenance of BBB integrity through upregulation of Angp1. To determine if H3 K27M mutations upregulate Angpt1 in DIPG mouse models, we performed brain imaging and functional analysis of Angpt1 in H3 K27M DIPG mouse models. We have initiated studies comparing H3 K27M DIPG mouse models to H3 WT and G44 cortical HGG mouse models, demonstrating that DIPG mouse models show minimal changes in vascular phenotype, including vessel density, branching, and diameter compared to cortical HGG models. Compared to cortical HGG models, purified endothelial transcriptomes, HGG ECs displayed enrichments of inflammatory signals and proliferation gene sets, and increased expression of tip cell identity genes. We identified Angpt1 as selectively upregulated in H3 K27M mouse models and derived cell lines. Preliminary data sug-
gests Angpt1 supports the maintenance of BBB integrity in DIPG models. BBB phenotype differences are present in DIPG and HGG mouse models. Uncovering mutation specific mechanisms that regulate BBB function in brain tumors will be critical to advance our understanding of brain tumor pathogenesis and treatment response.

HGG-23. IN VITRO AND IN VIVO PRECLINICAL SCREENING OF PROMISING THERAPEUTICS FOR DIFFUSE MIDLINE GLIOMA (DMG)
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Introduction: Diffuse midline gliomas (DMGs) are amongst the most unforgiving pediatric brain tumors, characterized by an intrinsic re-
sistance to therapy. Despite major advances in understanding of tumor biology, the prognosis remains exceedingly poor, and treatment options are limited. New therapeutics are being evaluated at a fast rate by dif-
f erent laboratories. In order to prioritize effective drug candidates for DMG treatment, we comprehensively characterized a panel of promising therapeutic agents in vitro in different disease models. We determined the sensitivity of primary DMG cell lines to a panel of 20 different compounds and possoy synapse effects were investigated by SystemFinder. Our study was an effort to highlight potential toxicities and associated mechanisms at a large scale, we performed a preclinical toxicity evaluation in zebrafish larvae, with a slightly modified version of the official Fish Embryo Acute Toxicity (FET) test. Drug toxicity was assessed by continuous and acute toxicity on zebrafish larvae to increasing concentrations of the different compounds. Survival curves, morphological analyses and behavioral tests were per-
f ormed at a maximum tolerated dose (MTD). To confirm the findings obtained in zebrafish, we performed a drug toxicity study on primary cultures from zebrafish models, using SystemFinder for improving candidates. Results: Among the tested drugs in vitro we found 10 drugs showing promising dose- dependent reduction in cell viability with IC50 in nM to µM range. These were further evaluated for toxicity in zebrafish. The zebrafish larvae toxicities observations strongly correlated with the findings in murine in vivo studies, reinforcing the importance of...