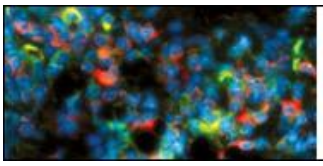


Targeting RAS-Driven Cancers

December 9-12, 2018 | San Diego, CA

AACR American Association for Cancer Research

Poster Session A

Monday, Dec. 10, 2018
1:30 p.m.-3:30 p.m.

A01 Novel state I structures of oncogenic KRAS4b mutants bound to GTP analog. Albert H. Chan, Frederick National Laboratory for Cancer Research, Frederick, MD.

A02 Probing amino acids residues chemical reactivity of KRAS 4b using N-hydroxysuccinimide esters. Oleg Chertov, Frederick National Laboratory for Cancer Research, Frederick, MD.

A03 Biochemical and structural analysis of the neurofibromin (NF1) protein and a potential role for protein destabilization in Rasopathy diseases. Dominic Esposito, Frederick National Laboratory for Cancer Research, Frederick, MD.

A04 Biophysical and biochemical characterization of Src-phosphorylated KRas. Teklab Gebregiworgis, Margaret Cancer Centre, University Health Network and Department of Medical Biophysics, University of Toronto, Toronto, ON, Canada.

A05 Context-dependent transformation with activated Ras isoforms in human normal epithelial cells. Minami Kumazaki, National Cancer Center Research Institute, Tokyo, Japan.

A06 Biophysical and biochemical characterization of KRAS G12C inhibition through the SMART™ platform. Earl W. May, Warp Drive Bio, Cambridge, MA.

A07 Inflammation enables pancreatic acinar cells to overcome resistance to oncogenic Kras by increasing its expression and plasma membrane localization. Mohamad Nabil Assi, Université Catholique de Louvain, de Duve Institute, Brussels, Belgium.

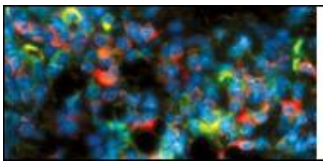
A08 Genetic drug resistance screen identifies LZTR1 as regulator of RAS ubiquitination and signaling. Johannes W. Bigenzahn, CeMM Center for Molecular Medicine, Vienna, Austria.

A09 Cooperative membrane interaction between G-domain and HVR defines unique diffusion behavior of KRAS4b. Debanjan Goswami, De Chen, John Columbus, Thomas Turbyville. FNLCR, NCI-Frederick, Frederick, MD.

A10 Quantitative biophysical analysis defining key components modulating KRAS recruitment to the plasma membrane. Frantz L. Jean-Francois, Frederick National Laboratory, Frederick, MD.

A11 Screening the Ras proteome microenvironment using APEX2. Stephanie P. Mo, University of Liverpool, Liverpool, United Kingdom.

A12 Mutations in *RABL3* alter KRAS prenylation and are associated with hereditary pancreatic cancer. Sahar Nissim, Brigham and Women's Hospital, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA.



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A13 KRAS4A directly regulates hexokinase 1. Mark R. Philips, NYU Perlmutter Cancer Center, New York, NY.

A14 Mutations in the ubiquitin ligase adaptor LZTR1 drive human disease by dysregulating RAS ubiquitination and signaling. Anna Sablina, KULeuven/VIB, Leuven, Belgium.

A15 Axl-mediated activation of TBK1 drives epithelial plasticity in pancreatic cancer. Rolf A. Brekken, UT Southwestern, Dallas, TX.

A16 Understanding the principles of tissue repair that accelerate tumor initiation. Sara Gallini, Yale University, New Haven, CT.

A18 Characterization of K-Ras^{G13D} as a unique activating allele in a mouse model of colorectal cancer. Yi-Jang Lin, Beth Israel Deaconess Medical Center, Boston, MA.

A19 Conditional inactivation of SHOC2 in adult mice to study its role in tissue homeostasis. Sibel Sari, UCL Cancer Institute, London, United Kingdom.

A20 An essential role for Argonaute 2 in mouse models of KRAS driven cancers. Sunita Shankar, University of Michigan, Ann Arbor, MI.

A21 Loss of Argonaute 2 leads to oncogene-induced senescence in mutant RAS-driven cancer. Ronald F. Siebenaler, University of Michigan, Ann Arbor, MI.

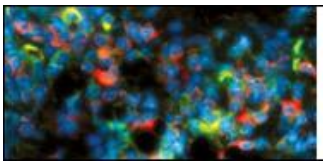
A22 Kras drives changes in acinar-specific gene regulatory networks in early pancreatic neoplasia in conjunction with Bmi1. Joyce K. Thompson, University of Michigan, Ann Arbor, MI.

A23 A second site *Kras^{G12D}* mutation that impairs PI3K binding rescues embryonic lethality, abrogates myeloproliferative disease, and delays lung tumorigenesis. Jasmine C. Wong, University of California, San Francisco, San Francisco, CA.

A24 New mouse models with *KRASG12D* or *KRASG12V* mutation in Amhr2-Cre mice develop different gynecologic tumors. Kwong-Kwok Wong, The University of Texas MD Anderson Cancer Center, Houston, TX.

A25 In vivo evidence validating the palmitoylation/depalmitoylation cycle as a therapeutic target in *NRAS* mutant hematologic cancers. Noemi A. Zambetti, Department of Pediatrics, University of California San Francisco, San Francisco, CA.

A26 Precise characterization and comparison of KRAS proteoforms by top-down mass spectrometry. Caroline J. DeHart, Northwestern University, Evanston, IL.



Poster Session A

Monday, Dec. 10, 2018
1:30 p.m.-3:30 p.m.

A28 USP21 promotes stemness of pancreatic cancer cells and bypass of KRAS extinction. Pingping Hou, University of Texas MD Anderson Cancer Center, Houston, TX.

A29 The gastric cancer-associated mutations R5W and Y42C in the RAS homologous RHOA protein cause distinct biochemical alterations, exhibit gain-of-function signaling and oncogenic activities. Antje Schaefer, University of North Carolina at Chapel Hill, Chapel Hill, NC.

A30 Neurofibromatosis type 1 (NF1) regulates the RAS-related GTPases, RRAS and RRAS2, independent of RAS activity in melanoma cells. Jillian M. Silva, University of California San Francisco, San Francisco, CA.

A31 Germline RASopathy mutations provide functional insights into the Raf cysteine-rich domain (CRD). Russell Spencer-Smith, NCI-Frederick, Frederick, MD.

A32 Selective contribution of the SHOC2 phosphatase complex to ERK pathway dynamics highlights its potential as a therapeutic target. Isabel Boned del Rio, University College London, Cancer Institute, London, United Kingdom.

A33 Combinations with CDK4/6 inhibitors to treat cancers with mutations in both KRAS and CDKN2A. Sean G. Buchanan, Eli Lilly, Indianapolis, IN.

A34 Defining KRAS mutation-specific kinome signatures and vulnerabilities in colorectal cancer. James Duncan, Fox Chase Cancer Center, Philadelphia, PA.

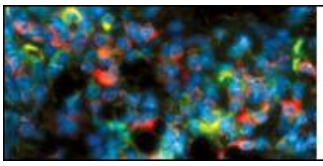
A36 Neoadjuvant-like Ezh2 inhibition in Kras-driven lung cancer amplifies inflammation and creates new therapeutic vulnerabilities. Gaetano Gargiulo, Max-Delbrück-Center for Molecular Medicine (MDC), Berlin, Germany.

A37 Mapping KRAS signaling pathways using the Mammalian-Membrane Two-Hybrid (MaMTH) assay to elucidate novel therapeutic targets. Ingrid Claudia Grozavu, University of Toronto, Toronto, ON, Canada.

A39 The role of YAP in regulating glycogen metabolism in pancreatic cancer. Sung Eun (Monica) Kim, University of California San Francisco, San Francisco, CA.

A40 Combinatorial knockout of Rap1GDS1 and RhoA leads to lethality in KRAS-driven non-small cell lung cancer. Kaja Kostyrko, University of California San Francisco, San Francisco, CA.

A41 Nucleotide metabolism heterogeneity in mutant KRAS pancreatic cancer. Thuc M. Le, University of California Los Angeles, Los Angeles, CA.



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A42 Bromodomain inhibitors suppress Nrf2-dependent HO-1 positive macrophage accumulation in murine models of KRAS-mutated pancreatic cancer. Ana S. Leal, Michigan State University, East Lansing, MI.

A43 Investigating novel inhibitors of the IMP-1-KRAS mRNA interaction. Victor Liu, University of Northern British Columbia, Prince George, BC, Canada.

A44 SHP2 inhibition overcomes RTK-mediated pathway reactivation in KRAS-mutant tumors treated with MEK inhibitors. Hengyu Lu, Novartis Institutes for BioMedical Research, Cambridge, MA.

A45 Protective autophagy elicited by RAF→MEK→ERK inhibition suggests a treatment strategy for RAS-driven cancers. Martin McMahon, Huntsman Cancer Institute, University of Utah, Salt Lake City, UT.

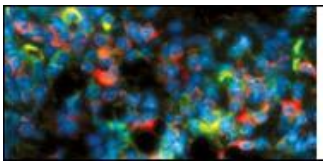
A46 A pan-cancer RAS mutant library elucidates the transformation potential of RAS variants. Amanda R. Moore, Genentech Inc, South San Francisco, CA.

A47 Targeting glutaminolysis potentiates the efficacy of chemotherapy in RAS-driven pancreatic cancers. Suman Mukhopadhyay, Frederick National Laboratory, Frederick, MD.

A48 Therapeutic reactivation of the protein phosphatase 2A (PP2A) for the treatment of KRAS-driven cancers. Goutham Narla, University of Michigan, Ann Arbor, MI.

A49 Specific Kras codon 12 and 13 mutations display different tumor initiation in pancreatic cancer Maria Paz Zafra Martin, Sandra and Edward Meyer Cancer Center, Department of Medicine, Weill Cornell Medicine, New York;

A50 Molecular Targeting of HuR Oncoprotein for Melanoma Treatment. Rebaz Ahmed, Univ. of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma.



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Poster Session B

Tuesday, Dec. 11
5:25 p.m.-7:25 p.m.

B01 Inhibition of RAS signaling and tumorigenesis through targeting vulnerabilities in RAS biochemistry. John P. O'Bryan. MUSC, UIC, Charleston, SC.

B02 Dissecting tumor cell heterogeneity to identify therapeutic vulnerabilities in Kras-mutant lung cancer. Aparna Padhye, University of Texas MD Anderson Cancer Center, Houston, TX.

B03 Biologic and biochemical interactions of NF1 GAP on KRAS G13x mutations. Dana Rabara, Frederick National Laboratory for Cancer Research, Frederick, MD.

B04 High-level expression of oncogenic KRAS is required to transform LKB1 mutant tissue in vivo. Briana B. Rackley, Emory University, Atlanta, GA.

B05 ASN007, an oral ERK1/2 inhibitor, shows strong antitumor activity across a panel of KRAS subtype mutant cancer models. Sanjeeva P. Reddy, Asana BioSciences, Lawrenceville, NJ.

B06 ING2 loss sensitizes KRAS-mutated NSCLC to WEE1 inhibition through regulation of CHK1 expression. Charles Ricordel, Université de Rennes 1, Rennes, France.

B07 Inhibition of Ras signalling by targeting Son of Sevenless with Affimers. Sophie E. Saunders, University of Leeds, Leeds, United Kingdom.

B08 ETC inhibitors alter oncogenic KRAS signal transduction. Kanika Sharma, Frederick National Laboratory for Cancer Research, Frederick, MD.

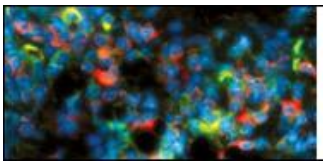
B09 Combining proteomics and genetic screens to identify *KRAS* synthetic lethal interactions. Shikha S. Sheth, Cancer Research Institute, Beth Israel Deaconess Cancer Center and Department of Medicine, Harvard Medical School, Boston, MA.

B10 Modeling the genetic heterogeneity of *KRAS* mutant lung adenocarcinomas for therapeutic discovery. Kate D. Sutherland, The Walter and Eliza Hall of Medical Research, Melbourne, VIC, Australia.

B11 O-GlcNAcylation is required for mutant KRAS-induced lung tumorigenesis. Phuoc T. Tran, Johns Hopkins University School of Medicine, Baltimore, MD.

B12 DOCK1 as a novel target for controlling RAS-driven cancer cell survival and invasion. Takehito Uruno, Kyushu University, Medical Institute of Bioregulation, Fukuoka-city, Japan.

B13 Parallel targeting of RAF/MEK/ERK pathway in RAS-mutant embryonal rhabdomyosarcoma. Angelina V. Vaseva, Greehey Children's Cancer Research Institute, The University of Texas Health Science Center, San Antonio, TX.



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B14 CRAF-mediated inactivation of epigenetic repressor complexes promotes KRAS-driven tumorigenesis. Avinashnarayan Venkatanarayan, Genentech, Inc., South San Francisco, CA.

B15 Dabrafenib-trametinib-induced pyrexia successfully treated with colchicine. Jesus Vera, Mayo Clinic, Rochester, MN.

B16 Role of RasGRF2 in AnxA6-mediated growth of TNBC cells. Diva S. Whalen, Meharry Medical College, Nashville, TN.

B17 MEK inhibition induces myogenic differentiation in RAS-driven rhabdomyosarcoma. Marielle E. Yohe, NCI, Bethesda, MD.

B18 *Clostridium perfringens* lethal toxin specifically targets RAS and disrupts RAS signaling pathway. Maria Abreu-Blanco, Frederick National Laboratory for Cancer Research, Frederick, MD.

B19 New tools to study the role of RAS/CRAF interaction in RAS-driven lung cancer. Romain Baer, The Francis Crick Institute, London, United Kingdom.

B20 Unbiased high-throughput screenings to identify combination therapies targeting RAS-mutated colorectal cancer. Rajat Bhattacharya, University of Texas MD Anderson Cancer Center, Houston, TX.

B21 Cancer-specific intracellular delivery of therapeutic antibodies against KRAS. Kathlynn C. Brown, SRI International, Harrisonburg, VA.

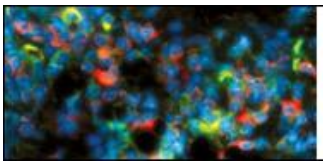
B22 Identifying protein interactors of oncogenic Kras in pancreatic cancer cells via proximity labelling. Derek K. Cheng, David A. Tuveson, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY.

B23 Insight towards therapeutic susceptibility of KRAS mutant cancers from MRTX1257: A prototype selective inhibitor of KRAS G12C. James G. Christensen, Mirati Therapeutics, San Diego, CA.

B24 Development of small-molecule RAS inhibitors using Affimer reagents. Katarzyna Haza, University of Leeds, Leeds, United Kingdom.

B25 Combined proteomic and genetic interaction mapping reveals new Ras pathway effectors and regulators. Peter K. Jackson, Stanford University, Stanford, CA.

B26 The SHOC2 phosphatase complex as a therapeutic target for ERK-pathway inhibition in RAS-driven tumors. Greg G. Jones, University College London, London, United Kingdom.



Poster Session B

Tuesday, Dec. 11
5:25 p.m.-7:25 p.m.

B27 A DARPin-based toolbox to understand and treat RAS-addicted cancers. Jonas N. Kapp, University of Zurich, Zurich, Switzerland.

B28 Direct targeting oncogenic Ras mutants by IgG-format cytosol-penetrating antibody. Yong-Sung Kim, Ajou University, Suwon, Republic of Korea.

B29 SHANK3 in oncogenic RAS signaling. Johanna Lilja, Turku Centre for Biotechnology, University of Turku, Turku, Finland.

B30 Structure-based drug discovery of MRTX1257, a selective, covalent KRAS G12C inhibitor with oral activity in animal models of cancer. Matthew A. Marx, Mirati Therapeutics, San Diego, CA.

B31 Combination inhibitor strategies targeting KRAS effector signaling in KRAS-mutant pancreatic cancer. Irem Ozkan-Dagliyan, University of North Carolina, Chapel Hill, NC.

B32 Silencing of oncogenic KRAS by a mutant-favoring short interfering RNA. Bjoern Papke, University of North Carolina at Chapel Hill, Chapel Hill, NC.

B33 Inhibition of Ras using Affimers. Ajinkya Rao, University of Leeds, Leeds, United Kingdom.

B34 Targeted destruction of endogenous K-RAS using an Affinity directed PROtein Missile (AdPROM). Sascha O. M. Roth, MRC Protein Phosphorylation and Ubiquitylation Unit, School of Life Sciences, University of Dundee, Dundee, United Kingdom.

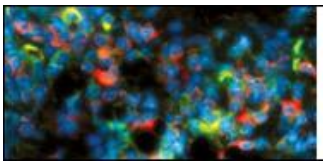
B35 Discovery of K-Ras(G12D)-targeting peptide KRpep-2d and its optimization strategy. Kotaro Sakamoto, ICHIMARU PHARCOS Co., Ltd., Motosu-shi, Gifu, Japan.

B36 Berberine induces apoptosis in cervical carcinoma cells by inducing DNA damage and inhibition of RAS MAPK pathway. Mayank Singh, All India Institute of Medical Sciences Delhi, New Delhi, India.

B37 Development of inhibitors of the activated form of KRAS G12C. Michelle L. Stewart, Warp Drive Bio, Cambridge, MA.

B38 Ras clipping by bacterial toxin RRSP reduces viability and proliferation of Ras-dependent cancer cell lines in 2D and 3D in vitro models. Vania Vidimar, Northwestern University, Chicago, IL.

B39 Characterization of the interaction between KRAS and Argonaute 2. Jessica Waninger, University of Michigan, Ann Arbor, MI.



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B40 Role of mutant HRAS in growth and drug sensitivity of head and neck squamous cell cancers (HNSCC). Adrienne D. Cox, University of North Carolina at Chapel Hill, Chapel Hill, NC.

B43 A systems biology approach to elucidate the mechanism of EGFR inhibitor sensitivity in mutant KRAS-driven colorectal cancer. Thomas McFall, Salk Institute, La Jolla, CA.

B44 KRAS and RAS signaling network is co-regulated and can be therapeutically blocked by targeting eIF4A dependent translation program. Kamini Singh, Cancer Biology and Genetics Program, Memorial Sloan Kettering Cancer Center, New York, NY.

B45 Surveillance of RAS-RAF dynamics in vivo: Tracking activity conformations and drug-induced interactions. Eduard Stefan, University of Innsbruck, Innsbruck, Austria.

B46 Systems modeling of Ras reveals systems mechanisms that dictate response to treatment. Edward C. Stites, Salk Institute for Biological Studies, La Jolla, CA.

B47 Systems-level dissection of tumor-macrophage crosstalk in ovarian cancer resistance to MEK inhibition. Stephanie J. Wang, Massachusetts Institute of Technology, Cambridge, MA.

B49 "Triple wild-type" co-mutational profile in early-stage *KRAS*-mutant lung cancer. Colin R. Lindsay, University of Manchester, Manchester, United Kingdom.

B50 ERK MAPK inhibition enhances the immunogenicity of KRAS-mutant colorectal cancer. Meagan B. Ryan, Massachusetts General Hospital Cancer Center, Boston, MA.

B51 MAPK regulation of an innate immune response in KRAS-mutant lung adenocarcinoma. Daniel Sisler, University of Colorado-Anschutz Medical Campus, Aurora, CO.

B52 KRAS-IRF2 axis drives immune suppression and immune therapy resistance in colorectal cancer. Alan Wang, University of Texas MD Anderson Cancer Center, Houston, TX.

B53 Differential response of distinct KRAS mutants to SHP2 inhibition. Sara Mainardi, Molecular Carcinogenesis Division, The Netherlands Cancer Institute, Amsterdam, The Netherlands.