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**BREAKING ADVANCES**

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**REVIEWS**

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**MOLECULAR AND CELLULAR PATHOBIOLOGY**

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<td>Calcium Promotes Human Gastric Cancer via a Novel Coupling of Calcium-Sensing Receptor and TRPV4 Channel</td>
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**Précis:** These results raise the possibility that daily calcium supplements may be harmful to patients at risk for gastric cancer.

**Précis:** This study identifies a signaling pathway that promotes prostate cancer, suggesting new directions to limit progression of this disease, which is the key issue in promoting patient survival.

**Précis:** This study describes a novel regulatory element in WNT oncogenic signaling that expands the perspective on how colon cancers develop.
Sleeping Beauty Insertional Mutagenesis in Mice Identifies Drivers of Steatosis-Associated Hepatic Tumors

Précis: Fatty liver disease is growing with the obesity epidemic and the inflammatory damage that it can create can influence the risks and genetic evolution of liver cancer, which is poised to increase in incidence in parallel with obesity.

R-Spondin1/LGR5 Activates TGFβ Signaling and Suppresses Colon Cancer Metastasis
Xiaolin Zhou, Liying Geng, Degeng Wang, Haowei Yi, Geoffrey Talmon, and Jing Wang

Précis: These findings establish a novel cross-talk between an important adult intestinal stem cell marker and a well-established tumor suppressor pathway in colon cancer.

Administering xCT Inhibitors Based on Circadian Clock Improves Antitumor Effects
Fumiyasu Okazaki, Naoya Matsunaga, Kengo Hamamura, Kayoko Suzuki, Takaharu Nakao, Hiyouki Okazaki, Masahiko Kutsukake, Shiro Fukumori, Yasuhiro Tsuji, and Hideto To

Précis: The circadian gene clock regulates the transcription of the essential cystine transporter xCT, the expression of which determines the effectiveness of the chemotherapy drug sulfasalazine.

Super-Enhancers Promote Transcriptional Dysregulation in Nasopharyngeal Carcinoma
Jiang Yuan, Yan-Yi Jiang, Anand Mayakonda, Moli Huang, Ling-Wen Ding, Han Lin, Fenggang Yu, Yanan Lu, Thomas Kwok Seng Loh, Marilynn Chow, Samantha Savage, Jeffrey W. Tyner, De-Chen Lin, and H. Phillip Koeffler

Précis: This study identifies a network of new candidate therapeutic targets in a cancer with high incidence in southeast Asia.

JAM-C Identifies Src Family Kinase-Activated Leukemia-Initiating Cells and Predicts Poor Prognosis in Acute Myeloid Leukemia
Maria De Grandis, Florence Bardin, Cyril Fauriat, Christophe Zemmour, Abdessamad El-Kaoutari, Arnauld Sérgé, Samuel Gzanjeaud, Laurent Pouyet, Camille Montersino, Anne-Sophie Chretien, Marie-Joelle Mozirconacci, Remy Castellano, Ghislain Bidaut, Jean-Marie Boher, Yves Collette, Stéphane J.C. Mancini, Norbert Vey, and Michel Aurrand-Lions

Précis: These findings define a gene signature for tumor-initiating cells in the early heterogeneous population of acute myeloid leukemias, with implications for fighting disease relapse.

MYC Inhibition Depletes Cancer Stem-like Cells in Triple-Negative Breast Cancer
Aimin Yang, Shenghui Qin, Bradley A. Schulte, Stephen P. Ethier, Kenneth D. Tew, and Gavin Y. Wang

Précis: A natural product described in this study may offer an opportunity to selectively kill drug-resistant cancer stem-like cells in triple-negative breast cancer by triggering degradation of the c-MYC oncoprotein.

EZH2 Modifies Sunitinib Resistance in Renal Cell Carcinoma by Kinome Reprogramming
Remi Adelaiye-Ogala, Justin Budka, Nur P. Damayanti, Justine Arrington, Mary Ferris, Chuan-Chih Hsu, Sreenivasulu Chintala, Ashley Orillion, Kiersten Marie Miles, Li Shen, May Elbanna, Eric Ciamprorco, Sreevani Arisa, Piergiorgio Pettazzoni, Giulio F. Dreacta, Mukund Seshadri, Bradley Hancock, Milan Radovich, Janaiah Kota, Michael Buck, Heike Keilhack, Brian P. McCanthy, Scott A. Persohn, Paul R. Territo, Yong Zang, Joseph Inudayraj, W. Andy Tao, Peter Hollenhorst, and Roberto Pili

Précis: These results offer a mechanistic rationale to target an oncogenic histone methyltransferase as a strategy to have an impact on sunitinib-resistance in kidney cancers.

IL10 Release upon PD-1 Blockade Sustains Immunosuppression in Ovarian Cancer
Purneshottam Lamichhane, Lavakumar Karyampudi, Barath Shreeder, James Kremps, Deborah Bahr, Joshua Daum, Kimberly R. Kall, Ellen L. Goode, Matthew S. Block, Martin J. Cannon, and Keith L. Knutson

Précis: These findings identify an actionable mechanism of resistance to anti-PD-1, with implications for broadening therapeutic responses to this immune checkpoint drug.
6679  Secretory Autophagy in Cancer-Associated Fibroblasts Promotes Head and Neck Cancer Progression and Offers a Novel Therapeutic Target
Jacob New, Levi Arnold, Megha Ananth, Sameer Alvi, Mackenzie Thornton, Lauryn Werner, Osama Tawfik, Hongying Dai, Yelizaveta Shnayder, Kian Kakarala, Terance T. Tsue, Douglas A. Girod, Wen-Xing Ding, Shrikant Anant, and Sufi Mary Thomas

Précis: These results establish an oncogenic function for secretory autophagy in the stromal fibroblasts in head and neck cancers, with possible implications to prevent malignant progression in this and other cancer settings.

6692  Astrocytes Promote Medulloblastoma Progression through Hedgehog Secretion

Précis: Astrocytes support the growth of medulloblastomas by secreting the developmental growth factor sonic hedgehog, enabling activation of a key progression pathway in this pediatric brain tumor.

6704  Mesenchymal Stem Cells Promote Hepatocarcinogenesis via IncRNA–MiF Interaction with ANXA2 and miR-34a
Xinlong Yan, Dongdong Zhang, Wei Wu, Shuheng Wu, Jingfeng Qian, Yaiing Hao, Fang Yan, Pingping Zhu, Jiayi Wu, Guanling Huang, Yinghui Huang, Jianjun Luo, Xinhui Liu, Benu Yu, Xiaomin Chen, Ying Du, Runsheng Chen, and Zusen Fan

Précis: These findings provide compelling evidence that long noncoding RNAs support liver carcinogenesis by facilitating contributions from mesenchymal stem cells in the tumor microenvironment.

INTEGRATED SYSTEMS AND TECHNOLOGIES

6717  Chemotherapeutic Dose Scheduling Based on Tumor Growth Rates Provides a Case for Low-Dose Metronomic High-Entropy Therapies
Jeffrey West and Paul K. Newton

Précis: A game theory mathematical model shows how the effectiveness of cytotoxic drugs in killing cancer cells is affected more by changes in dose density than dose concentration, especially in faster growing tumors.

6729  SMYD5 Controls Heterochromatin and Chromosome Integrity during Embryonic Stem Cell Differentiation
Benjamin L. Kidder, Runsheng He, Darawalee Wangsa, Hesed M. Padilla-Nash, M. Margarida Bernardo, Shijie Sheng, Thomas Ried, and Keji Zhao

Précis: Changes in a repressive chromatin structure in embryonic stem cells leads to genome instability during differentiation.

6746  Glutamine Addiction in Kidney Cancer Suppresses Oxidative Stress and Can Be Exploited for Real-Time Imaging
Omran Abu Aboud, Samy L. Habib, Josephine Trott, Benjamin Stewart, Sitai Liang, Abhijit J. Chaudhari, Julie Sutcliffe, and Robert H. Weiss

Précis: Glutamine consumed by clear cell renal tumors to support an antioxidant survival pathway can be exploited for functional PET imaging.

6759  Modeling Cytostatic and Cytotoxic Responses to New Treatment Regimens for Ovarian Cancer
Francesca Falcetta, Francesca Bizzaro, Elisa D’Agostini, Maria Rosa Bani, Raffaella Giavazzi, and Paolo Ubezio

Précis: A comparative preclinical study of several treatment regimens for ovarian cancer with paclitaxel, cisplatin, and bevacizumab alone or in combination decodes tumor growth curves via mathematical modeling of the proliferation process.

PREVENTION AND EPIDEMIOLOGY

6770  Disparities in Prostate, Lung, Breast, and Colorectal Cancer Survival and Comorbidity Status among Urban American Indians and Alaskan Natives
Marc A. Emerson, Matthew P. Banegas, Neetu Chawla, Ninah Achacoso, Stacey E. Alexeeff, Alyce S. Adams, and Laurel A. Habel

Précis: These findings address a critical gap in information concerning the cancer experience of the majority of Native Americans and Alaskan Natives in the U.S. who live in urban areas.

6777  Oral Microbiome Composition Reflects Prospective Risk for Esophageal Cancers
Brandilyn A. Peters, Jing Wu, Zhiheng Pei, Liying Yang, Mark P. Purdue, Neal D. Freedman, Eric J. Jacobs, Susan M. Capstur, Richard B. Hayes, and Jiyoung Ahn

Précis: A prospective study of the relationship between the oral microbiome and risks of developing esophageal cancers has potential implications for early detection and prevention.
CORRECTIONS

6788 Correction: miR-103/107 Promote Metastasis of Colorectal Cancer by Targeting the Metastasis Suppressors DAPK and KLF4

6789 Correction: Myc Induces miRNA-Mediated Apoptosis in Response to HDAC Inhibition in Hematologic Malignancies

ABOUT THE COVER

8-Oxo7,8-dihydro-2'-deoxyguanosine (8-oxodG), an oxidized form of deoxyguanosine, is a major product of DNA oxidation and is used as a biomarker for oxidative stress in cancer. The level of 8-oxodG in cellular DNA reflects the balance between the rate of DNA damage and the efficiency of DNA repair. This merged image of double fluorescent-labeled murine xenografted human kidney cancer cells shows a high abundance of 8-oxodG (stained green with FITC) within the nuclei (identified by red propidium iodide staining of all DNA). A higher level of orange to green staining within the kidney tumor section as compared with the normal kidney (not shown) indicates more oxidative DNA damage within the tumor. The image was taken using a Nikon research microscope equipped for epifluorescence with excitation and band pass filters. For details, see article by Abu Aboud and colleagues on page 6746.
### Cancer Research

**77 (23)**

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