



An AACR Special Conference on  
**Targeting RAS**  
March 5-8, 2023 | Philadelphia, PA

**AACR**  
American Association  
for Cancer Research®  
21090485

### **Conference Cochairs:**

Mariano Barbacid, Spanish National Cancer Center (CNIO), Madrid, Spain  
Dafna Bar-Sagi, New York University Langone Medical Center, New York, NY  
Frank McCormick, UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, CA  
Deborah K. Morrison, National Cancer Institute, Frederick, MD

**[U]= Recording will be unavailable to view on-demand**

### **SUNDAY, MARCH 5, 2023**

#### **Registration**

3:30 pm-7:30 pm Liberty Ballroom Foyer

#### **Welcome and Opening Keynote Lectures**

6:00 pm-7:30 pm Liberty Ballroom

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| 6:00-6:10  | Welcome from Conference Cochairs   |
| 6:10       | Introduction of Keynote Speaker<br>Frank McCormick, UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, CA                        |
| 6:10 -6:50 | Keynote Lecture<br><b>Targeting KRAS: Light at the end of the tunnel</b><br>Mariano Barbacid, Spanish National Cancer Center (CNIO), Madrid, Spain |
| 6:50 -7:00 | Discussion / Q&A   |
| 7:00       | Introduction of Rising Star Lecturer<br>Dafna Bar-Sagi, New York University Langone Medical Center, New York, NY                                   |
| 7:00-7:20  | Rising Star Lecture<br><b>Targeting RAS in cancer: Opportunities and challenges</b><br>Andrew Aguirre, Harvard Medical School, Boston, MA          |
| 7:20-7:30  | Discussion / Q&A   |

#### **Opening Reception**

7:30 pm-9:00 pm Franklin Hall A

### **MONDAY, MARCH 6, 2023**

#### **Breakfast**

7:00 am-8:00 am Franklin Hall A

*\*Short talk selected from proffered abstracts*



### Plenary Session 1: Biochemistry, Function, and Structure

8:00 am-10:15 am Liberty Ballroom

*Session Chair: Frank McCormick, UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, CA*

- 8:00-8:25      **Treating mutant KRAS tumors with RAS inhibitors, alone or in combination**  
Neal Rosen, Memorial Sloan Kettering Cancer Center, New York, NY
- 8:25-8:35      Discussion / Q&A
- 8:35-9:00      **Emerging therapeutics shed light on the allosteric regulation of KRAS**  
Piro Lito, Memorial Sloan Kettering Cancer Center, New York, NY
- 9:00-9:10      Discussion / Q&A
- 9:10-9:35      **Uncovering new structural insights into RAS interactions with effectors and regulators**  
Dhirendra K. Simanshu, Frederick National Laboratory for Cancer Research, Frederick, MD
- 9:35-9:45      Discussion / Q&A
- 9:45-9:55      **Structural plasticity of KRAS oncogenic mutants – a case of misleading conclusions from GTP analogues\***  
Alok K. Sharma, Frederick National Laboratory for Cancer Research, Frederick, MD
- 9:55-10:00      Discussion / Q&A
- 10:00-10:10    **Factors modulating RAF dimerization downstream of RAS\***  
Jawahar Sudhamsu, Genentech Inc., South San Francisco, CA
- 10:10-10:15    Discussion / Q&A

### Break

10:15 am-10:35 am Liberty Ballroom Foyer

### Plenary Session 2: Signaling Networks

10:35 am-12:55 pm Liberty Ballroom

*Session Chair: Deborah K. Morrison, National Cancer Institute, Frederick, MD*

- 10:35-11:00    **Targeting the ERK-MYC signaling network for the treatment of KRAS-mutant cancers**  
Channing J. Der, University of North Carolina Lineberger Comprehensive Cancer Center, Chapel Hill, NC
- 11:00-11:10    Discussion / Q&A

*\*Short talk selected from proffered abstracts*



- 11:10-11:35 **Molecular characterization of acquired resistance to KRAS<sup>G12C</sup>-EGFR inhibition in colorectal cancer**  
Sandra Misale, Memorial Sloan Kettering Cancer Center, New York, NY
- 11:35-11:45 Discussion / Q&A
- 11:45-12:10 **Paradoxical activation of oncogenic signaling as a cancer treatment strategy**  
René Bernards, The Netherlands Cancer Institute, Amsterdam, The Netherlands
- 12:10-12:20 Discussion / Q&A
- 12:20-12:45 **Direct covalent inhibitors of mutant K-Ras**  
Kevan M. Shokat, University of California, San Francisco, CA
- 12:45-12:55 Discussion / Q&A

#### **Lunch on Own / Free Time**

12:55 pm-2:15 pm

#### **Plenary Session 3: Tackling RAS Using a Disease-specific Approach**

2:15 pm-4:35 pm Liberty Ballroom

*Session Chair: Christin E. Burd, The Ohio State University, Columbus, OH*

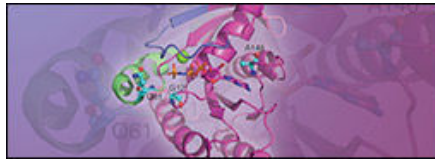
- 2:15-2:40 **Allelic specificity: The key to NRAS-mutant melanoma initiation?**  
Christin E. Burd, The Ohio State University, Columbus, OH
- 2:40-2:50 Discussion / Q&A
- 2:50-3:15 **K-RAS hyperexchange mutants in colorectal cancer**  
Kevin M. Haigis, Dana-Farber Cancer Institute, Boston, MA
- 3:15-3:25 Discussion / Q&A
- 3:25-3:50 **Three-dimensional genomic mapping of human pancreatic tissue reveals striking multifocality and genetic heterogeneity in precancerous lesions**  
Laura D. Wood, Johns Hopkins University School of Medicine, Baltimore, MD
- 3:50-4:00 Discussion / Q&A
- 4:00-4:25 **Developing combinatorial therapies for KRAS-mutant cancers**  
Karen M. Cichowski, Brigham and Women's Hospital, Boston, MA
- 4:25-4:35 Discussion / Q&A

#### **Poster Session A / Reception**

4:45 pm-7:00 pm Franklin Hall A

#### **TUESDAY, MARCH 7, 2023**

*\*Short talk selected from proffered abstracts*



## Breakfast

7:00 am-8:00 am Franklin Hall A

## Plenary Session 4: Metabolism

8:00 am-10:15 am Liberty Ballroom

*Session Chair: Dafna Bar-Sagi, New York University Langone Medical Center, New York, NY*

- 8:00-8:25      **Identifying metabolic dependencies in pancreatic cancer**  
Alec C. Kimmelman, New York University Langone Medical Center, New York, NY
- 8:25-8:35      Discussion / Q&A
- 8:35-9:00      **Host autophagy mediates organ wasting and nutrient mobilization for tumor growth [U]**  
Tor Erik Rusten, Norwegian Radium Hospital, Oslo, Norway
- 9:00-9:10      Discussion / Q&A
- 9:10-9:35      **Coordinated transcriptional and catabolic programs support iron dependent adaptation to RAS-MAPK pathway inhibition in pancreatic cancer**  
Rushika M. Perera, University of California, San Francisco, CA
- 9:35-9:45      Discussion / Q&A
- 9:45-9:55      **Cooperative anti-tumor effects of combined inhibition of KRAS<sup>G12C</sup> plus autophagy in preclinical models of KRAS<sup>G12C</sup>-driven lung cancer\***  
Phaedra C. Ghazi, University of Utah, Salt Lake City, UT
- 9:55-10:00      Discussion / Q&A
- 10:00-10:10      **A bimodal mechanism of RAS inactivation by monoubiquitination\***  
Wout Magits, VIB-KU Leuven Center for Cancer Biology, Leuven, Belgium
- 10:10-10:15      Discussion / Q&A

## Break

10:15 am-10:35 am Liberty Ballroom Foyer

## Plenary Session 5: RASopathies / RAS Superfamily

10:35 am-12:15 pm Liberty Ballroom

*Session Chair: Marco Tartaglia, Bambino Gesù Children's Hospital, Rome, Italy*

- 10:35-11:00      **RASopathies: the other face of RAS signaling upregulation**  
Marco Tartaglia, Bambino Gesù Children's Hospital, Rome, Italy
- 11:00-11:10      Discussion / Q&A

*\*Short talk selected from proffered abstracts*



**[CANCELLED]**

**Use of RAS isoforms in nerve tumors**

Nancy Ratner, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

11:10-11:35 **Somatic predisposition to germline mutations in the RTK/RAS/MAPK pathway**  
Anne Goriely, MRC Weatherall Institute of Molecular Medicine, University of Oxford, Oxford, England

11:35-11:45 Discussion / Q&A

11:45-11:55 **The role of the RAS GTPase RIT1 in RASopathies and cancer\***  
Pau Castel, New York University School of Medicine, New York, NY

11:55-12:00 Discussion / Q&A

12:00-12:10 **Germline RASopathy mutations provide insights into the differential regulation of RAF family kinases\***

Russell Spencer-Smith, National Cancer Institute-Frederick, Frederick, MD

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

**Lunch on Own / Free Time**

12:15 pm-2:15 pm

**Plenary Session 6: RAS and Tumor Immunity**

2:15 pm-4:30 pm Liberty Ballroom

*Session Chair: Julian Downward, The Francis Crick Institute, London, England*

2:15-2:40 **Oncogenic KRAS and the regulation of the pancreatic cancer microenvironment**  
Marina Pasca di Magliano, University of Michigan Medical School, Ann Arbor, MI

2:40-2:50 Discussion / Q&A

2:50-3:15 **The impact of RAS inhibition on tumor immune evasion**  
Julian Downward, The Francis Crick Institute, London, England

3:15-3:25 Discussion / Q&A

3:25-3:50 **Immune rewiring of mutant Ras tumors: Mechanisms and translational implications**

Dafna Bar-Sagi, New York University Langone Medical Center, New York, NY

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

4:00-4:10 **How oncogenic Kras shapes the tumor microenvironment in lung adenocarcinoma\***

Rachael K. Baliira, University of Michigan, Ann Arbor, MI

4:10-4:15 Discussion / Q&A

*\*Short talk selected from proffered abstracts*



- 4:15-4:25 **TCR1020 specific for KRAS G12V restricted to HLA-A\*11:01 exhibits potent and precise antigen specificity for clinical development\***  
Adham S. Bear, University of Pennsylvania, Philadelphia, PA
- 4:25-4:30 Discussion / Q&A

### Poster Session B / Reception

4:45 pm-7:00 pm Franklin Hall A

## WEDNESDAY, MARCH 8, 2023

### Breakfast

7:00 am-8:00 am Franklin Hall A

### Plenary Session 7: Targeting RAS

8:00 am-9:40 am Liberty Ballroom

*Session Chair: David A. Tuveson, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY*

- 8:00-8:25 **Challenges and opportunities in treating KRAS mutant tumors [U]**  
Shiva Malek, Novartis Institutes for BioMedical Research, Cambridge, MA
- 8:25-8:35 Discussion / Q&A
- 8:35-9:00 **Selectively targeting KRAS mutant alleles: contribution of both cell autonomous and pro-immunogenic MOAs in an expanded spectrum of human cancers**  
James G. Christensen, Mirati Therapeutics, San Diego, CA
- 9:00-9:10 Discussion / Q&A
- 9:10-9:20 **KRAS-targeted PROTAC degraders are broadly efficacious against KRAS-dependent tumor models\***  
Kathryn Smith, Arvinas Operations, Inc., New Haven, CT
- 9:20-9:25 Discussion / Q&A
- 9:25-9:35 **IK-595, a MEK-RAF complex inhibitor, obviates CRAF mediated resistance resulting in superior RAS/MAPK pathway inhibition and anti-tumor activity in RAS/RAF altered cancers\***  
X. Michelle Zhang, Ikena Oncology, Boston, MA
- 9:35-9:40 Discussion / Q&A

### Break

9:40 am-10:00 am Liberty Ballroom Foyer

*\*Short talk selected from proffered abstracts*



## Plenary Session 8: Resistance Mechanisms and Emerging Clinical Data

10:00 am-11:45 am Liberty Ballroom

*Session Chair: Mariano Barbacid, Spanish National Cancer Center (CNIO), Madrid, Spain*

- 10:00-10:25 **KRAS<sup>G12C</sup> inhibitors- Becoming “Therapeutic” : Lesson from the bedside**  
Melissa L. Johnson, Sarah Cannon Research Institute, Nashville, TN
- 10:25-10:35 Discussion / Q&A
- 10:35-11:00 **Systemic interrogation of KRAS function**  
William C. Hahn, Dana-Farber Cancer Institute, Boston, MA
- 11:00-11:10 Discussion / Q&A
- 11:10-11:35 **Exploiting altered metabolism as a therapeutic strategy for RAS-driven cancers**  
Kirsten L. Bryant, University of North Carolina Lineberger Comprehensive Cancer Center, Chapel Hill, NC
- 11:35-11:45 Discussion / Q&A

### Break

11:45 am-12:00 pm

### Closing Keynote Lecture

12:00 pm-12:50 pm Liberty Ballroom

- 12:00 Introduction of Keynote Speaker  
Mariano Barbacid, Spanish National Cancer Center (CNIO), Madrid, Spain
- 12:00-12:40 **Beating KRAS- it's a Toreo**  
David A. Tuveson, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY
- 12:40-12:50 Discussion / Q&A

### Closing Remarks and Departure

12:50 pm Liberty Ballroom

Dafna Bar-Sagi, New York University Langone Medical Center, New York, NY

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