AACR Special Conference in Cancer Research
Expanding and Translating Cancer Synthetic Vulnerabilities
June 10-13, 2024 | Doubletree by Hilton Montreal | Montreal, QC, Canada

**clemConference Cochairs:**
Michael A. Erb, The Scripps Research Institute, La Jolla, California
Kimberly Stegmaier, Dana-Farber Cancer Institute, Boston, Massachusetts
E. Alejandro Sweet-Cordero, University of California, San Francisco, California
Kris C. Wood, Duke University School of Medicine, Durham, North Carolina

**Monday, June 10, 2024**

**Opening Keynote Address**
6:00-7:00 p.m. | Grand Salon Opera AB
*CME-eligible*

6:00-6:05  
**Introduction of Keynote Speaker**  
Kimberly Stegmaier, Dana-Farber Cancer Institute, Boston, Massachusetts

6:05-6:50  
**Exploiting pathway activation as a new form of synthetic lethality**  
William R. Sellers, Broad Institute and Dana-Farber Cancer Institute, Cambridge, Massachusetts

6:50-7:00  
Discussion/Q&A

**Opening Reception**
7:00-8:30 p.m. | Soprano AB  
*Not CME-eligible*

**Tuesday, June 11, 2024**

**Continental Breakfast**
7:00-8:00 a.m. | Grand Salon Opera C  
*Not CME-eligible*

**Plenary Session 1: Chemical Biology Tools to Advance Synthetic Lethality**
8:00-10:00 a.m. | Grand Salon Opera AB
*Session Chair: Fleur M. Ferguson, UC San Diego, La Jolla, California*
*CME-eligible*

8:00-8:20  
**Overcoming the K-Ras inhibitor resistant cell state in PDAC with molecular glu**es  
Fleur M. Ferguson

8:20-8:30  
Discussion/Q&A

8:30-8:50  
**Chemoproteomic discovery of a covalent allostéric inhibitor of WRN helicase**
Matthew P. Patricelli, Vividion Therapeutics, San Diego, California
8:50-9:00 Discussion/Q&A

9:00-9:20 **Redirecting FOXA1 pioneering function with covalent small molecules**
Michael A. Erb, The Scripps Research Institute, La Jolla, California
9:20-9:30 Discussion/Q&A

9:30-9:40 **KIF18A inhibition, via ATX020, leads to mitotic arrest and robust anti-tumor activity through a synthetic lethal interaction with chromosome instability***
Maureen Lynes, Accent Therapeutics, Lexington, Massachusetts
9:40-9:45 Discussion/Q&A

9:45-9:55 **Nimbolide targets RNF114 to induce the trapping of PARP1 and synthetic lethality in BRCA-mutated cancer***
Yonghao Yu, Columbia University Vagelos College of Physicians and Surgeons, New York, New York
9:55-10:00 Discussion/Q&A

Break
10:00-10:30 a.m. | Grand Salon Opera Foyer
*Not CME-eligible*

**Plenary Session 2: Mechanisms of Synthetic Lethality**
10:30 a.m.-12:30 p.m. | Grand Salon Opera AB
*Session Chair: Zuzana Tothova, Dana-Farber Cancer Institute, Boston, Massachusetts CME-eligible*

10:30-10:50 **Therapeutic vulnerabilities of cohesin-mutant myeloid malignancies**
Zuzana Tothova
10:50-11:00 Discussion/Q&A

11:00-11:20 **Synthetic lethalties for SWI/SNF mutant cancers**
Charles W.M. Roberts, St. Jude Children's Research Hospital, Memphis, Tennessee
11:20-11:30 Discussion/Q&A

11:30-11:50 **The long isoform of RAP1GDS1 is a synthetic vulnerability in RAS-driven lung adenocarcinoma**
E. Alejandro Sweet-Cordero, University of California San Francisco, San Francisco, California
11:50-12:00 Discussion/Q&A

12:00-12:10 Mechanisms of therapeutic vulnerability of mismatch repair defective cancers to RNA polymerase I inhibitors*
Marikki Laiho, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University, Baltimore, Maryland

12:10-12:15 Discussion/Q&A

12:15-12:25 Computational discovery of paralog dependencies drives target identification in lung cancer*
Siobhan O’Brien, Fred Hutchinson Cancer Center, Seattle, Washington

12:25-12:30 Discussion/Q&A

Lunch Break (lunch on your own)
12:30-2:30 p.m.
Not CME-eligible

Plenary Session 3: Clinical Translation of DNA Damage Synthetic Lethality
2:30-4:30 p.m. | Grand Salon Opera AB
Session Chair: Michael A. White, Ideaya Biosciences, South San Francisco, California
CME-eligible

2:30-2:50 Exploiting tumor selective vulnerabilities with structure based drug design
Michael A. White

2:50-3:00 Discussion/Q&A

3:00-3:20 Single strand DNA GAP accumulation as a functional biomarker for DNA repair inhibitors
Alan D. D’Andrea, Dana-Farber Cancer Institute, Boston, Massachusetts

3:20-3:30 Discussion/Q&A

3:30-3:50 Targeting genome instability in cancer: Translating synthetic lethal biology into the clinic
Michael J. Zinda, Repare Therapeutics Inc., Cambridge, Massachusetts

3:50-4:00 Discussion/Q&A

4:00-4:10 CX-5461 sensitizes DNA damage repair-proficient castrate-resistant prostate cancer to PARP inhibition*
Luc Furic, Peter MacCallum Cancer Centre, Melbourne, Australia

4:10-4:15 Discussion/Q&A
4:15-4:25 DNA repair inhibition via targeting ATR activates cGAS/STING signaling, promotes anti-tumor immunity, and is a synthetic lethal strategy to augment immunotherapy response in preclinical models and clinical samples of small cell lung cancer*
Triparna Sen, Icahn School of Medicine at Mount Sinai, New York, New York

4:25-4:30 Discussion/Q&A

Poster Session A (with light refreshments)
4:30-7:00 p.m. | Soprano ABC
Not CME-eligible

Wednesday, June 12, 2024

Continental Breakfast
7:00-8:00 a.m. | Grand Salon Opera C
Not CME-eligible

Plenary Session 4: Synthetic Lethality at Scale
8:00-10:00 a.m. | Grand Salon Opera AB
Session Chair: Francisca Vazquez, Broad Institute, Cambridge, Massachusetts
CME-eligible

8:00-8:20 Towards mapping the landscape of cancer vulnerabilities
Francisca Vazquez

8:20-8:30 Discussion/Q&A

8:30-8:50 Mapping genetic dependencies and Interactions in childhood brain cancers
Ron Firestein, Hudson Institute of Medical Research, Clayton, Australia

8:50-9:00 Discussion/Q&A

9:00-9:20 Identifying novel therapeutic vulnerabilities in AML: From discovery to targeting
Aniruddha Deshpande, Sanford Burnham Prebys Medical Discovery Institute, La Jolla, California

9:20-9:30 Discussion/Q&A

9:30-9:40 Delineating functional drivers of esophageal adenocarcinoma to identify synthetic lethal interactions*
Nicholas Clemons, Peter MacCallum Cancer Centre, Melbourne, Australia

9:40-9:45 Discussion/Q&A
### 9:45-9:55  
**Targeting mechanisms of dosage compensation to selectively kill aneuploid cancer cells**  
Hajime Okada, Tel Aviv University, Tel Aviv, Israel

### 9:55-10:00  
Discussion/Q&A

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### Break
10:00-10:30 a.m.  
| Grand Salon Opera Foyer  
*Not CME-eligible*

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### Plenary Session 5: New Concepts in Synthetic Lethality
10:30 a.m.-12:30 p.m.  
| Grand Salon Opera AB  
*Session Chair: Kimberly Stegmaier, Dana-Farber Cancer Institute, Boston, Massachusetts  
CME-eligible*

#### 10:30-10:50  
**Synthetic lethal vulnerabilities in pediatric cancer**  
Kimberly Stegmaier

#### 10:50-11:00  
Discussion/Q&A

#### 11:00-11:20  
**Identifying and targeting synthetic lethalities of aneuploid (cancer) cells**  
Uri Ben-David, Sackler Faculty of Medicine Tel Aviv University, Tel Aviv, Israel

#### 11:20-11:30  
Discussion/Q&A

#### 11:30-11:50  
**Emerging synthetic vulnerabilities in oncogene-driven lung cancer**  
Trever G. Bivona, University of California San Francisco, San Francisco, California

#### 11:50-12:00  
Discussion/Q&A

#### 12:00-12:10  
**Cytidine diphosphate diacylglycerol synthase 2 is a synthetic lethal target in mesenchymal cancers**  
Tim Arnoldus, Netherlands Cancer Institute, Amsterdam, Netherlands

#### 12:10-12:15  
Discussion/Q&A

#### 12:15-12:25  
**CDK12 loss promotes prostate cancer development while exposing vulnerabilities to paralog-based synthetic lethality**  
Jean C. Tien, University of Michigan, Ann Arbor, Michigan

#### 12:25-12:30  
Discussion/Q&A

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### Lunch Break (lunch on your own)
12:30-2:30 p.m.  
*Not CME-eligible*
Plenary Session 6: Synthetic Lethality of Residual Disease and Novel Drug Combinations
2:30-4:30 p.m. | Grand Salon Opera AB
Session Chair: Kris C. Wood, Duke University, Durham, North Carolina
CME-eligible

2:30-2:50 Synthetic dependencies arising during tumor evolution
Kris C. Wood
2:50-3:00 Discussion/Q&A

3:00-3:20 Vulnerabilities of TP53-mutated AML and therapeutic implications
Shruti Bhatt, National University of Singapore (NUS), Singapore
3:20-3:30 Discussion/Q&A

3:30-3:50 Identification of metabolic adaptation mechanisms that confer resistance to glutathione depletion in Ewing sarcoma
Poul H.B. Sorensen, British Columbia Cancer Research Institute and University of British Columbia, Vancouver, British Columbia, Canada
3:50-4:00 Discussion/Q&A

4:00-4:10 Inhibiting eIF4E phosphorylation sensitizes triple-negative breast cancer to CDK4/6 inhibition*
Qiyun Deng, McGill University, Montreal, Quebec, Canada
4:10-4:15 Discussion/Q&A

4:15-4:25 KAT6A/B and Menin-MLL complexes coordinately regulate estrogen receptor-driven gene expression programs in breast cancer*
Sarah Naomi Olsen, Dana-Farber Cancer Institute, Boston, Massachusetts
4:25-4:30 Discussion/Q&A

Poster Session B (with light refreshments)
4:30-7:00 p.m. | Soprano ABC
Not CME-eligible

Thursday, June 13, 2024

Continental Breakfast
7:00-8:00 a.m. | Grand Salon Opera C
Not CME-eligible
Plenary Session 7: New Technologies to Discover Synthetic Lethality
8:00-10:00 a.m. | Grand Salon Opera AB
Session Chair: Francisco J. Sánchez-Rivera, Koch Institute for Integrative Cancer Research at MIT, Cambridge, Massachusetts
CME-eligible

8:00-8:20  Functional studies of genetic variation using precision genome editing
           Francisco J. Sánchez-Rivera

8:20-8:30  Discussion/Q&A

8:30-8:50  Environmental challenge rewires functional connections among human genes
           Luke A. Gilbert, UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, California

8:50-9:00  Discussion/Q&A

9:00-9:20  Mechanisms of splicing dysregulation and dependency in cancer
           Kristen L. Karlin, Baylor College of Medicine, Houston, Texas

9:20-9:30  Discussion/Q&A

9:30-9:40  Detecting pairwise and higher-order antagonistic epistatic effects among somatic cancer genotypes to discover synthetic lethality*
           Jorge A. Alfaro-Murillo, Yale University, New Haven, Connecticut

9:40-9:45  Discussion/Q&A

9:45-9:55  Combinatorial genetic screens to map synthetic lethal interactions and identify new cancer drug targets in KRAS mutant cancers*
           Rand Arafeh, Dana Farber Cancer Institute, Harvard Medical School, Boston, Massachusetts

9:55-10:00 Discussion/Q&A

Break
10:00-10:30 a.m. | Grand Salon Opera Foyer
Not CME-eligible

Plenary Session 8: Translating the Next Synthetic Lethalities
10:30 a.m.-12:30 p.m. | Grand Salon Opera AB
Session Chair: Jolanta E. Grembecka, University of Michigan, Ann Arbor, Michigan
CME-eligible

10:30-10:50 Targeting epigenetic complexes in leukemia
10:50-11:00 Discussion/Q&A

11:00-11:20 RNA-modifying enzyme inhibitors as synthetic lethal cancer therapeutics
Serena J. Silver, Accent Therapeutics, Lexington, Massachusetts
11:20-11:30 Discussion/Q&A

11:30-11:50 Identifying and deconstructing chemical synthetic lethal interactions for the development of combinatorial therapies
Karen M. Cichowski, Brigham and Women's Hospital, Boston, Massachusetts
11:50-12:00 Discussion/Q&A

12:00-12:10 Discovery of LY4050784 (FHD-909), a selective BRM (SMARCA2) ATPase inhibitor for the treatment of BRG1(SMARCA4) mutant cancers*
Janice Y. Lee, Foghorn Therapeutics, Cambridge, Massachusetts
12:10-12:15 Discussion/Q&A

12:15-12:25 Investigating vulnerabilities associated with chromosome arm aneuploidy in cancer*
Nadja Zhakula, Columbia University Vagelos College of Physicians and Surgeons, New York, New York
12:25-12:30 Discussion/Q&A

Closing Remarks
12:30-12:45 p.m. | Grand Salon Opera AB
Not CME-eligible

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