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Georgina D. Barnabas, Joo Sang Lee, Tamar Shami, Michal Harel, Lir Beck, Michael Selitrennik, Livnat Jerby-Arnon, Neta Erez, Eytan Ruppim, and Tamar Geiger
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1486 **HDAC5 Loss Impairs RB Repression of Pro-Oncogenic Genes and Confers CDK4/6 Inhibitor Resistance in Cancer**
Yingke Zhou, Xin Jin, Jian Ma, Donglin Ding, Zhenlin Huang, Haoyue Sheng, Yuqian Yan, Yunqian Pan, Ting Wei, Ligu Wang, Heshui Wu, and Haojie Huang
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Priyanka Kulkarni, Pritha Dasgupta, Yutaka Hashimoto, Marisa Shiina, Varahram Shahryari, Z. Laura Tabatabai, Soichiro Yamamura, Yuichiro Tanaka, Sharanjot Saini, Rajvir Dahiya, and Shahana Majid

This study's investigation of noncoding RNA interactions in renal cell carcinoma identify miRNA-155-lncRNA TCL6-mediated regulation of the Src-Akt-EMT network as a novel mechanism of disease progression and metastasis.

TUMOR BIOLOGY AND IMMUNOLOGY

1513 **Oncogenic Ras Disrupts Epithelial Integrity by Activating the Transmembrane Serine Protease Hepsin**

Topi A. Tervonen, Shishir M. Pant, Denis Belitškin, Johanna I. Englund, Katja Närhi, Caj Haglund, Panu E. Kovanen, Emmy W. Verschuren, and Juha Klefström

These findings identify the cell-surface serine protease hepsin as a potential therapeutic target for its role in oncogenic Ras-mediated deregulation of epithelial cell-cell and cell-matrix interactions and cohesion of epithelial structure.

1528 **Therapy-Induced Transdifferentiation Promotes Glioma Growth Independent of EGFR Signaling**

Hwanhee Oh, Inah Hwang, Ja-Young Jang, Lingxiang Wu, Dongqing Cao, Jun Yao, Haoqiang Ying, Jian Yi Li, Yu Yao, Baoli Hu, Qianghu Wang, Hongwu Zheng, and Jihye Paik

This study demonstrates that molecular reprogramming and lineage transdifferentiation underlie anti-EGFR therapy resistance and are clinically relevant to the development of new combinatorial targeting strategies against malignant gliomas with aberrant EGFR signaling.

1540 **The *BRCA1* Pseudogene Negatively Regulates Antitumor Responses through Inhibition of Innate Immune Defense Mechanisms**

Yoo Jane Han, Jing Zhang, Jung-Hyun Lee, Jennifer M. Mason, Olga Karginova, Toshio F. Yoshimatsu, Qinyu Hao, Ian Hurley, Laia Paré Brunet, Aleix Prat, Kannanganattu V. Prasanth, Michaela U. Gack, and Olufunmilayo I. Olopade

This study identifies a novel mechanism of innate immunity driven by a host pseudogene RNA that inhibits innate immune defense mechanisms and antitumor responses through regulation of antiviral gene expression.

TRANSLATIONAL SCIENCE

1552 **Bladder Tumor Subtype Commitment Occurs in Carcinoma *In Situ* Driven by Key Signaling Pathways Including ECM Remodeling**

Adrian Wullweber, Reiner Strick, Fabienne Lange, Danijel Sikic, Helge Taubert, Sven Wach, Bernd Wullich, Simone Bertz, Veronika Weyerer, Robert Stoehr, Johannes Breyer, Maximilian Burger, Arndt Hartmann, Pamela L. Strissel, and Markus Eckstein

This study demonstrates that CIS is the stage of commitment for determining MIBC tumor subtype, which is relevant for patient prognosis and therapy response.

1567 **Mesenchymal Stem Cell-Secreted Extracellular Vesicles Instruct Stepwise Dedifferentiation of Breast Cancer Cells into Dormancy at the Bone Marrow Perivascular Region**

Oleta A. Sandiford, Robert J. Donnelly, Markos H. El-Far, Lisa M. Burgmeyer, Garima Sinha, Sri Harika Pamarthi, Lauren S. Sherman, Alejandra I. Ferrer, Dariana E. DeVore, Shyam A. Patel, Yahaira Naaldijk, Sara Alonso, Pradeep Barak, Margarette Bryan, Nicholas M. Ponzio, Ramaswamy Narayanan, Jean-Pierre Etchegaray, Rakesh Kumar, and Pranela Rameshwar

These findings describe how the initial process of dormancy and dedifferentiation of breast cancer cells at the bone marrow perivascular niche requires mesenchymal stem cell-derived exosomes, indicating a potential target for therapeutic intervention.

1583 **Ferroptosis Inducers Are a Novel Therapeutic Approach for Advanced Prostate Cancer**

Ali Ghoochani, En-Chi Hsu, Merve Aslan, Meghan A. Rice, Holly M. Nguyen, James D. Brooks, Eva Corey, Ramasamy Paulmurugan, and Tanya Stoyanova

These findings reveal that induction of ferroptosis is a new therapeutic strategy for advanced prostate cancer as a monotherapy and in combination with second-generation antiandrogens.

1595 **EMT Transcription Factor ZEB1 Represses the Mutagenic *POLθ*-Mediated End-Joining Pathway in Breast Cancers**

Mélanie K. Prodhomme, Roxane M. Pommier, Camille Franchet, Frédérique Fauvet, Valérie Bergoglio, Pierre Brousset, Anne-Pierre Morel, Anne-Cécile Brunac, Mojgan Devouassoux-Shisheboran, Virginie Petrilli, Caroline Moyret-Lalle, Jean-Sébastien Hoffmann, Alain Puisieux, and Agnès Tissier

These findings uncover an original mechanism of TMEJ regulation, highlighting ZEB1 as a key player in genome stability during cancer progression via its repression of *POLQ*.

See related commentary, p. 1441

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POPULATION AND PREVENTION SCIENCE

1607 **Assessing Lung Cancer Absolute Risk Trajectory Based on a Polygenic Risk Model**

Rayjean J. Hung, Matthew T. Warkentin, Yonathan Brhane, Nilanjan Chatterjee, David C. Christiani, Maria Teresa Landi, Neil E. Caporaso, Geoffrey Liu, Mattias Johansson, Demetrius Albanes, Loic Le Marchand, Adonina Tardon, Gad Rennert, Stig E. Bojesen, Chu Chen, John K. Field, Lambertus A. Kiemeny, Philip Lazarus, Shanbeth Zienolddiny, Stephen Lam, Angeline S. Andrew, Susanne M. Arnold, Melinda C. Aldrich, Heike Bickeböller, Angela Risch, Matthew B. Schabath, James D. McKay, Paul Brennan, and Christopher I. Amos
Three large-scale datasets reveal that, after accounting for risk factors, an individual's genetics can affect their lung cancer risk trajectory, thus may inform the optimal timing for LDCT screening.

1616 **Light at Night and Risk of Pancreatic Cancer in the NIH-AARP Diet and Health Study**

Qian Xiao, Rena R. Jones, Peter James, and Rachael Z. Stolzenberg-Solomon
Our study suggests that higher LAN is a risk factor for pancreatic cancer, contributing to the growing literature that demonstrates the potentially adverse health effects of light pollution.

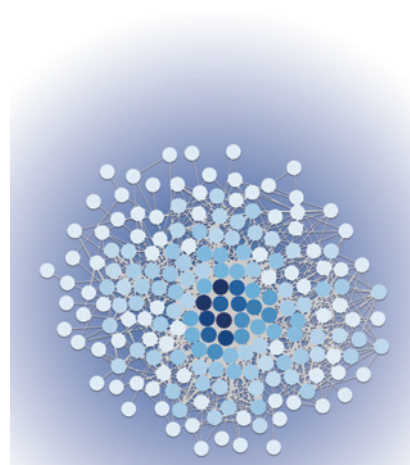
RETRACTION

1623 **Retraction: A Glycolytic Mechanism Regulating an Angiogenic Switch in Prostate Cancer**

Jianhua Wang, Jincheng Wang, Jinlu Dai, Younghun Jung, Chuen-Long Wei, Yu Wang, Aaron M. Havens, Phillip J. Hogg, Evan T. Keller, Kenneth J. Pienta, Jacques E. Nor, Cun-Yu Wang, and Russell S. Taichman

ABOUT THE COVER

Association of breast cancer subtypes with distinct metabolic phenotypes identified isocitrate dehydrogenase 2 (IDH2) as a key player in triple-negative breast cancer (TNBC) and HER2 subtypes. Wild-type IDH2 promoted cell proliferation, anchorage-independent growth, glycolysis, mitochondrial respiration, and antioxidant defense, thus revealing its protumorigenic role in TNBC cells. Serine biosynthesis pathway proteins were found to be metabolic synthetic dosage lethal partners of IDH2. Pharmacological inhibition of PHGDH sensitized cells with high IDH2 and inhibited tumor growth *in vivo*, emphasizing PHGDH inhibition as a therapeutic approach for triple-negative breast tumors with high IDH2. For details, see article by Barnabas and colleagues on page 1443.



Cancer Research

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