3rd CNS Anticancer Drug Discovery and Development

November 14-15, 2018
Marriott Hotel
New Orleans, Louisiana

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Department of Neurosurgery, UCSF Medical School

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Departments of Chemistry and Radiology
Stony Brook School of Medicine
**CNS ANTICANCER DRUG DISCOVERY**

Wednesday, November 14, 2018

**Chair:** Victor Levin  
Mardi Gras A-D

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<th>Time</th>
<th>Event</th>
<th>Speaker/Institution</th>
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<td>7:00 - 8:00am</td>
<td>REGISTRATION AND LIGHT CONTINENTAL BREAKFAST</td>
<td>Ballroom Foyer</td>
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<tr>
<td>8:00 - 8:10am</td>
<td>Welcome and Opening Remarks</td>
<td>Victor Levin</td>
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<tr>
<td>8:10 - 10:00am</td>
<td>Session 1: Approaches to Solve the Regulatory and Pharmaceutical/Biotech Drug Discovery/Development Conundrum</td>
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<tr>
<td>8:10 - 8:25am</td>
<td>Attracting industry to the platform approach in the setting of low patient numbers</td>
<td>Gary Gordon, GCAR/GBM AGILE</td>
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<td>8:25 - 8:40am</td>
<td>Platform trials for glioblastoma - what they have to offer and what we can learn from them</td>
<td>Howard Colman, Huntsman Cancer Institute</td>
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<td>8:40 - 8:55am</td>
<td>Understanding the statistical challenges and opportunities of platform trials</td>
<td>Pallavi Mishra-Kalyani, Division of Biometrics, CDER/FDA</td>
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<td>8:55 - 9:10am</td>
<td>From patient to pharma-a stakeholders round table of drug development in GBM AGILE</td>
<td>Melissa Paoloni, Berry Consultants</td>
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<td>9:10 - 9:25am</td>
<td>The challenge of repurposing drugs for CNS neoplasms</td>
<td>Jeffrey Bacha, DelMar Pharmaceuticals</td>
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<tr>
<td>10:00 - 10:20am</td>
<td>Session 1 Discussion</td>
<td>Victor Levin, Moderator</td>
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<tr>
<td>10:20 - 12:15pm</td>
<td>Session 2: Drug Delivery, The Blood-brain Barrier, and Other Pharmacokinetic Considerations</td>
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<tr>
<td>10:20 - 10:40am</td>
<td>The blood-brain barrier and its effect on drug delivery to brain and tumor</td>
<td>Quentin Smith, Texas Tech University</td>
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<td>10:40 - 11:00am</td>
<td>Factors influencing the distribution of free drug to tumors in the CNS</td>
<td>William Elmquist, University of Minnesota</td>
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<td>11:00 - 11:20am</td>
<td>Understanding brain penetrance of anticancer agents for infiltrative gliomas</td>
<td>Victor Levin, MD Anderson Cancer Center, UCSF School of Medicine</td>
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<td>11:20 - 11:35am</td>
<td>Development of a translational PK model for characterizing and predicting protein therapeutics in the brain</td>
<td>Dhaoul K. Shah, University of Buffalo</td>
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<td>11:35 - 12:15pm</td>
<td>Drug penetration into human brain tumors: Mechanistic and quantitative insights from in vitro, in silico, and patients</td>
<td>Jing Li, Wayne State University</td>
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<td>12:15 - 1:20pm</td>
<td>Session 2 - Part 1 Discussion</td>
<td>James Gallo, Moderator</td>
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<td>1:20 - 1:30pm</td>
<td>Mechanisms of enhanced drug delivery in brain tumors with focused ultrasound-induced transient blood-tumor barrier disruption</td>
<td>Costas Arvanitis, Georgia Institute of Technology</td>
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<td>1:30 - 1:40pm</td>
<td>A versatile and modular targeted nanoparticle platform for delivery of combination therapies to adult and pediatric CNS tumors</td>
<td>Fred Lam, Massachusetts Institute of Technology</td>
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### CNS Anticancer Drug Discovery and Delivery

**Wednesday, November 14, 2018**

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| 1:40 - 1:50pm | PD-L1 checkpoint blockade using a single-chain variable fragment targeting PD-L1 delivered by retroviral replicating vector (Toca 521) enhances anti-tumor effect in cancer models  
*Amy Lin, Tocagen, Inc.* |
| 1:50 - 2:00pm | Low intensity pulsed ultrasound using an implantable device to temporarily disrupt the blood-brain barrier: A new tool for enhancing delivery of drugs to the brain  
*Michael Canney, CarThera, Inc.* |
| 2:00 - 2:20pm | Session 2 - Part 2 Discussion  
*James Gallo, Moderator* |
| 2:20 - 2:50pm | BREAK  
*Ballroom Foyer* |

#### Session 3: Biophysical Modeling to Guide Drug Discovery and Development

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| 2:50 - 3:10pm | Protein folding and aggregation in stressed and aging cells  
*Ken A. Dill, Stony Brook University* |
| 3:10 - 3:30pm | Simulating cancer cell migration  
*David Odde, University of Minnesota* |
| 3:30 - 3:50pm | Cell mechanical targets for brain tumors  
*Steven Rosenfeld, Mayo Clinic* |
| 3:50 - 4:05pm | Extracting predictive biomarkers of cancer immunotherapy from tumor spatial heterogeneity using a multi-scale systems biology model  
*Chang Gong, Johns Hopkins University* |
| 4:05 - 4:15pm | Reaching the subarachnoid space: a role for intrathecal delivery of drug loaded nanoparticles  
*Rachael Sirianni, University of Texas Health Science Center* |
| 4:15 - 4:45pm | Session 3 Discussion  
*Peter Tonge, Moderator* |
| 5:00 - 8:00pm | POSTER AND NETWORKING RECEPTION  
*Mardi Gras A-D* |
A new bioanalytical method and single-dose pharmacokinetics for oxaloacetate
David Conway

Vismodegib loaded Polyoxazoline (POx) micelles enhance efficacy of vismodegib and prolong mice survival, emphasize potential of POx micelles to improve drug delivery to brain tumors
Duhyeong Hwang

Targeting Nrf2 antioxidative pathway as a novel therapeutic strategy for IDH1-mutated cancers
Chunzhang Yang

Combined inhibition of nicotinamide phosphoribosyltransferase (NAMPT) and poly (ADP-ribose) polymerase (PARP) impairs glioblastoma cell growth
Lee Hwang

Dual PI3K/Akt inhibition to overcome the P-gp/BCRP drug efflux system for improved drug delivery in glioblastoma therapy
Bjoern Bauer

MP-Pt(IV): A MAOB sensitive mitochondrial smart bomb for treating glioma
Martyn Sharpe

Proteasome inhibition is a targeted therapy for PTEN-deficient glioblastomas
Jorge Benitez

A novel dopamine receptor 3 antagonist inhibits the growth of primary and temozolomide resistant glioblastoma cells
Sarah Scott

G-quadruplex DNA drives genomic instability and represents a targetable molecular abnormality in ATRX-deficient malignant glioma
Jason Huse

Melatonin: Targeting the cell’s powerhouse to fight glioblastoma
Beatriz I. Fernandez-Gil

Radiation enhances the delivery of unmodified antisense morpholino oligonucleotides to reduce MGMT protein expression in a rat xenograft brain tumor model
Prakash Ambady

Utilising novel materials to dynamically measure drug delivery to gliomas: A proposal
Lawrence M Cher

Efficacy of mutant interleukin-13 alpha-2 receptor–targeted liposomal doxorubicin in the intracranial brain tumor model
Darya Nesterova

Compounds identified by structure based virtual screening decrease GBM growth and glucose uptake
Catherine Libby

Development of local treatment for glioblastoma using supramolecular hydrogels
Paula Schiapparelli

NetZen: A comprehensive network-based pathway and target discovery platform
David Tran

Localization of erlotonib relative to MRI-based tumor extent in PDX glioblastoma model: Towards a mathematical model for the interface between MRI and drug distribution
Pamela Jackson

MicroRNA-34a packaged in bacterial nanocells overcomes therapeutic resistance in glioblastoma
Muhammad Babar Khan

An old story (MGMT) in an expanded context (National Cancer Database)
Santhi Konduri

Macrocyclic natural products as molecular probes to target ER proteostasis in GBM
Jane Ishmael

Development and early clinical experience with PAC-1, a Procaposase Activating Compound with activity against malignant glioma
M. Kelly Nicholas

Glioblastoma tumorigenesis – Lessons from reproductive immunology
Na Tosha Gatson

Phase 1b clinical trial of IV OKN-007 in recurrent malignant glioblastoma (GBM)
James Battiste

Low serum 25 (OH) vitamin D level is associated with increased risk of primary CNS malignancy: A retrospective cohort study in a veteran population
Emmanuel Mantilla

Intra-arterial NEO100 transiently opens the blood brain barrier
Thomas Chen

Preclinical development of miR-10b antagonist for the treatment of glioblastoma
Danling Wang
7:00 - 8:00am **REGISTRATION AND LIGHT CONTINENTAL BREAKFAST**  
*Preservation Hall*

**Session 4: Novel Targets, Approaches and Discovery Paradigms**

8:00 - 8:20am Correlating time-dependent target engagement and drug activity  
Peter Tonge, Stony Brook University

8:20 - 8:30am Nanoparticle delivery of miRNAs to inhibit GBM stem cells  
Hernando Lopez, Kennedy Krieger Institute

8:30 - 8:40am CD97 perturbation by novel fusion protein DAF-Fc inhibits GBM invasion and induces antibody dependent cellular cytotoxicity  
Michael Safaee, University of California, San Francisco

8:40 - 9:00am Therapeutic targets in primary and metastatic brain tumors: genomics as a tool  
Priscilla K. Brastianos, Massachusetts General Hospital

9:00 - 9:10am Translational discovery of therapeutic targets for glioblastoma  
Maria-Magdalena Georgescu, Louisiana State University

9:10 - 9:25am Protein target identification and target interaction from linear modeling of protein targets from rodent tumors  
Forest White, Massachusetts Institute of Technology

9:25 - 9:35am Targeting the CD200 checkpoint for the fight against central nervous system tumors  
Michael Olin, University of Minnesota

9:35 - 9:50am The PROTAC drug approach  
Chris Nasveschuk, C4 Therapeutics

9:50 - 10:05am Session 4 - Part 1 Discussion  
Peter Tonge, Moderator

10:05 - 10:20am **BREAK**  
*Preservation Hall*

10:20 - 10:40am Nativis Voyager®: A disruptive approach to cancer treatment  
Mike Butters, Nativis, Inc.

10:40 - 10:50am Personalized pharmacogenomics using glioma patient-derived orthotopic xenografts (PDOXs)  
Ann-Christin Hau, Luxembourg Institute of Health

10:50 - 11:10am A key to tumor cell immortality: How it might inform new drug targets  
Joseph F. Costello, University of California, San Francisco

11:10 - 11:20am Developing Zika virus as a potential cancer stem cell therapy  
Milan Chheda, Washington University

11:20 - 11:30am Multi-modality analysis of heterogeneous EGFR inhibitor delivery and efficacy in GBM  
Jann Sarkaria, Mayo Clinic

11:30 - 11:50am Selective dependency and conceptual approaches to target identification  
Jeremy Rich, Sanford Consortium for Regenerative Medicine

11:50 - 12:00pm The development of personalized CAM Avatar model to predict chemotherapeutic drug sensitivity/resistance of gliomas  
Martine Charbonneau, University of Sherbrooke

12:00 - 12:15pm Principles of epigenetics and chromatin in development and human disease  
Ali Shilatifard, Northwestern University
12:15 - 12:30pm  Session 4 - Part 2 Discussion  
Jann Sarkaria, Moderator

12:30 - 1:30pm  LUNCH  Preservation Hall

Session 5: Drug Discovery Efforts and Preclinical and Clinical Accomplishments

1:30 - 1:50pm  Building on the success of osimertinib: Achieving CNS exposure in oncology drug discovery  
Nicola Colclough, AstraZeneca

1:50 - 2:10pm  Discovery of AZD1390, a potent, selective and brain penetrant inhibitor of ATM kinase  
Kurt G. Pike, AstraZeneca

2:10 - 2:30pm  BMI-1 modulation by PTC596 as a new approach to the treatment of GBM  
Young-Choon Moon, PTC Therapeutics

2:30 - 2:50pm  Therapeutic challenges and opportunities for pediatric high-grade glioma  
Suzanne Baker, St. Jude Children's Research Hospital

2:50 - 3:00pm  2-hydroxyoleic acid, a novel membrane lipid regulator, demonstrates clinical activity in high-grade glioma  
Derek Hanson, Hackensack University Medical Center

3:00 - 3:10pm  Small molecule epigenetic targeting of methyl-CpG binding protein 2 (MBD2) for medulloblastoma therapy  
Erwin Van Meir, Emory University

3:10 - 3:20pm  CT-179: an inhibitor of the OLIG2 transcription factor with potent anti-tumour activity in brain cancer  
Terrance Johns, Telethon Kids Institute

3:20 - 3:30pm  Re-programing chromatin with a bifunctional LSD1/HDAC inhibitor induces therapeutic differentiation in DIPG  
Jamie Anastas, Boston Children's Hospital

3:30 - 3:40pm  Identification and validation of azoles as HK2 inhibitors in glioblastoma in vitro and in vivo  
Alireza Mansouri, University of Toronto

3:40 - 3:50pm  The efficacy of therapy with ABT-414, an EGFR-targeting ADC, is potentially altered by heterozygous deletion of the endocytic trafficking regulator RBSN  
Gaelle Muller-Greven, Cleveland Clinic

3:50 - 4:00pm  PAM-OBG: A MAOB-specific prodrug inhibitor of O6-methylguanine DNA methyltransferase (MGMT) that sensitizes GMB to BCNU/CCNU  
Martyn Sharpe, Houston Methodist Hospital

4:00 - 4:30pm  Session 5 Discussion  
Zoran Rankovic, Moderator

4:30 - 4:35pm  Closing Remarks  
Victor Levin

4:35pm  ADJOURN
The Society for Neuro-Oncology gratefully acknowledge the following organizations for their support of this program.

PLATINUM

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SILVER

The Brain Tumour Charity
Oligo Nation Uniting for a Cure