BREAKING INSIGHTS
6055 Highlights from Recent Cancer Literature

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6057 Mitohormesis, UPRmt, and the Complexity of Mitochondrial DNA Landscapes in Cancer
Timothy C. Kenny, Maria L. Gomez, and Doris Germain

6067 Circulating Tumor Cell-Neutrophil Tango along the Metastatic Process
Massimo Saini, Barbara M. Szczersba, and Nicola Aceto

CANCER RESEARCH HIGHLIGHTS
6074 Targeting Mitochondrial Fission to Trigger Cancer Cell Death
V. Ashutosh Rao
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CONTROVERSY AND CONSENSUS
6079 E-Cigarettes: Unstandardized, Under-Regulated, Understudied, and Unknown Health and Cancer Risks
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GENOME AND EPIGENOME
6084 Epigenomic Profiling Discovers Trans-lineage SOX2 Partnerships Driving Tumor Heterogeneity in Lung Squamous Cell Carcinoma
Takashi Sato, Seungyeul Yoo, Ranron Kong, Abhilasha Sinha, Prashanth Chandramani-Shivlingappa, Ayushi Patel, Maya Fridrikh, Osamu Nagano, Takashi Masuko, Mary Beth Beasley, Charles A. Powell, Jun Zhu, and Hideo Watanabe


6101 Histone-Related Genes Are Hypermethylated in Lung Cancer and Hypermethylated HIST1H4F Could Serve as a Pan-Cancer Biomarker
Shihua Dong, Wei Li, Lin Wang, Jie Hu, Yuanlin Song, Raolong Zhang, Xiaoguang Ren, Shimeng Ji, Jin Li, Peng Xu, Ying Liang, Gang Chen, Jia-Tao Lou, and Weniqiang Yu
Significance: These findings identify a new biomarker for cancer detection and show that hypermethylation of histone-related genes seems to persist across cancers.

6113 Follistatin-like Protein 1 Inhibits Lung Cancer Metastasis by Preventing Proteolytic Activation of Osteopontin
Jean Chiou, Yu-Chan Chang, Hsing-Fang Tsai, Yuan-Feng Lin, Ming-Shyan Huang, Chih-Jen Yang, and Michael Hsiao
Significance: These findings describe the novel interaction between FSTL1 and SPP1 and its role in the metastatic progression of lung adenocarcinoma.

6126 Mcl-1 Interacts with Akt to Promote Lung Cancer Progression
Guo Chen, Donglyouo Park, Andrew T. Magis, Madhusmita Behera, Suresh S. Ramalingam, Taopeek K. Owonikoko, Gabriel L. Sica, Kejiing Ye, Chao Zhang, Zhengjia Chen, Walter J. Curran, and Xingming Deng
Significance: These findings indicate that targeting Mcl-1/Akt interaction by employing small molecules such as PH-687 represents a potentially new and effective strategy for cancer treatment.

6139 MK5 Regulates YAP Stability and Is a Molecular Target in YAP-Driven Cancers
Jimyung Seo, Min Hwan Kim, Hyunsoo Cho, Seongyeol Park, Sang Kyum Kim, and Joon Kim
Significance: These findings reveal MK5 is a novel kinase that regulates YAP in a LATS-independent manner and can be targeted for cancer therapy.
**TUMOR BIOLOGY AND IMMUNOLOGY**

6153  
PGC1α Suppresses Prostate Cancer Cell Invasion through ERRα Transcriptional Control  

**Significance:** These findings describe how downregulation of the prostate tumor suppressor PGC1 drives invasiveness and migration of prostate cancer cells.

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**TRANSLATIONAL SCIENCE**

6166  
A Novel MYCN-Specific Antigene Oligonucleotide Deregulates Mitochondria and Inhibits Tumor Growth in MYCN-Amplified Neuroblastoma  
Luca Montemurro, Salvatore Raieli, Silvia Angelucci, Damiano Bartolucci, Camilla Amadesi, Silvia Lampis, Anna Lisa Scardovi, Leonardo Venturelli, Giammario Nieddu, Lucia Cerisoli, Matthias Fischer, Gabriella Teti, Mirella Falconi, Andrea Pession, Patrizia Hrelia, and Roberto Tonelli  

**Significance:** A second generation antigene peptide oligonucleotide targeting MYCN induces mitochondrial damage and inhibits growth of MYCN-amplified neuroblastoma cells.

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6178  
A Microbial Siderophore-Inspired Self-Gelling Hydrogel for Noninvasive Anticancer Phototherapy  
Seungbeom Ko, Joo Yeon Park, and Yu-Kyoung Oh  

**Significance:** These findings provide new insights into noninvasive anticancer phototherapy using self-gelling hydrogels. Application of these hydrogels in preclinical models reduces the sizes of solid tumors and skin cancers without surgery, radiation, or chemotherapy.

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6190  
Parallel Signaling through IRE1α and PERK Regulates Pancreatic Neuroendocrine Tumor Growth and Survival  

**Significance:** The UPR is upregulated in pancreatic neuroendocrine tumors and its inhibition significantly reduces tumor growth in preclinical models, providing strong rationale for targeting the UPR in these cancers.

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**RESOURCE REPORTS**

6204  
YAP1 Mediates Resistance to MEK1/2 Inhibition in Neuroblastomas with Hyperactivated RAS Signaling  
Grace E. Coggins, Alvin Farrel, Komal S. Rathi, Colin M. Hayes, Laura Scolaro, Jo Lynne Rokita, and John M. Maris  

**Significance:** High-risk neuroblastomas with hyperactivated RAS signaling escape the selective pressure of MEK inhibition via YAP1-mediated transcriptional reprogramming and may be sensitive to combination therapies targeting both YAP1 and MEK.

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6215  
MFF Regulation of Mitochondrial Cell Death Is a Therapeutic Target in Cancer  
Jae Ho Seo, Young Chan Chae, Andrew V. Kossenkov, Yu Geon Lee, Hsin-Yao Tang, Ekta Agarwal, Dmitry I. Gabrilovich, Lucia R. Languino, David W. Speicher, Prashanth K. Shastrula, Alessandra Maria Storaci, Stefano Ferrero, Gabriella Gaudioso, Manuela Caroli, Davide Tosi, Massimo Giorda, Valentina Vaira, Vito W. Rebecca, Meenhard Herlyn, Min Xiao, Dylan Figner, Alessandra Martorella, Emmanuel Skordalakes, and Dario C. Altieri  

**Significance:** These findings describe mitochondrial fission regulation using a peptidomimetic agent that disturbs the MFF-VDAC complex and displays anticancer activity in multiple tumor models.  
See related commentary, p. 6074

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6227  
Modeling Cellular Response in Large-Scale Radiogenomic Databases to Advance Precision Radiotherapy  
Venkata SK. Manem, Meghan Lambie, Ian Smith, Petr Smirnov, Victor Kofia, Mark Freeman, Marianne Koritzinsky, Mohamed E. Abazeed, Benjamin Haibe-Kains, and Scott V. Bratman  

**Significance:** The RadioGx computational platform enables integrative analyses of cellular response to radiation with drug responses and genome-wide molecular data.  
See related commentary, p. 6076

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6238  
Comprehensive Benchmarking and Integration of Tumor Microenvironment Cell Estimation Methods  
Alejandro Jiménez-Sánchez, Oliver Cast, and Martin L. Müller  

**Significance:** This work shows an independent and comprehensive benchmarking of recently developed and widely used tumor microenvironment cell estimation methods based on bulk expression data and integrates the tools into a consensus approach.
ABOUT THE COVER

Cancer Research selects a cover image for each issue from suggestions submitted by our authors. This month's cover features a montage of our covers from 2019. We thank all authors who submitted cover art suggestion during this past year and look forward to receiving submissions in the coming year.