

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 glues Fleur M. Ferguson
8:20-8:30	Discussion/Q&A
8:30-8:50	Chemoproteomic discovery of a covalent allosteric inhibitor of WRN helicase

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8:50-9:00	Matthew P. Patricelli, Vividion Therapeutics, San Diego, California 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 lethality 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

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- 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

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- 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

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- 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

Break

10:00-10:30 a.m. | Grand Salon Opera Foyer

Not CME-eligible

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 lethality 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**
Trevor 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

Lunch Break (lunch on your own)

12:30-2:30 p.m.

Not CME-eligible

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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

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| 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

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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
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- 10:50-11:00 Jolanta E. Grembecka
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

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