

CANCER RESEARCH

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See related article, *Cancer Res* 80(23):5367–79.

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- 268 **Single-Cell Transcriptomic Heterogeneity in Invasive Ductal and Lobular Breast Cancer Cells**
Fangyuan Chen, Kai Ding, Nolan Priedigkeit, Ashuvinee Elangovan, Kevin M. Levine, Neil Carleton, Laura Savariau, Jennifer M. Atkinson, Steffi Oesterreich, and Adrian V. Lee
This study represents a key step towards understanding heterogeneity in cancer cell lines and the role of E-cadherin depletion in contributing to the molecular features of invasive lobular breast carcinoma.

- 282 **Misannotated Multi-Nucleotide Variants in Public Cancer Genomics Datasets Lead to Inaccurate Mutation Calls with Significant Implications**

Sujaya Srinivasan, Natallia Kalinava, Rafael Aldana, Zhipan Li, Sjoerd van Hagen, Sander Y.A. Rodenburg, Megan Wind-Rotolo, Xiaozhong Qian, Ariella S. Sasson, Hao Tang, and Stefan Kirov

Identification of incorrect mutation calls in TCGA, including clinically relevant *BRAF* V600 and *KRAS* G12, will influence research and potentially clinical decisions.

METABOLISM AND CHEMICAL BIOLOGY

- 289 **2-Hydroxylation of Fatty Acids Represses Colorectal Tumorigenesis and Metastasis via the YAP Transcriptional Axis**
Liang Sun, Xiaoqin Yang, Xiaoheng Huang, Yizhou Yao, Xiangyu Wei, Shugao Yang, Diyan Zhou, Wei Zhang, Zhimin Long, Xiaoyan Xu, Xinguo Zhu, Songbing He, and Xiong Su

These findings identify a novel metabolic mechanism regulating the tumor suppressor function of FA 2-hydroxylation in colorectal cancer.

- 303 **Targeting Subtype-Specific Metabolic Preferences in Nucleotide Biosynthesis Inhibits Tumor Growth in a Breast Cancer Model**
Martin P. Ogrodzinski, Shao Thing Teoh, and Sophia Y. Lunt

These findings uncover differences in nucleotide salvage and *de novo* biosynthesis using a histologically heterogeneous breast cancer model, highlighting metabolic vulnerabilities in these pathways as promising targets for breast cancer subtypes.

MOLECULAR CELL BIOLOGY


- 315 **RNA-Binding RING E3-Ligase DZIP3/hRUL138 Stabilizes Cyclin D1 to Drive Cell-Cycle and Cancer Progression**
Srinivasa P. Kolapalli, Rinku Sahu, Nishant R. Chauhan, Kautilya K. Jena, Subhash Mehto, Saroj K. Das, Ashish Jain, Manaswini Rout, Rupesh Dash, Rajeeb K. Swain, David Y. Lee, Tor Erik Rusten, Santosh Chauhan, and Swati Chauhan
 **A C**
- These findings show that DZIP3 is a novel driver of cell-cycle and cancer progression via its control of cyclin D1 mRNA and protein stability in a cell-cycle phase-dependent manner.

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- 332** **Loss of ARID1A Promotes Epithelial–Mesenchymal Transition and Sensitizes Pancreatic Tumors to Proteotoxic Stress**
A C Hideo Tomihara, Federica Carbone, Luigi Perelli, Justin K. Huang, Melinda Soeung, Johnathon L. Rose, Frederick S. Robinson, Yonathan Lissanu Deribe, Ningping Feng, Mitsunobu Takeda, Akira Inoue, Edoardo Del Poggetto, Angela K. Deem, Anirban Maitra, Pavlos Msaouel, Nizar M. Tannir, Giulio F. Draetta, Andrea Viale, Timothy P. Heffernan, Christopher A. Bristow, Alessandro Carugo, and Giannicola Genovese
This study identifies ARID1A loss as a promising biomarker for the identification of PDAC tumors that are potentially responsive to treatment with proteotoxic agents.
- 344** **circIGHG-Induced Epithelial-to-Mesenchymal Transition Promotes Oral Squamous Cell Carcinoma Progression via miR-142-5p/IGF2BP3 Signaling**
A C Jingpeng Liu, Xiao Jiang, Ailing Zou, Zhaoyi Mai, Zhijie Huang, Liying Sun, and Jianjiang Zhao
These findings broaden our insights regarding regulation of OSCC progression by circular RNA and serve as a reference for future clinical research in OSCC diagnosis and treatment.
- 356** **Nucleoporin 210 Serves a Key Scaffold for SMARCB1 in Liver Cancer**
Seong Hwi Hong, Keun Hong Son, Sang Yun Ha, Tae In Wee, Sung Kyung Choi, Ji Eun Won, Hee Dong Han, Youngtae Ro, Yeong-Min Park, Jung Woo Eun, Suk Woo Nam, Jeung-Whan Han, Keunsoo Kang, and Jueng Soo You
This study reveals a novel protumorigenic role for SMARCB1 and describes valuable links between nucleoporins and chromatin remodelers in cancer by identifying NUP210 as a critical coregulator of SMARCB1 chromatin remodeling activity.
- 371** **Pleiotropic Mechanisms Drive Endocrine Resistance in the Three-Dimensional Bone Microenvironment**
A C Eugen Dhimolea, Ricardo de Matos Simoes, Dhvanir Kansara, Xiang Weng, Shruti Sharma, Pallavi Awate, Zhiyi Liu, Dong Gao, Nicholas Mitsiades, Joseph H. Schwab, Yu Chen, Rinath Jeselsohn, Aedin C. Culhane, Myles Brown, Irene Georgakoudi, and Constantine S. Mitsiades
This study uncovers a previously underappreciated dependency of tumor cells on HR signaling for anchorage-independent growth and highlights how the metastatic microenvironment restores this malignant property of cancer cells during hormone therapy.
- 384** **Frizzled-7 Identifies Platinum-Tolerant Ovarian Cancer Cells Susceptible to Ferroptosis**
Yinu Wang, Guangyuan Zhao, Salvatore Condello, Hao Huang, Horacio Cardenas, Edward J. Tanner, JianJun Wei, Yanrong Ji, Junjie Li, Yuying Tan, Ramana V. Davuluri, Marcus E. Peter, Ji-Xin Cheng, and Daniela Matei
Frizzled-7 marks platinum-tolerant cancer cells harboring stemness features and altered glutathione metabolism that depend on GPX4 for survival and are highly susceptible to ferroptosis.
- 400** **Loss of Aurora Kinase Signaling Allows Lung Cancer Cells to Adopt Endoreplication and Form Polyploid Giant Cancer Cells That Resist Antimitotic Drugs**
Vural Tagal and Michael G. Roth
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- 414** **Unconventional Secretion of PKC δ Exerts Tumorigenic Function via Stimulation of ERK1/2 Signaling in Liver Cancer**
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PKC δ secretion from liver cancer cells behaves as a humoral growth factor that contributes to cell growth via activation of proliferative signaling molecules, which may be potential diagnostic or therapeutic targets.
- 426** **The Cancer-Associated ATM R3008H Mutation Reveals the Link between ATM Activation and Its Exchange**
Maja Milanovic, Lisa M. Houghton, Demis Menolfi, Ji-Hoon Lee, Kenta Yamamoto, Yang Li, Brian J. Lee, Jun Xu, Verna M. Estes, Dong Wang, Peter J. Mckinnon, Tanya T. Paull, and Shan Zha
This study functionally characterizes the most common ATM missense mutation R3008H in cancer and identifies a unique role of PI3-kinase regulatory domain in ATM activation.

TUMOR BIOLOGY AND IMMUNOLOGY

- 438** **Glutamine-Directed Migration of Cancer-Activated Fibroblasts Facilitates Epithelial Tumor Invasion**
Aida Mestre-Farrera, Marina Bruch-Oms, Raúl Peña, José Rodríguez-Morató, Lorena Alba-Castellón, Laura Comerma, Miguel Quintela-Fandino, Mireia Duñach, Josep Baulida, scar J. Pozo, and Antonio García de Herreros
Cancer-associated fibroblasts migrate and invade toward free glutamine and facilitate invasion of tumor epithelial cells, accounting for their movement away from the hostile conditions of the tumor towards nutrient-rich adjacent tissues.
- 452** **Chemotherapy-Induced Upregulation of Small Extracellular Vesicle-Associated PTX3 Accelerates Breast Cancer Metastasis**
Carson A. Wills, Xiaoming Liu, Longgui Chen, Yuanjun Zhao, Christopher M. Dower, Jeffrey Sundstrom, and Hong-Gang Wang
These findings show that chemotherapy-induced small extracellular vesicles accelerate breast cancer metastasis, and targeted inhibition of tumor-derived vesicles may be a promising therapeutic strategy to improve the efficacy of chemotherapy treatment.

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Nathan Harmston, Jun Yi Stanley Lim, Oriol Arqués, Héctor G. Palmer, Enrico Petretto, David M. Virshup, and Babita Madan

These findings show that Wnt/ β -catenin signaling causes widespread gene repression via inhibition of MAPK signaling, thus fine tuning the RAS-MAPK pathway to optimize proliferation in cancer.

476 **Cell Softness Prevents Cytolytic T-cell Killing of Tumor-Repopulating Cells**

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Yuying Liu, Tianzhen Zhang, Haizeng Zhang, Jiping Li, Nannan Zhou, Roland Fiskesund, Junwei Chen, Jiadi Lv, Jingwei Ma, Huafeng Zhang, Ke Tang, Feiran Cheng, Yabo Zhou, Xiao-hui Zhang, Ning Wang, and Bo Huang
Tumor-repopulating cells evade CD8⁺ cytolytic T-cell killing through a mechanical softness mechanism, underlying the impediment of perforin pore formation at the immune synapse site.

TRANSLATIONAL SCIENCE

489 **E74-Like Factor 3 Is a Key Regulator of Epithelial Integrity and Immune Response Genes in Biliary Tract Cancer**

Masami Suzuki, Mihoko Saito-Adachi, Yasuhito Arai, Yuko Fujiwara, Erina Takai, Shinsuke Shibata, Masahide Seki, Hirofumi Rokutan, Daichi Maeda, Masafumi Horie, Yutaka Suzuki, Tatsuhiro Shibata, Tohru Kiyono, and Shinichi Yachida

These findings show that ELF3 regulates epithelial integrity and host immune responses and functions as a tumor suppressor in biliary tract cancer.

501 **Inhibition of G Protein-Coupled Receptor Kinase 2 Promotes Unbiased Downregulation of IGF1 Receptor and Restrains Malignant Cell Growth**

Caitrin Crudden, Takashi Shibano, Dawei Song, Mihnea P. Dragomir, Sonia Cismas, Julianna Serly, Daniela Nedelcu, Enrique Fuentes-Mattei, Andrei Tica, George A. Calin, Ada Girnita, and Leonard Girnita

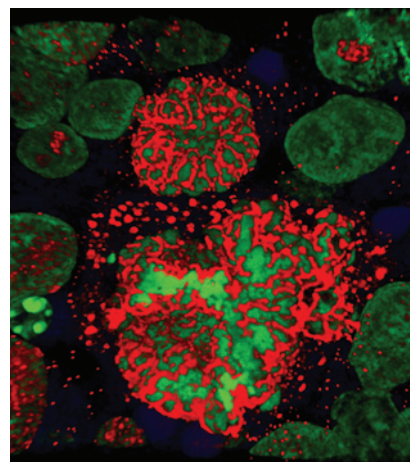
This work provides insight into the molecular and biological roles of biased signaling downstream RTK and provides a novel "system bias" strategy to increase the efficacy of anti-IGF1R-targeted therapy in cancer.

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ABOUT THE COVER

During mitosis, Ki-67 (red) is necessary for the formation of the perichromosomal layer and prevents chromosomes from collapsing into a single chromatin mass. Thus, the cells undergoing mitosis can be easily recognized using Ki-67 immunostaining, as the nucleus (blue) gives a floral appearance. A significantly higher number of mitotic floral cells were observed in control tumors as compared with the DZIP3 knockdown tumors. For details, see the article by Kolapalli and colleagues on page 315.



Cancer Research

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