remained elusive. Here we present one possible cause: MAPK-driven *KT stress*. The hallmarks of KT stress include chronic KT-MT attachment instability in mitosis, dramatic changes in KT morphology, and increases in merotelic KT attachments and chromosome segregation errors. KT stress is lethal to cancer cells. However, stressed cells survive by relying on BUB1B/BubR1 activity to strengthen KT-MT attachments. We first observed KT stress in GBM patient isolates, where ~60–70% display its hallmarks. We subsequently found that RAS or MEK activity is sufficient to induce KT stress in both CNS and non-CNS derived cell types. We propose that KT stress is caused by aberrant *mitotic* RAS/MAPK activity, which likely targets one or more KT proteins resulting in KT-MT attachment defects and chromosome instability. In addition, Dr. Jun Zhu's lab has also created a computational classifier that can identify KT stressed cells and tumors based on the expression of 838 genes associated with KT stress, which can be also used to identify orthogonal therapeutic sensitivities. We will present these findings as well at this meeting.

CBIO-25. INTEGRATED MOLECULAR AND BH3 PROFILING OF THE INTRINSIC APOPTOTIC MACHINERY IDENTIFIES THERAPEUTIC VULNERABILITIES IN GLIOBLASTOMA

Elizabeth Fernandez[1], Wilson Mai[1], Nicholas Bayley[1], Christopher Tse[1], Linda Liau[1], Timothy Cloughesy[1], Anthony Letai[4], and David Nathanson[1]; [1]University of California Los Angeles, Los Angeles, CA, USA, [2]Dana-Farber Cancer Institute, Boston, MA, USA

Resistance to apoptosis is a hallmark of cancer. However, the underlying molecular mechanisms of intrinsic-apoptotic resistance in glioblastoma (GBM) are largely unknown. Here we performed integrated molecular and functional characterization (via BH3 profiling) of the intrinsic apoptotic machinery in 50 GBM patient specimens. We found that, despite significant genetic heterogeneity of our GBM samples, all GBMs have a cross compensatory reliance on BCLXL and MCL1 for basal survival. Treatment with standard of care (e.g., temozolomide or radiation) caused minimal apoptosis, yet ablated the MCL-1 block in a p53-dependent manner, thus creating an exclusive dependence on BCLXL for survival in p53 wild-type GBM tumors (65% of GBM tumors). Consequently, BCLXL inhibition caused synergistic cell death with IR/TMZ in GBM tumors with intact p53 signaling. Importantly, the degree of synergistic cell kill was best predicted by combining molecular features with BH3 profiling, providing an integrated predictive signature of response to this novel therapeutic approach. Collectively, these studies identify mechanisms of intrinsic apoptosis resistance in both basal and treatment states of GBM and demonstrate how functional and molecular data can be complementary to robustly predict therapy-induced cell death.

COVID-19 AND NEURO-ONCOLOGY

COVD-01. ADAPTATION OF A GAMMA KNIFE ICON STEREOTACTIC RADIOSURGERY PROGRAM IN THE FACE OF A GLOBAL PANDEMIC

Rodney Wegner, Zachary Horne, Linda Xu, Alexander Yu, Matthew Goss, Yun Liang, Jason Sohn, Athanasios Colonias[1], Russell Fuhrer, and Stephen Karlovits; Allegheny Health Network Cancer Institute, Pittsburgh, PA, USA

PURPOSE: The COVID-19 pandemic necessitated drastic and rapid changes throughout the field of radiation oncology, some of which were unique to the discipline of radiosurgery. Available guidelines called for reduced frame use, postponing non-urgent cases, and reducing the number of fractions delivered. Our institution enacted many of these guidelines, and herein we show the resultant effect on patient treatments on our Gamma Knife Icon system. METHODS & MATERIALS: In early to mid-March of 2020 our institution rapidly implemented suggested changes according to ASTRO and other consensus guidelines as they relate specifically to stereotactic radiosurgery in the COVID-19 era. We reviewed the GK Icon schedule at our institution between January 01 and April 30, 2020. We documented age, condition treated, technique (frame vs. mask), and number of fractions. We then tabulated and graphed the number of patients, framed cases, and fractions across that time period. RESULTS: Seventy-seven patients were treated on the GK Icon between January and April 2020, for a total of 231 fractions. The number of unique patients per month varied from 18 (April) to 22 (January). Of the 77 patients only 5 were treated using a frame. The number of fractions per month decreased significantly over time, from 70 in January to 36 in April. Likewise, the percentage of single fraction cases increased from 4.5% per month in January to 67% in April. CONCLUSIONS: The results presented here show that it is possible to quickly and efficiently change work flows to allow for reduced fractionation and frame use in the time of a global pandemic. Multidisciplinary cooperation and ongoing communication are integral to the success of such programs.

COVD-02. ADAPTING RNA-NANOPARTICLE VACCINES FROM GLIOBLASTOMA TO SARS-COV-2

Hector Mendez-Gomez[1], Paul Castillo[2], Noah Jones[1], Sadeem Qdaisat[1], Frances Weidert[1], Duane Mitchell[3], and Elias Sayour[1]; [1]University of Florida, Gainesville, FL, USA, [2]University of Florida, Department of Pediatrics, Gainesville, FL, USA, [3]University of Florida, Department of Neurosurgery, Gainesville, FL, USA

BACKGROUND: Glioblastoma (GBM) can be an effective teacher in the war on COVID-19, as an operative vaccine for either must elicit near-immediate protective responses that overcomes disease heterogeneity and immune suppression. Current prophylactic strategies against COVID-19 utilize mRNA vaccines targeting small fragments of the SARS-CoV-2 genome, but these may not induce robust T cell responses or elicit immunity quickly enough. OBJECTIVE: We sought to adapt an FDA-IND approved mRNA vaccine in GBM against COVID-19 for: 1) activation of near immediate immune responses, 2) targeting of full-length SARS-CoV-2 structural proteins, and 3) induction of bidirectional (B and T cell) adaptive immunity. METHODS: We utilized a novel engineering design that layers mRNA into a lipid-nanoparticle (NP) shell (much like an onion); this allows greater packaging of mRNA per particle to quickly boost innate/adaptive immune responses against full-length glioblastoma antigens or SARS-CoV-2 structural proteins. RESULTS: In small and large animal models, RNA-NPs safely mimic viremia activating the quiescent immune system in only a few hours for induction of protective immunity against its mRNA payload. RNA-NPs activate dendritic cells (DCs), upregulate critical innate gene signatures, and induce antigen-specific cellular and humoral immunity. We found that mice receiving SARS-CoV-2 spike RNA-NPs had more effector T cells after vaccination with significant memory recall expansion after in vitro re-stimulation with overlapping SARS-CoV-2 spike peptide mix. We also found increased release of MIP-1-alpha (i.e. CCL3) previously shown by our group (Mitchell et al. *Nature* 2015) to be responsible for Th1 mediated memory recall to infectious vaccine antigens in GBM patients. CONCLUSION: SARS-CoV-2 RNA-NPs elicit memory recall response after vaccination. We have obtained FDA-IND approval (BB-19304, Sayour) in GBM with SARS-CoV-2 specific amendment (BB-20871) underway to support first-in-human trials of RNA-NPs targeting both GBM and COVID-19.

COVD-03. ASSESSING THE IMPACT OF CORONAVIRUS 19 PANDEMIC ON NEURO-ONCOLOGY AT GUY'S CANCER CENTRE LONDON

Jessica Little[1], Omar Al-Salihi[2], Lucy Brazil[2], and Angela Swampillai[2]; [1]Guy's Hospital London, London, England, United Kingdom, [2]Guy's Hospital, GSTT, London, London, United Kingdom

BACKGROUND: Immunosuppressive treatment increases COVID-19 risk. Neuro-oncology patients may not qualify for ITU if they deteriorate, but without oncological treatment, prognosis is poor. The pandemic has seen the introduction of new guidelines; including alternative treatment schedules which balance risks of contracting COVID-19, against safely delivering effective cancer treatment. We assess COVID-19 impact on neuro-oncology treatment at Guy's Cancer Centre, London. METHODS: Notes of patients seen March-April 2020 were reviewed. Demographic data, tumour grade, treatment and changes due to COVID-19 recorded. RESULTS: 111 patients were identified (69 male: 42 female, median age 51years). 65 were WHO Grade 4, 24 Grade 3, 17 Grade 2, 2 Grade 1, 1 metastatic-neuroblastoma, 1 anaplastic-medulloblastoma and 1 radiological diagnosis of high-grade-glioma. 14% (32) of consultations were in person (16 new, 7 consents, 9 attending for treatment); 86% (198) were telephone. 8 had concurrent chemo-radiotherapy, 22 radiotherapy alone, 64 chemotherapy alone, 15 had active-surveillance and 2 best-supportive-care. To minimise COVID-19 risk, 22.5% (25) had treatment altered: - A 76-year-old had a radiological diagnosis; - 4 had hypofractionated radiotherapy (30Gy in 6#) to minimise hospital visits; - 7 had no chemotherapy (5 were unmethylated /age, 2 patient choice); - 4 switched from PCV to Lomustine; - 11 stopped chemotherapy early; - 50% (36) were given prophylactic GCS-F; - No patients were recruited for trials. 19 reported possible COVID-19 symptoms – 7 had delays and 3 stopped treatment. 4 tested COVID-19 positive (although not all tested). 1 died of COVID-19 (off treatment). Review of March-April 2020 service showed similar new patient referrals compared to the same time in 2019 (16 and 19 respectively). CONCLUSION: Despite concern about decreasing new referrals during the pandemic, this wasn't the case for our service. 77.5% of patients had no treatment changes due to COVID-19 and all 22 patients on trial were able to continue treatment throughout this period.

COVD-04. REAL-WORLD PERSPECTIVES: TUMOR TREATING FIELDS (TTFIELDS) UTILITY TO OPTIMIZE TREATMENT OF PATIENTS WITH GLIOBLASTOMA (GBM) AMIDST COVID-19 PANDEMIC

Peggy Frongillo, Melissa Shackelford, and Lindsay Rain; Novocure Inc, New York, NY, USA

INTRODUCTION: Due to the unprecedented, COVID-19 pandemic and resulting health/safety guidelines, rapid-adjustments to treatment plans