Program Schedule
Poster viewing and social hour: 5:00 – 6:00pm
Welcome and opening remarks: 6:00 – 6:05pm
Platform presentations 1: 6:05 – 7:25pm
Break and additional poster viewing: 7:25 – 7:50pm
Platform presentations 2: 7:50 – 9:10 pm
Meeting adjourns: 9:10 pm

Platform Presentations 1

6:05 – 6:15 Presenter: Erik Ladomersky
Department and Institution: Department of Neurological Surgery, Northwestern University
Title: IDO1 inhibition synergizes with radiation and pd1 blockade to durably increase survival against advanced GBM
Category: Immunotherapy
Abstract: We evaluated a triple immunotherapeutic approach that combines IDO1 enzyme inhibition, PD-1 blockade and whole brain radiation (WBRT) in syngeneic, immunocompetent mouse models of GBM. Our results demonstrate a robust survival benefit in immunocompetent GBM models after triple treatment with IDO1i, RT and PD-1 blockade, but not for any single- or dual-agent combination. These data also form the basis of a soon-to-open, phase I/II trial evaluating the simultaneous treatment with IDOl1, RT and PD-1 blockade in GBM patients at our institution.

6:15 – 6:25 Presenter: Chunzhang Yang
Department and Institution: Neuro-Oncology Branch, National Cancer Institute
Title: Microenvironment-derived mitochondria prime glioma vhemoresistance by augmenting NAD+ metabolism and PARP-dependent DNA repair
Category: Tumor microenvironment, angiogenesis, epigenetics
Abstract: We demonstrate that mitochondria are released from normal astrocytes through extracellular vesicles, and are adopted by neighboring glioma cells. Mitochondrial transfer not only improves oxidative metabolism in recipient glioma cells, but also supports the detoxification of chemotherapeutic agents by fueling PARP-dependent DNA repair with ATP and NAD+. Targeting astrocyte mitochondria-releasing pathways increased the cytotoxic effects of chemotherapy, reduced xenograft progression, and prolonged overall survival.

6:25 – 6:35 Presenter: Shuli Xia
Department and Institution: Neurology, Johns Hopkins
Title: Heterozygous IDH1 mutR132H/WT created by single base editing inhibits human astroglial growth by downregulating YAP
Category: Tumor Microenvironment, Angiogenesis and Epigenetics
Abstract: We employed a modified CRISPR/Cas9 genome editing technique called "single base editing", and efficiently (20%) introduced heterozygous IDHI R132H mutation in human astroglial cells. We identified Yes-associated protein (YAP) and its downstream signaling pathway Notch to mediate biological functions of IDHI[R132H/WT]. Our isogenic cellular systems that differ in a single nucleotide in one allele of the IDH1 gene provide a valuable model for novel discoveries of IDHI[R132H/WT]-driven events.
6:35 – 6: 45 Presenter: Jian Hu  
**Department and Institution:** Cancer Biology, MD Anderson  
**Title:** The role of unsaturated fatty acids in regulating stemness of glioma cells  
**Category:** Cancer Stem Cells, Metabolism and Heterogeneity  
**Abstract:** GSCs are also able to sustain their stemness in the suboptimal environments they encounter outside their niches during invasion, however the underpinning mechanism of the maintenance of stemness in GSCs outside the niches remains unclear. To identify potential glioma suppressors that affect interaction of GSCs and niches, we discovered that RNA-binding protein Quaking (QKI) is a key regulator of endocytosis that controls receptor trafficking, degradation, and signaling desensitization. Mechanistically, QKI regulates pre-mRNA stability of genes that regulate lipid components of endolysosomes, particularly the unsaturated fatty acids (UFAs), and consequently we showed that depletion of QKI and inhibition of UFA biosynthesis led to the enrichment of cytoplasmic membrane-bound receptors that are required for maintaining stemness.

6: 45 – 6:55 Presenter: Yuxiang Wang  
**Department and Institution:** Radiation Oncology, Memorial Sloan Kettering  
**Title:** Therapeutically Exploiting the Intrinsic Deficiency of IDH1 Mutant Glioma  
**Category:** Novel Agents and Translational Approaches  
**Abstract:** I will present our new findings of promising agents that target IDH1 mutant tumors based on the concept of synthetic lethality, one regarding G-quadruplex and ATRX interaction, and the other regarding PARP inhibition for IDH1 mutant glioma and cholangiocarcinoma. I will introduce data from in vitro characterization, as well as various in vivo models including orthotopic xenografts and genetic engineered mice with RCAS gene delivery.

6:55 – 7:05 Presenter: Paul Kongkham  
**Department and Institution:** Neurosurgery, University of Toronto  
**Title:** 5-hydroxymethylcytosine profiling identifies differential targeting in IDH1 mutant vs IDH1 wild-type high-grade gliomas  
**Category:** Tumor Microenvironment, Angiogenesis and Epigenetics  
**Abstract:** 5-hydroxymethylcytosine (5hmC) represents a novel variant of DNA methylation, recently implicated in cancer including glioma pathogenesis. We performed a quantitative, locus-specific genome-wide screen of 5hmC in a cohort of IDH1 mutant versus IDH1 wild-type high-grade gliomas. Our study identified differential targeting of this epigenetic mark between IDH1 cohorts, with 5hmC targeting enhancer regions, contributing to overall ‘methylation’ of G-CIMP target genes, and associated with increased gene expression for genes overexpressed in IDH1 mutant tumors.

7:05 – 7:15 Presenter: Giselle Lopez  
**Department and Institution:** Pathology, University of California San Francisco  
**Title:** Genetic Landscape of Gliomas Arising After Therapeutic Radiation for Pediatric Malignancies  
**Category:** Other – Secondary Malignancies  
**Abstract:** Radiation-associated gliomas develop years after administration of craniospinal irradiation for other malignancies, and most commonly are high-grade astrocytomas that are highly aggressive. Targeted next-generation sequencing of 12 gliomas arising after therapeutic radiation for other childhood cancers revealed a high frequency of TP53 mutation and BRAF gene fusions, along with multiple genomic amplifications per tumor commonly including PDGFRA, MET, and CDK4, while lacking alterations in several class-defining genes including IDH1/2, EGFR, PTEN, TERT promoter, H3F3A, and HIST1H3B. In combination with a pattern of frequent intrachromosomal breaks often resembling the chromosome shattering that has been termed chromothripsis, these findings suggest that radiation-associated gliomas represent a distinct molecular subgroup of gliomas that may benefit from different treatment modalities and targeted therapies than spontaneous gliomas.

7: 15- 7:25 Presenter: Shiv Gupta  
**Department and Institution:** Radiation Oncology, Mayo Clinic - Rochester  
**Title:** Metabolic vulnerabilities in IDH1 mutant glioblastoma prevent in vivo TMZ sensitizing efficacy of veliparib  
**Category:** Novel Agents and Translational Approaches  
**Abstract:** 2-Hydroxy glutarate production in IDH mutant tumors decreases homologous recombination efficiency, thus providing strong rationale for evaluation of PARP inhibitors in IDH-mutant gliomas. Using PDX models
established from IDH1 mutant glioblastoma patients, we have investigated single agent activity of veliparib and its combinatorial effect with TMZ. Findings from our in vitro and in vivo studies suggest that despite HR deficiency, metabolic vulnerabilities in 1DH-mutant cells act against therapeutic potential of PARP inhibitors.

7:25 – 7:50: Break for Refreshments and Additional Poster Viewing

Platform Presentations 2

7:50 – 8:00 Presenter: Simone Sredni
Department and Institution: Neurosurgery, Lurie Children’s Hospital
Title: Inhibiting PLK4: A new therapeutic option for embryonal brain tumors
Category: Pediatric Tumors
Abstract: We performed a partial functional screening of the kinome by individually mutating 160 kinases in a well-characterized rhabdoid tumor (RT) cell line using lentiviral CRISPR/Cas9, and observed that the polo-like kinase 4 (PLK4) - a critical regulator of centriole duplication and consequently mitotic progression - was the kinase gene that, when edited, resulted in the most significant impairment of cell proliferation. Follow up studies showed upregulation of PLK4 in RT, MB and other embryonal brain tumors. An orally bioavailable small molecule, PLK4 inhibitor, was tested in multiple embryonal tumor cell lines, as well as in an orthotopic xenograft model of AT/RT demonstrating: (1) impairment of cell proliferation, viability, migration and invasion; (2) induction of apoptosis, senescence and polyploidy increasing tumor cell susceptibility to DNA-damaging agents in vitro and (3) efficacy in vivo.

8:00 – 8:10 Presenter: Dusten Unruh
Department and Institution: Neurological Surgery, Northwestern
Title: Methylation-dependent suppression of tissue factor is a key contributor to the less aggressive phenotype of IDH1 mutant gliomas
Category: CNS Metastases, Tumor Microenvironment, Angiogenesis, and Epigenetics
Abstract: Gliomas with isocitrate dehydrogenase 1 mutations (IDH1mut) are much less malignant than gliomas wild-type for this mutation (IDH1wt), though the basis for this is still unclear. Our data indicate that suppression of the promalignant protein, Tissue Factor (TF), and signaling via the TF receptor, protease-activated receptor 2 (PAR2), contribute to the less aggressive nature of IDH1mut gliomas. Furthermore, a small molecule inhibitor of TF-PAR2 signaling shows promise as a novel therapeutic strategy, especially in aggressive IDH1wt gliomas with high TF-PAR2 activity.

8:10 – 8:20 Presenter: Elizabeth Pluhar
Department and Institution: Veterinary Clinical Sciences, University of Minnesota
Title: CD200 (OX2) peptide enhances the response to vaccine-based immunotherapy in dogs with high-grade glioma
Category: Novel Agents and Translational Approaches
Abstract: We developed a novel checkpoint blockade (CD200) inhibitor, a peptide of the native molecule, which overrides CD200 immunosuppression in CNS tumors. We added this peptide to our tumor lysate vaccines to enhance the immune response allowing for normal T- and antigen presenting cell activity in a spontaneous large animal model of high-grade glioma, pet dogs with naturally occurring disease. Addition of the peptide to autologous tumor lysate vaccines resulted in regression of residual tumor after surgery, radiographic evidence of an immune response and significantly longer survival times compared to lysate vaccines alone.

8:20 – 8:30 Presenter: Xiaolong Li
Department and Institution: Neuro-Oncology, MD Anderson
Title: The FGFR1-Tie2 interaction induces acquired PI3K inhibitor resistance through Aurora kinases/Plk1/CDK signaling in GBM
Category: Other – drug resistance
Abstract: In this study, we established an in vivo intracranial mice xenograft GSC (Glioma Stem-like Cells) model of PI3K inhibitor resistance. By integrating RNA-seq and high throughput drug screening data, we efficiently ruled
out the noises of non-specific gene alterations, and precisely identified the most specific signaling pathway and effective drug combinations to overcome the resistance in vitro and in vivo. Further studies showed that the interaction of FGFR1 with Tie2 promotes Aurora kinases expression through phosphorylation of STAT3 in the resistant GSCs serves as a survival signal upon P13K inhibition in GBM.

8:30 – 8:40 Presenter: Chirag Patel
Department and Institution: Neurology, Stanford
Title: TTFIELDS induces changes in GBM metabolism as measured by [18F]DASA-23
Category: Cancer Stem Cells, Metabolism, and Heterogeneity
Abstract: Tumor treating fields (TTFIELDS) is emerging as the fourth therapeutic modality in glioblastoma (GBM), but its effects on cancer metabolism are not well understood; pyruvate kinase M2 (PKM2) is a key enzyme involved in the glycolytic reprogramming of GBM. Human GBM cells were exposed or unexposed to 200 kHz TTFIELDS for 3 days, followed by evaluation of cellular uptake of [18F]DASA-23, a PKM2-specific radiopharmaceutical. There was a significant reduction in the cellular uptake of [18F]DASA-23 and PKM2 expression after 3 days of TTFIELDS compared to control, indicating the potential for non-invasive measurement of PKM2 expression with [18F]DASA-23 to serve as an early imaging biomarker of alterations in GBM metabolism.

8:40 – 8:50 Presenter: Lawrence Lamb
Department and Institution: Hematology & Oncology, University of Alabama Birmingham
Title: The combination of chemotherapy and gene-modified cell therapy for eradication primary GBM following resection and standard radiation + temozolomide
Category: Cell and Virus-based Therapies
Abstract: We will present a new Phase I clinical protocol to test a novel combination of temozolomide (TMZ) chemotherapy and MGMT-modified γ6 T cells administered simultaneously during maintenance phase TMZ for primary GBM. This approach, which has shown a significant improvement in disease-free survival in James primary and TMZ-resistant xenograft models, is designed to leverage TMZ-induced NKG2D-ligands (NKG2DL) upregulation on glioma cells and glioma stem cells while targeting with TMZ-resistant γ6 T cells that recognize NKG2DL via the γ6-T cell receptor and surface NKG2D. Data from animal models and significant components of the clinical trial and cell manufacturing protocols will be presented.

8:50 – 9:00 Presenter: Saumya Bollam
Department and Institution: Translational Genomics Research Institute (TGEN)
Title: Targeting the TERT promoter mutation for treatment in glioblastoma
Category: Immunotherapy
Abstract: Approximately 86% of primary glioblastomas present with a hotspot mutation 124bp or 146bp upstream from the ATG start site of telomerase reverse transcriptase (TERT). These mutations result in misfolding the G-quadruplex structure which naturally occurs in the wild-type TERT promoter. Using a pharmacological chaperone molecule that selectively restores the natural G-quadruplex structure of the TERT promoter, we demonstrate a novel approach to targeting this genetic vulnerability of glioblastoma.

9:00 – 9:10 Presenter: Wataru Ishida
Department and Institution: Department of Neurosurgery, Johns Hopkins
Title: In vivo synergistic effect of checkpoint blockade and RT against chordomas in a humanized mouse model
Category: Immunotherapy
Abstract: Currently, there are no well-established murine chordoma cell lines or transgenic mouse chordoma, which prevents us from investigating the interaction between murine chordomas and murine immune cells, and thus, the development of a humanized mouse model of chordomas, where human thymus and CD34+ stem cells as well as human chordomas are co-transplanted to engraft human immune system into mice, is imperative to scrutinize immunotherapy (IT) against chordoma. We aimed to develop this model and investigate synergistic effect between IT and radiation therapy (RT) against chordomas using this model. Based on our analyses such as tumor volume measurement, flow cytometry of blood and tumor infiltrating lymphocytes, qRT-PCR, and immunohistochemistry in these humanized mice, we demonstrated that this humanized mouse model could be a revolutionary platform to investigate IT against rare cancers such as chordomas and the direct synergistic effect between IT and RT against chordoma as well as potential abscopal effect was observed in this study.

9:10 Meeting Adjourns
Poster Presentations

IMM – 01 Presenter: Jason Miska
Department and Institution: Neurological Surgery, Northwestern
Title: HIF1a directs regulatory T-cells metabolism towards lipid oxidation in glioblastoma
Category: Immunotherapy
Abstract
1. Regulatory T-cells depend on lipid oxidation for immunosuppression in glioblastoma
2. Hypoxia inducible Factor 1a is responsible for lipid metabolic choices by Regulatory T-cells
3. Targeting lipid metabolic pathways may be advantageous for promoting immunity against GBM

IMM – 02 Presenter: Natacha Le Moan
Department and Institution: Omniox Inc.
Title: The oxygen carrier OMX restores anti-tumor immunity and when combined with checkpoint inhibitors improves anti-tumor efficacy in GL261 orthotopic tumor model
Category: Immunotherapy
Abstract
Hypoxia promotes immune tolerance by altering the recruitment and function of innate and adaptive immune effector and suppressor cells in the tumor microenvironment. Therefore, activating tumor immune microenvironment by reversing tumor hypoxia provides an attractive combinatorial approach to improve immunotherapy response in solid tumors. Our data in late-stage GL261 brain tumor-bearing mice, in which the aPD-1 therapy is ineffective, show that by delivering oxygen to hypoxic tumor regions, the oxygen carrier OMX immunosensitizes tumor microenvironment (increases CTL infiltration, proliferation and cytotoxic activity, and secretion of IFN-γ-related inflammatory cytokines), leading to tumor responses and cures.

IMM – 03 Presenter: Zhihua Chen
Department and Institution: School of Medicine, Shanghai Jiao Tong University
Title: Immune system response to mTOR inhibitor combined with PD-I inhibitor therapy to recurrent glioblastoma
Category: Immunotherapy
Abstract
Target and PD-1 inhibitor combination therapy lead to strong immune system activation and tumor lysis response for recurrent GBM. A large number of activated T cells and T memory cells, B cells, NK cells present in tumor lesion, without T reg cells. IL-6, IL-8, MCP-1, SDF-1, M1P-1beta, GRO-a, IP-10, RANTES, IFN-gamma significantly elevate in the treatment period, and 1L-5, 1L-9, IL-21, IL-22, 1L-23, IL-2, TNF-a/b, GM-CSF appear peak-changing.

IMM – 04 Presenter: Irina Balyasnikova
Department and Institution: Neurological Surgery, Northwestern
Title: Challenges and Advances in CAR T cell Therapy for Glioblastoma
Category: Immunotherapy
Abstract
The outstanding efficacy of chimeric antigen receptor (CAR)-modified T cells against hematological malignancies brings hope that they can be programmed to target solid tumors like malignant glioma (MG), the most common type of brain tumor. Preclinical models and early phase clinical studies demonstrate the feasibility of this approach for patients with MG. However, challenges, such as the limited persistence of T cells, immunosuppressive tumor environment, antigen escape, and inefficiency of T cell trafficking to tumors after systemic delivery, need to be overcome for the successful translation of CAR T cell therapy into the clinic.

IMM – 05 Presenter: Lijie Zhai
Department and Institution: Neurological Surgery, Northwestern
Title: Non-enzyme IDO1 activity and its immunosuppressive effects in glioblastoma
Category: Immunotherapy
Abstract
Indoleamine 2,3 dioxygenase 1 (IDO1), the rate-limiting tryptophan catabolic enzyme, has been reported as a pivotal regulator in GBM immunosuppression. Accumulating evidence has indicated that tumor cell-derived IDO1 may exert its suppressive function via an enzyme-independent mechanism. This preliminary study further tests the non-enzymatic hypothesis of IDO1’s immunosuppressive role by dissecting the underlying molecular and biochemical mechanisms.
IMM – 06 Presenter: Yvonne Reiss  
**Department and Institution:** Institute of Neurology / Edinger Institute, Goethe University  
**Title:** Improved survival and immunostimulatory reprogramming in a preclinical glioblastoma model by combining anti-angiogenic with immune checkpoint therapy  
**Category:** Immunotherapy  
**Abstract:** We provide evidence that checkpoint inhibition in a preclinical GBM model led to significantly extended survival post dual anti-VEGF and Ang-2 therapy by creating an immunostimulatory microenvironment with enriched CD8+ IFN-γ expressing cytotoxic T lymphocytes and abated immunosuppressive MDSC and FoxP3+ T reg cells. Moreover, anti-angiogenic therapy led to vascular normalization at the morphological and gene expression level that was further enhanced by anti-PD-1 therapy.

MAE – 01 Presenter: Viive Howell  
**Department and Institution:** Neuro-Oncology, University of Sydney  
**Title:** Glioblastoma progression correlates with an increased immunosuppressive microenvironment  
**Category:** Tumor Microenvironment, Angiogenesis and Epigenetics  
**Abstract:** To understand how glioblastomas adapt to withstand the pressures of treatment, leading inevitably to progression, we undertook molecular profiling of 19 matched pre- and post-treatment glioblastomas and in vitro studies. Our finding of increased expression post-treatment of M2 macrophage markers points to an increasingly immunosuppressive microenvironment post-treatment that favors tumor aggression and progression, and suggests that immune-altering therapies may be of value in recurrent disease.

MAE – 02 Presenter: Paul Clark  
**Department and Institution:** Neurosurgery, University of Wisconsin  
**Title:** Neurovascular-targeting antibodies discovered using yeast biopanning enhance drug delivery and improve survival for glioblastoma  
**Category:** Tumor Microenvironment, Angiogenesis and Epigenetics  
**Abstract:** Targeting antigens of the neurovascular extracellular matrix (nvECM) within GBM-disrupted blood-brain barrier (BBB) may localize and enhance efficacy of therapeutic agents. Using yeast biopanning techniques, we identified multiple nvECM antibodies that were used via combination with chemotherapeutic doxorubicin (DOX) liposomes. Administration of nvECM-DOX liposomes significantly improve d survival of mice bearing U87 orthotopic xenografts, compared to non-targeted antibody-DOX (Kaplan-Meier, p<0.01), and therefore this approach could potentially be used to enhance drug delivery and improve survival for GBM patients.

MAE – 03 Presenter: Catalina Lee-Chang  
**Department and Institution:** Neurological Surgery, Northwestern  
**Title:** Identification of glioma-associated regulatory B cells  
**Category:** Tumor Microenvironment, Angiogenesis and Epigenetics  
**Abstract:** This fundamental work describes the existence of glioma-supporting regulatory B cells in two different glioma experimental model, GL261 and CT2A. Glioma-associated B cells are a unique B-cell subset that produce immunoregulatory cytokines IL-10, TGFB and IL35; and inhibitory ligands PD-L1 and the polivirus receptor CD155. They interact with activated CD8 T cells and strongly suppress their expansion and cytotoxic function, suggestive of their pro-tumorigenic function.

MAE – 04 Presenter: Zhihua Chen  
**Department and Institution:** School of Medicine, Shanghai Jiao Tong University  
**Title:** Characterizing the immune microenvironment in cystic glioblastoma  
**Category:** Tumor Microenvironment, Angiogenesis and Epigenetics  
**Abstract:** We found overall survival time in cystic GBM group is longer than noncystic group. Cystic GBM are PTEN strong positive, CD3, CD4, CD8 surrounding vessel and infiltrate in to tumor, PD-L1+ expression rate is higher than noncystic GBM group. Active T cells subtypes in cystic fluid are higher than in patient's self-control blood. T memory cells, not Treg cells, exist in the cystic fluid, MDSC populations are lower in cyst fluid than in blood. 8 cytokines in cystic are higher than in blood, 10 cytokines only exist in cyst, CCLS exist both in cyst and blood of cystic GBM patient, IL-10/22 are non-existent.
MAE – 05 Presenter: Edgar Gonzalez-Buendia  
**Department and Institution:** Neurological Surgery, Northwestern  
**Title:** Development of biomarkers to personalize chemotherapy for glioblastoma  
**Category:** Tumor Microenvironment, Angiogenesis and Epigenetics  
**Abstract:**  
1. TOP2B regulates transcription in gliomas.  
2. Pharmacological targeting of TOP2 in gliomas can modulate PDGFRA and MYC expression.  
3. Expression baseline of oncogenes PDGFRA and MYC serve as biomarkers to predict susceptibility to TOP2 inhibitors therapy

SCMH – 01 Presenter: Tianzhi Huang  
**Department and Institution:** Neurology, Northwestern  
**Title:** Targeting oncogenic autophagy signaling in glioblastoma  
**Category:** Cancer Stem Cells, Metabolism and Heterogeneity  
**Abstract:**  
- MST4 (STK26) kinase is critical in GBM tumorigenicity and prognosis  
- MST4 phosphorylates ATG4B and induces autophagy  
- Target ATG4B enhanced anti-tumor activity of radiation therapy

SCMH – 02 Presenter: Anh Nhat Tran  
**Department and Institution:** Cell, Developmental and Integrative Biology, University of Alabama Birmingham  
**Title:** Glioblastoma, cancer stem cells and reactive species balances: a case for GTP cyclohydrolase 1  
**Category:** Cancer Stem Cells, Metabolism, and Heterogeneity  
**Abstract:** GTP cyclohydrolase 1 (GCH1), the first and rate-limiting enzyme of the pathway producing of NOS cofactor producing pathway, play important roles in GBM stem cell phenotypes via redox balances. Upregulation of GCH1 in GSCs promotes tumor maintenance and is a key regulator of reactive oxygen species in GBM, and GCH1 pathway is a potential target for therapy.

SCMH – 03 Presenter: Catherine Libby  
**Department and Institution:** Cell, Developmental, & Integrative Biology, University of Alabama Birmingham  
**Title:** Novel glucose transport inhibitors decrease GBM growth in vitro  
**Category:** Cancer Stem Cells, Metabolism, and Heterogeneity  
**Abstract:** Therapeutic development for GBM has been hindered by the high degree of heterogeneity within these tumors, which is partially attributed to a subset of tumor cells known as brain tumor initiating cells (BTICs). BTICs express elevated levels of GLUT3 and this allows them to better survive in low nutrient tumor microenvironments, leading to tumor promotion and progression. Through structure based virtual screening, we identified potential novel GLUT inhibitors that can preferentially inhibit the growth and glucose uptake of BTICs with minimal toxicity to non-malignant cells.

SCMH – 04 Presenter: Lindsay Stetson  
**Department and Institution:** Center for Proteomics and Bioinformatics, Case Western  
**Title:** Profiles of protein heterogeneity and invasiveness in glioblastoma  
**Category:** Cancer Stem Cells, Metabolism, and Heterogeneity  
**Abstract:** While protein markers are an effective readout of cellular function and an effective marker of tumor heterogeneity, high-throughput proteomics have been under-utilized in glioblastoma (GBM) research. GBM patients were prospectively recruited (Ohio Brain Tumor Study) and proteomics discovery using liquid chromatography mass spectrometry analysis (LC MS/MS) was performed in a discovery set of 27 patients including 13 short-term survivors (< 9 months, STS) and 14 long-term survivors (≥ 18 months, LTS). In order to further study and demonstrate the heterogeneous distribution of our discovered prognostic proteins and other GBM biomarkers/drug targets we performed LC MS/MS on 18 GBM samples micro-dissected from distinct portions of n=6 patient tumors.
SCMH – 05 Presenter: Ana DeCarvalho  
**Department and Institution:** Neurosurgery, Henry Ford Hospital  
**Title:** Integrated molecular analysis of longitudinal glioblastoma samples  
**Category:** Cancer Stem Cells, Metabolism, and Heterogeneity  
**Abstract:** Dynamic clonal evolution based on exonic SNV was determined for 8 samples derived from the same patient. These data were integrated with copy number alteration, DNA methylation (EPIC), transcriptome and targeted proteomics for a complex picture of molecular changes and clonal composition over time and upon microenvironmental changes.

SCMH – 06 Presenter: Joseph McAbee  
**Department and Institution:** National Cancer Institute, University of Cambridge  
**Title:** Influence of radiation on the evolution of orthotopic xenografts initiated from glioblastoma stem-like cells  
**Category:** Cancer Stem Cells, Metabolism and Heterogeneity  
**Abstract:** This study seeks to better understand the impact of radiotherapy on GBM evolution by investigating changes that occur following irradiation of brain tumor xenografts initiated from glioma stem-like cells (GSCs) in nude mice. In addition to providing a significant survival advantage (+34.2 days), we observed that radiation led to histologic changes in invasion patterns and a reduction in the overall number of clones detected by viral integration site analysis when compared to control tumors and in vitro tumor lines. Our results demonstrate that radiation, a treatment component for almost all glioblastoma patients, can have wide-ranging effects on the evolution of this dynamic tumor which may have future implications for tumor evolution and the treatment of recurrent GBM.

SCMH – 07 Presenter: Subhas Mukherjee  
**Department and Institution:** Pathology, Northwestern  
**Title:** CDK5 inhibition attenuates self-renewal of brain tumor stem cells  
**Category:** Cancer Stem Cells, Metabolism and Heterogeneity  
**Abstract:** Glioma stem cells are biologically potent and support GBM tumor growth, in part by deregulating asymmetric stem cell division and self-renewal. Using Drosophila brain tumor model, human GSCs isolated from tumor spheres and mouse xenografts, we found that CDK5 suppression promotes neurogenesis and CDK5 directly phosphorylates CREB 1 independent of cAMP and stops stem cell renewal. A highly specific CDK5 inhibitor such as CP681301 could potentially become a better treatment strategy for patients and improve their cognitive function as well.

PED – 01 Presenter: Harpreet Kaur  
**Department and Institution:** Pediatric Oncology, Johns Hopkins  
**Title:** Targeting the lethal pediatric ATRTs with the DNA minor-groove binding agent quinacrine  
**Category:** Pediatric Tumors  
**Abstract:** Atypical teratoid/rhabdoid tumors (AT/RT) are rare, incurable, and highly proliferative pediatric brain tumors, warranting identification of novel therapeutic targets and improved therapies urgently. We found increased expression of the developmentally important, DNA-binding, oncofetal protein HMGA2 in AT/RT primary tumors and cell lines, and using loss of function approaches like shRNA-mediated reduction and pharmacological inhibition of HMGA2 by DNA minor groove binding agent quinacrine (anti-malarial, penetrates the brain at micromolar levels after oral administration, does not affect normal cells), we showed that disrupting HMGA2 increases apoptotic cell death and inhibits growth, proliferation, colony formation, and suppresses in vivo tumorigenicity in ATRT cell lines. Our studies are the first to use patient derived central nervous system (CNS) AT/RT cell lines to validate HMGA2 as a potential therapeutic target in AT/RT and the first to show that quinacrine and other minor groove binding agents can be effective therapeutics for HMGA2-expressing fatal pediatric AT/RT tumors.

PED – 02 Presenter: Sidharth Mahapatra  
**Department and Institution:** University of Nebraska, Omaha  
**Title:** MiR-1253, a putative tumor suppressor gene in medulloblastoma  
**Category:** Pediatric Tumors  
**Abstract:** MiR-1253, located on chromosome 17p, sustains high degree of silencing via hypermethylation in medulloblastoma. While de-methylation results in a recovery of tumor cell invasiveness, in the presence of miR-
1253 inhibitor, this effect is abolished. Restoring miR-1253 levels in vitro via transient transfection leads to a punctuated decline in medulloblastoma tumor cell viability, proliferation, migration, and invasion; in the presence of a specific miR-1253 inhibitor, this effect is lost.

**PED – 03 Presenter:** Nundia Louis  
**Department and Institution:** Neurological Surgery, Northwestern  
**Title:** DNA damage repair inhibition by chromatin modification in DIPG  
**Category:** Pediatric Tumors  
**Abstract** All patients who suffer from diffuse intrinsic pontine glioma (DIPG) show evidence of disease progression within months of completing focal radiation therapy, the only treatment that results in tumor shrinkage and symptomatic relief. We investigated the effects of the JMJD3 demethylase inhibitor, GSK-J4, on radiation-induced DNA damage repair in DIPG. The results of our investigation highlight GSK-J4 as a potential radiosensitizer in DIPG treatment.

**PED – 04 Presenter:** Sabrina Wang  
**Department and Institution:** Pediatric Oncology, Johns Hopkins  
**Title:** Disrupting glutamine metabolism depletes glutathione and sensitizes atypical teratoid/rhabdoid tumor to carboplatin  
**Category:** Pediatric Tumors  
**Abstract:** High MYC expression has recently been identified in an especially aggressive sub-group of AT/RT and has been shown to drive cancer cell reliance on glutamine for metabolic needs. We show that the glutamine metabolic inhibitor, 6-diazo-5-oxo-L-norleucine (DON) targets high MYC expressing AT/RT to slow cell growth, induce apoptosis, and deplete intra-cellular glutathione. Weekly intraperitoneal dosing of DON in high MYC expressing xenograft models of AT/RT nearly doubles survival, and DON combines synergistically in vitro with carboplatin to induce high rates of apoptosis and further slow AT/RT cell growth, suggesting that DON and carboplatin may be an efficacious therapy for AT/RT.

**PED – 05 Presenter:** Rachel Maynard  
**Department and Institution:** Pathology, Johns Hopkins  
**Title:** Tak228 shows combinatorial efficacy with carboplatin in MYC driven medulloblastoma  
**Category:** Pediatric Tumors  
**Abstract** To target mTOR in aggressive Medulloblastoma, we are using the TORC1/2 kinase inhibitor TAK228/sapanisertib. In MYC driven Medulloblastoma, we find that TAK228 suppresses both TORC1 and TORC2 targets including P-S6 and P-AKT(473) as well as inhibiting tumor growth and inducing apoptosis. MTO inhibition is known to deplete glutathione, and we find TAK228 shows combinatorial efficacy with Carboplatin suggesting that TAK228 may enhance the efficacy of traditional chemotherapy in Medulloblastoma.

**PED – 06 Presenter:** Antjie Arnold  
**Department and Institution:** Neuropathology, Johns Hopkins  
**Title:** Synergistic growth inhibitor effect on a patient derived NF1 pilocytic astrocytoma cell line with the dual mTORC1/2 inhibitor TAK228 and MEK inhibitor trametinib  
**Category:** Pediatric Tumors  
**Abstract** The combination of the dual mTORC1/2 inhibitor TAK228 and the FDA approved MEK inhibitor trametinib shows synergistic growth inhibition in pediatric low-grade glioma cell lines in vitro and in vivo. To our knowledge, our laboratory has derived the first non-genetic modified patient derived NF1 pilocytic astrocytoma cell line which shows synergistic growth inhibition in therapeutic relevant doses.

**PED – 07 Presenter:** Hope Robinson  
**Department and Institution:** Cancer Biology, Emory  
**Title:** HElls is up-regulated in Sonic hedgehog-associated medulloblastoma and proliferating cerebellar progenitors in a YAP-dependent manner  
**Category:** Pediatric Tumors  
**Abstract** In our studies of Sonic Hedgehog (SHH) induced medulloblastoma, we discovered elevated levels of HElls (Lymphoid specific helicase), a chromatin remodeler with multiple epigenetic functions. Importantly, YAP1 is a downstream effecter of SHH signaling and our further investigation revealed that upregulation of HElls could be modulated by treatment of primary cell culture with the YAP1 inhibitor Verteporfin. Future
studies to understand the function of HELLS in cerebellar development and in medulloblastoma have the potential to provide a better understanding of the epigenetic processes underlying SHH driven medulloblastoma.

**PED – 08 Presenter:** Hiroaki Katagi  
**Department and Institution:** Neurological Surgery, Northwestern  
**Title:** Targeted inhibition of JMJD3 and BET bromodomain proteins for the treatment of diffuse intrinsic pontine gliomas  
**Category:** Pediatric Tumors  
**Abstract:** We have shown that the JMJD3 demethylase inhibitor, GSKJ4, acts to restore K27 methylation in DIPG cells, while demonstrating potent anti-tumor activity, in vitro and in vivo. In addition to H3K27 methylation, increase level of H3K27 acetylation and bromodomain proteins in K27M-containing nucleosomes suggests that inhibitor of BET bromodomain protein 4 (BRD4), JQI, could be useful for the treatment of K27M DIPG. The results of our investigation highlight the combined GSKJ4 + JQI have greater anti-tumor activity in vitro and in vivo than either monotherapy and reduce the likelihood of drug resistance.

**PED – 09 Presenter:** Anup Pathania  
**Department and Institution:** Pediatrics, Children’s Hospital of Los Angeles  
**Title:** PID1, a novel brain tumor growth suppressor, is a target for phosphorylation by a newly identified binding partner  
**Category:** Pediatric Tumors  
**Abstract:** In 2014, our group established the link between PID1 and cancer for the first time, and showed its tumor inhibitory effect in pediatric brain tumor cell lines and direct correlations with patient survival. In this study, we found a novel interacting protein binding partner of PID1, GRK2, that binds and phosphorylates PID1, firstly identified by prediction algorithms, confirmed by in vitro kinase assays and followed by co-IPs in 293FT cells and in native pediatric glioblastoma (CHLA-07-BSGBM cells). siGRK2 caused a poptosis in MEFs, medulloblastoma and glioma cells, that was mitigated in Pid1 ko compared to Pid1 wt MEFs, suggesting that PID1 functions downstream of GRK2 to negatively regulate its pro-survival effect.

**PED – 10 Presenter:** Xingyao He  
**Department and Institution:** Neurological Surgery, Northwestern  
**Title:** New therapeutic approach for brainstem glioma: Intranasal delivery of nanoliposomal SN-38  
**Category:** Pediatric Tumors  
**Abstract:** Intranasal delivery (ND) is a practical, noninvasive method to deliver therapeutic agents into the brain along with the olfactory and trigeminal nerves pathway, with the advantages of reducing systemic side effects and convenient self-administration for patients. In vitro and in vivo experiments were carried out using nanoliposomal SN38 (LS-SN38) compared with nanoliposomal CPT11 (LS-CPT11) treating DIPG models. Results indicate the potential of IND of LS-SN38 being a new therapeutic approach for brainstem glioma.

**PED – 11 Presenter:** Allison Hanaford  
**Department and Institution:** Pathology, Johns Hopkins  
**Title:** In vivo metabolomics reveals a potentially potent combination therapy for MYC-driven medulloblastoma  
**Category:** Pediatric Tumors  
**Abstract:** The glutamine analog 6-diaz0-5-oxo-l-norleucine increases apoptosis in MYC-driven medulloblastoma tumors and increases the survival of orthotopic xenograft bearing animals. Stable isotope in vivo flux metabolomic analysis of DON-treated MYC-driven medulloblastoma tumors showed decreased levels of asparagine, suggesting that DON therapy could be combined with asparaginase for increased anti-tumor efficacy. L-asparaginase effectively penetrates the brain, and we find that treatment with the combination of low-dose DON and asparaginase causes significantly more apoptosis than treatment with either drug alone via activation of the amino acid response pathway, suggesting a novel, metabolism-based approach to MYC-driven medulloblastoma therapy.

**PED – 12 Presenter:** Maria Tsoli  
**Department and Institution:** Lowy Cancer Research Centre, University of New South Wales  
**Title:** Integrated genomics — drug screening and personalised xenograft development approach to identify precision treatments for aggressive paediatric brain tumours.  
**Category:** Pediatric Tumors
Abstract: Brain tumors represent the most common solid tumor of childhood and account for significant morbidity and mortality. Personalized medicine approaches have the potential to enhance diagnostic, prognostic and/or therapeutic information. The TARGET study focused on the development of a comprehensive genomic platform, combined with high throughput drug screening (HTS), and PDX models to identify personalized therapies for patients with aggressive pediatric tumours. 59 patients were enrolled of which 28 had brain tumours. The use of the comprehensive platform significantly increased discovery of actionable findings compared with testing for somatic DNA mutations alone. An integrated approach based on genomic, in vitro and in vivo drug efficacy testing is useful to guide the management of aggressive pediatric brain tumours.

PED – 13 Presenter: Maria Tsoli
Department and Institution: Lowy Cancer Research Centre, University of New South Wales
Title: Targeting the polyamine pathway as a novel therapeutic treatment against Diffuse Intrinsic Pontine Glioma
Category: Pediatric Tumors
Abstract: Diffuse intrinsic pontine glioma (DIPG) is an incurable pediatric brainstem tumor. We found that the polyamine pathway is an important driver of DIPG tumor growth. Using a strategy of dual targeting of the polyamine pathway, by inhibiting polyamine synthesis, and blocking polyamine cellular uptake we were able to potently block DIPG growth with unprecedented activity seen in our highly aggressive DIPG orthotopic animal models. A clinical trial based on this powerful new anti-DIPG treatment is being planned.

PED – 14 Presenter: Huizi Guo
Department and Institution: Psychological and Brain Sciences, Johns Hopkins
Title: The minor groove binding agent quinacrine inhibits growth and increases apoptotic death in diffuse intrinsic pontine glioma cells
Category: Pediatric Tumors
Abstract: Diffuse intrinsic pontine glioma (DIPG) is an invasive, incurable and aggressive pediatric brain tumor found in the brainstem, necessitating development of novel treatments urgently. Based on our group’s previous results that shRNA-mediated inhibition of the DNA binding stem cell factor HMGA2 (high protein levels in DIPG) decreases proliferation and increases apoptosis in DIPG cell lines, we show here that inhibiting HMGA proteins using minor groove binding agents like quinacrine increase apoptotic cell death (cleaved caspase-3 and cleaved PARP) and inhibit proliferation (BrdU incorporation) of DIPG cell lines in a dose-dependent manner. Our results suggest that quinacrine and other minor groove-binding agents may be effective therapeutics for HMGA2-expressing DIPG tumors.

NNT – 01 Presenter: Rimas Lukas
Department and Institution: Neurology, Northwestern
Title: Advanced tryptophan imaging in glioblastoma patients treated with Indoximod
Category: Neuroimaging and Novel Technologies
Abstract: The enzyme indoleamine 2,3 dioxygenase (IDO1) coverts tryptophan to kynurenine, which contributes to the immunosuppressive tumor microenvironment via a number of mechanisms. PET imaging utilizing the tryptophan analog, a-[11C]-methyl-L-Trp (AMT), can be utilized to monitor and visualize tryptophan metabolism in patients with glioblastoma. We present pre- and post-treatment AMT-PET and corresponding MRI images which may help delineate areas with true vs. pseudo-progression in patients with recurrent glioblastoma treated with the tryptophan mimetic indoximod for inhibition of the IDO pathway.

NNT – 02 Presenter: David Kamson
Department and Institution: Neurology, University of Chicago
Title: Imaging correlates of autopsy findings in glioblastoma patients treated with bevacizumab
Category: Neuroimaging and Novel Technologies
Abstract: It is a presentation of 3 GBM patients who received 6 or more cycles of bevacizumab and had autopsies. MRI and autopsy results were correlated and showed tumor infiltration, even solid tumor beyond abnormalities detected by T1w-gadolinium enhanced images or FLAIR. ADC maps provided minimal additional information with highly reduced ADC being consistent with tumor and highly increased ADC suggesting tissue injury without tumor infiltration.
NNT – 03 Presenter: Carlen Yuen  
Department and Institution: Neurology, University of Chicago  
Title: Patient Parameters associated with Tumor Growth in Incidental Meningiomas  
Category: Neuroimaging and Novel Technologies  
Abstract: This study aims to evaluate a set of patient characteristics for predicting tumor growth and to assess whether or not these characteristics may provide added information to radiographic data for the prediction of progression free survival (PFS). Our preliminary data suggests that population data such as age, gender, height and BMI may have value independent of radiographic characteristics to predict progression in incidental meningiomas. Of these parameters, BMI is a modifiable risk factor and weight loss could be evaluated as a potential intervention to slow meningioma growth.

NNT – 04 Presenter: Ze’ev Bomzon  
Department and Institution: Novocure  
Title: Of Fields and of Phantoms: Using Numerical Simulations to Improve Delivery of Tumor Treating Fields (TTFields)  
Category: Neuroimaging and Novel Technologies  
Abstract:  
- Overview on the fundamentals of simulating TTFields distribution with the brain.  
- TTFields distribution within the brain is heterogeneous and depends on the patient anatomy and the position of transducer arrays on the scalp.  
- A recent study utilizing numerical simulations of TTFields distributions within a large patient population suggests that delivery of high TTField intensities to the tumor is associated with improved patient outcome.

NNT – 05 Presenter: Moshe Giladi  
Department and Institution: Novocure  
Title: Two decades of tumor treating fields (TTFields) research - insights into the mechanisms of action  
Category: Neuroimaging and Novel Technologies  
Abstract:  
- TTFields act on microtubules and septin fibers to induce mitotic catastrophe, which could result in mitotic cell death, or the formation of abnormal daughter cells.  
- The resulting daughter cells express cellular stress and cell death of various form: endoplasmic reticulum stress, autophagy, immunogenic cell death and caspase independent cell death.  
- Beyond mitosis: TTFields inhibit DNA damage repair by altering homologous recombination of DNA repair genes in the BRCA1 pathway; impairing cell migration and invasion by inhibiting MMP via NF-KB pathways; and dysregulation of epithelial-to-mesenchymal transition-related genes.

NNT – 06 Presenter: Nikola Mikic  
Department and Institution: Neurosurgery, Aarhus University  
Title: Optimal array layouts for tumor treating field therapy oblique array layouts are superior to standard LR and AP positions.  
Category: Neuroimaging and Novel Technologies  
Abstract: We used computer modeling to investigate the impact of systematic changes in the array layout for tumor treating field distribution in the head of GBM patients. We found that electrode -edge effects" were highly important determinants of the effectiveness of the individual layouts and we identified a single oblique array configuration, which was effective for most tumor positions. Using this oblique layout, field intensities were 30-40% higher compared to the standard anterior/posterior and left/right positions.

NATA – 01 Presenter: Erin Smithberger  
Department and Institution: Pathobiology and Translational Science, University of North Carolina  
Title: Kinome profiling of non-germline, genetically engineered mouse models of glioblastoma driven by Cdkn2a, Egrf, and/or Pten mutations reveals genotype-dependent kinase targets  
Category: Novel Agents and Translational Approaches  
Abstract: Glioblastoma is difficult to treat for many reasons including intratumoral heterogeneity and acquired treatment resistance, both of which can be related to differences in cell genotypes. To investigate the consequences of these varying genotypes, we used RNA sequencing, multiplex inhibitor bead/mass
spectrometry (MIB-MS), and various imaging techniques to identify differences in cell signaling and drug response. We found several potential targets that are differentially expressed or activated that could be used to personalize treatment and/or develop combination therapies to target drug resistance.

NATA – 02 Presenter: Damian Almiron  
Department and Institution: Molecular and Systems Biology, Dartmouth  
Title: Benztropine enhances temozolomide sensitivity by restricting the growth of drug-resistant glioma stem cells  
Category: Novel Agents and Translational Approaches  
Abstract: Glioblastomas (GBMs) are characterized by the presence of primitive glioma stem-like cell subpopulations that resist chemotherapy and sustain disease progression. In this study, we found that Benztropine, a muscarinic acetylcholine receptor (mAChR) inhibitor, suppresses glioma cell proliferation and sensitizes these cells to treatment with Temozolomide. Our results suggest that Benztropine might be targeting glioma stem cells by altering the glioma stem cell microenvironment supporting a potential role for the use of adjuvant Benztropine for the clinical management of GBM.

NATA – 03 Presenter: Abhinav Dey  
Department and Institution: Pediatric Oncology, Emory  
Title: Applications of Organotypic Slice Cultures in Precision Medicine and Diagnostics  
Category: Novel Agents and Translational Approaches  
Abstract: For the childhood brain tumors that are refractory to standard therapy, there is an unmet need to rapidly identify and validate effective new tumor-targeting combination therapies for clinical investigation. The current paradigm for personalized pre-clinical drug screening is either incapable of mimicking the tumor microenvironment or is exceedingly slow due to the time required to develop patient-derived xenograft mouse models. To address these roadblocks, we are employing organotypic slice cultures derived from genetically engineered mouse models and human medulloblastoma patients to identify novel drug targets, to screen for inhibitors and to develop high-throughput drug screening devices.

NATA – 04 Presenter: Olga Gusyatiner  
Department and Institution: Swiss Institute of Bioinformatics, University of Lausanne  
Title: BET Inhibitors Synergize with HDAC Inhibitors and Down-Regulate Expression of Interferon Response Genes in Glioblastoma.  
Category: Novel Agents and Translational Approaches  
Abstract: In this project we aim at targeting enhancer elements, which are crucial for epigenetic regulation of gene expression, by small molecule inhibitors of BET proteins in various glioblastoma models. Interestingly, we show that BET inhibitors repress expression of interferon-stimulated genes in glioblastoma cells both in vitro and in vivo. Moreover, histone deacetylase inhibitors act synergistically with BET inhibitors to reduce viability of glioblastoma derived sphere lines.

NATA – 05 Presenter: Awah Chidiebere  
Department and Institution: Neurological Surgery, Northwestern  
Title: Development of biomarkers to personalize chemotherapy for glioblastoma  
Category: Novel Agents and Translational Approaches  
Abstract:  
1. We have developed a systematic unbiased approach for investigating potential biomarkers for etoposide susceptibility in gliomas, a drug that has shown promising yet unpredictable responses in these tumors.  
2. Our novel approach: We combined whole genome CRISPR KO with expression-susceptibility correlation analysis of glioma cell lines treated with etoposide.  
3. We discovered DNA-damage response and repair genes are over-represented among the genes that confer susceptibility to etoposide in the CRISPR screen. We found translation-related genes whose expression might serve as potential biomarkers for predicting etoposide susceptibility for this disease.

NATA – 06 Presenter: Uri Weinberg  
Department and Institution: Novocure  
Title: Overview of the clinical development of Tumor treating Fields  
Category: Novel Agents and Translational Approaches
Abstract

- Tumor Treating Fields (TTFields) are a non-invasive, regional antimitotic treatment modality, delivering alternating electric fields which predominantly disrupt the formation of the mitotic spindle in tumor cells.
- TTFields (200 kHz) have been demonstrated to extend overall survival in newly diagnosed glioblastoma patients in a phase 3 trial, and are approved by FDA for newly diagnosed and recurrent glioblastoma.
- TTFields have also been investigated in clinical studies in pancreatic, ovarian, lung and liver cancers, as well as in brain metastasis and mesothelioma.

NATA – 07 Presenter: Juliana Guimaraes  
Department and Institution: Federal Fluminense University  
Title: Ketogenic Diet with Concomitant Intranasal Perillyl Alcohol: Strategy Therapy for Delaying Growth of Recurrent Glioblastoma  
Category: Novel Agents and Translational Approaches  
Abstract: Glioblastoma (GBM) is a highly aggressive primary brain cancer that is difficult to treat. Perillyl alcohol (POH) is a non-toxic, naturally-occurring, hydroxylated monoterpene that exhibits cytotoxicity against temozolomide-resistant glioma cells, regardless of 06-methylguanine-methyltransferase promoter methylation status. This study aimed to evaluate the therapeutic efficacy of intranasal POH administered in combination with a ketogenic diet (KD) program for the treatment of patients with recurrent glioblastoma.

NATA – 08 Presenter: Varun Kumar  
Department and Institution: Bergen County Academies  
Title: The chemosensitizing and oncolytic effects of dihydrotanshinone in glioblastoma  
Category: Novel Agents and Translational Approaches  
Abstract: Dihydrotanshinone (DHT) is extracted from Salvia miltiorrhiza, a Chinese medicinal plant, and has been shown to have antiproliferative effects on various cancer cell lines, and can reportedly sensitize cells to temozolomide. MTS cellular proliferation assays or trypan blue viability assays were used to determine the effects of DHT/temozolomide combinatorial treatment. Enzyme-linked immunosorbent assay (ELISA) was used to determine effects on MGMT, P-glycoprotein, AKT, p65, and IlkB levels after singular and combinatorial treatment. DNA microarray was used to gauge gene expression and miRNA levels. DHT had a selectively cytotoxic synergistic oncolytic effect in a MGMT-deficient cell line and a sensitizing effect in a MGMT-expressing cell line. Cytotoxicity due to DHT was shown to be reactive oxygen species-dependent, while the combinatorial effect of DHT and temozolomide synergistically reduced MGMT and P-glycoprotein expression and protein levels. In addition, the NFkB complex was sensitive to combinatorial treatment, while AKT activity and gene expression was downregulated in response to treatment. Temozolomide in combination with DHT may represent a promising therapeutic option for glioblastoma.

NATA – 09 Presenter: Tae Jin Lee  
Department and Institution: Neurosurgery, University of Texas Health Science Center at Houston  
Title: RNA nanoparticle based targeted therapy for glioblastoma  
Category: Novel Agents and Translational Approaches  
Abstract: Systemic administration of therapeutic siRNA/microRNA for targeted treatment of glioblastoma, one of the most deadly cancers, requires robust and efficient delivery platform without immunogenicity. Here we report newly emerged multivalent naked RNA nanoparticle (RNP), named FA-pRNA-3WJ, based on pRNA 3-way-junction (3WJ) from bacteriophage phi29 to target glioblastoma cells with folate (FA) ligand and deliver siRNA/microRNA for tumor cell killing. Systemically injected FA-pRNA-3WJ RNPs successfully targeted and delivered siRNA into brain tumor cells in mice, and efficiently reduced target gene expressions leading to improved survival rate.

TM – 01 Presenter: Jacqueline Brosnan-Cashman  
Department and Institution: Pathology, Johns Hopkins  
Title: ATRX loss induces hallmarks associated with alternative lengthening of telomeres (ALT) in human glioma cell lines in a cell line-specific manner  
Category: Tumor Models  
Abstract: Loss of ATRX is associated with the activation of the alternative lengthening of telomeres (ALT) telomere maintenance mechanism in high grade gliomas. Two (out of seven) high grade glioma cell lines
developed features associated with the ALT pathway after ATRX knockout and/or knockdown, providing the first in vitro evidence that ATRX loss can be sufficient for features of ALT to develop. These two ALT-competent cell lines, along with our five ALT-resistant cell lines, will facilitate the identification of additional ALT-suppressors or ALT-facilitators in glioma.

**TM – 02 Presenter:** Mateusz Koptyra  
**Department and Institution:** Center for Data Driven Discoveries in Biomedicine, Children’s Hospital of Philadelphia  
**Title:** High grade glioma cell line cohort as an example of children’s brain tumor tissue consortium tumor specimen processing pipeline  
**Category:** Tumor Models  
**Abstract:** We would like to present pediatric high grade glioma cell line cohort as an example of children’s brain tumor tissue consortium (CBTTC) tumor specimen processing pipeline. The CBTTC is the multi-institutional research program dedicated to the study and treatment of childhood brain tumors. The cell lines and PDX models developed by consortium provide research models for preclinical testing and tumor biology studies in pediatric brain tumor field.