

BREAKING INSIGHTS

- 2777** Highlights from Recent Cancer Literature

REVIEWS

- 2779** **Pericytes in the Premetastatic Niche**
 Ana E. Paiva, Luiza Lousado, Daniel A.P. Guerra,
 Patrick O. Azevedo, Isadora F.G. Sena, Julia P. Andreotti,
 Gabryella S.P. Santos, Ricardo Gonçalves, Akiva Mintz, and
 Alexander Birbrair
- 2787** **Glycosylation of Recombinant Anticancer
 Therapeutics in Different Expression Systems with
 Emerging Technologies**
 Tariq Nadeem, Mohsin Ahmad Khan, Bushra Ijaz,
 Nadeem Ahmed, Zia ur Rahman,
 Muhammad Shahzad Latif, Qurban Ali, and
 Muhammad Adeel Rana

METABOLISM AND CHEMICAL BIOLOGY


- 2799** **Transketolase Regulates the Metabolic Switch to
 Control Breast Cancer Cell Metastasis via the
 α -Ketoglutarate Signaling Pathway**
 Chien-Wei Tseng, Wen-Hung Kuo, Shih-Hsuan Chan,
 Hong-Lin Chan, King-Jen Chang, and Lu-Hai Wang
Significance: These findings uncover the clinical significance
 of TKT in breast cancer progression and metastasis and
 demonstrate effective therapy by inhibiting TKT or by
 adding α KG.

MOLECULAR CELL BIOLOGY

- 2813** **Human Elongation Factor 4 Regulates Cancer
 Bioenergetics by Acting as a Mitochondrial
 Translation Switch**
 Ping Zhu, Yongzhang Liu, Fenglin Zhang, Xiufeng Bai,
 Zilei Chen, Fugen Shanguan, Bo Zhang, Lingyun Zhang,
 Qianqian Chen, Deyao Xie, Linhua Lan, Xiangdong Xue,
 Xing-Jie Liang, Bin Lu, Taotao Wei, and Yan Qin
Significance: Dysregulated mitochondrial translation drives
 tumor development and progression.

- 2825** **Acetylation within the N- and C-Terminal
 Domains of Src Regulates Distinct Roles of
 STAT3-Mediated Tumorigenesis**
 Chao Huang, Zhe Zhang, Lihan Chen, Hank W. Lee,
 Marina K. Ayrapetov, Ting C. Zhao, Yimei Hao,
 Jinsong Gao, Chunzhang Yang, Gautam U. Mehta,
 Zhengping Zhuang, Xiaoren Zhang, Guohong Hu, and
 Y. Eugene Chin

Significance: CBP-mediated acetylation of lysine clusters in
 both the N-terminal and C-terminal regions of c-Src provides
 additional levels of control over STAT3 transcriptional
 activity.

- 2839** **The Circular RNA circPRKCI Promotes Tumor
 Growth in Lung Adenocarcinoma**

 Mantang Qiu, Wenjia Xia, Rui Chen, Siwei Wang,
 Youtao Xu, Zhifei Ma, Weizhang Xu, Erbao Zhang,
 Jie Wang, Tian Fang, Jingwen Hu, Gaochao Dong,
 Rong Yin, Jun Wang, and Lin Xu


Significance: These findings reveal high expression of the
 circular RNA circPRKCI drives lung adenocarcinoma
 tumorigenesis.

- 2852** **The MDA-9/Syntenin/IGF1R/STAT3 Axis Directs
 Prostate Cancer Invasion**
 Swadesh K. Das, Anjan K. Pradhan, Praveen Bhoopathi,
 Sarmistha Talukdar, Xue-Ning Shen, Devanand Sarkar,
 Luni Emdad, and Paul B. Fisher

Significance: This study provides new mechanistic insight
 into the proinvasive role of MDA-9/syntenin-1 in prostate
 cancer and has the potential for therapeutic application to
 prevent prostate cancer metastasis.

- 2864** **Plk1-Mediated Phosphorylation of TSC1
 Enhances the Efficacy of Rapamycin**
 Zhiguo Li, Yifan Kong, Longzhen Song, Qian Luo,
 Jinghui Liu, Chen Shao, Xianzeng Hou, and Xiaoqi Liu

Significance: This seminal report shows that activation
 of mTORC1 can be independent of AKT during mitosis.

- 2876** **RIPK1 Binds MCU to Mediate Induction of
 Mitochondrial Ca^{2+} Uptake and Promotes
 Colorectal Oncogenesis**

 Fanxin Zeng, Xiao Chen, Weiyi Cui, Wei Wen, Fujian Lu,
 Xueting Sun, Dongwei Ma, Ye Yuan, Zezhong Li,
 Ning Hou, Hong Zhao, Xinyu Bi, Jianjun Zhao,
 Jianguo Zhou, Yan Zhang, Rui-Ping Xiao, Jianqiang Cai,
 and Xiuqin Zhang

Significance: RIPK1-mediated cell proliferation through
 MCU is a central mechanism underlying colorectal cancer
 progression and may prove to be an important therapeutic
 target for colorectal cancer treatment.

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- 2886** Therapeutic Targeting of Sunitinib-Induced AR Phosphorylation in Renal Cell Carcinoma
Remi Adelaiye-Ogala, Nur P. Damayanti, Ashley R. Orillion, Sreevani Arisa, Sreenivasulu Chintala, Mark A. Titus, Chinghai Kao, and Roberto Pili

Significance: These findings highlight the therapeutic potential of targeting the androgen receptor to overcome RCC resistance to receptor tyrosine kinase inhibitors.

- 2897** Peli1 Modulates the Subcellular Localization and Activity of Mdmx

Dawei Li, Omid Tavana, Shao-Cong Sun, and Wei Gu

Significance: Peli1-mediated regulation of Mdmx, a major inhibitor of p53, provides critical insight into activation of p53 function in human cancers.

TUMOR BIOLOGY AND IMMUNOLOGY

- 2911** Osteoblast-Secreted Factors Mediate Dormancy of Metastatic Prostate Cancer in the Bone via Activation of the TGF β RIII–p38MAPK–pS249/T252RB Pathway

Li-Yuan Yu-Lee, Guoyu Yu, Yu-Chen Lee, Song-Chang Lin, Jing Pan, Tianhong Pan, Kai-Jie Yu, Bin Liu, Chad J. Creighton, Jaime Rodriguez-Canales, Pamela A. Villalobos, Ignacio I. Wistuba, Eulalia de Nadal, Francesc Posas, Gary E. Gallick, and Sue-Hwa Lin

Significance: These findings provide mechanistic insights into the dormancy of metastatic prostate cancer in the bone and offer a rationale for developing strategies to prevent prostate cancer recurrence in the bone.

- 2925** Tight Junction Protein Claudin-2 Promotes Self-Renewal of Human Colorectal Cancer Stem-like Cells

Sophie Paquet-Fifield, Shir Lin Koh, Lesley Cheng, Laura M. Beyit, Carolyn Shembrey, Christina Mølck, Corina Behrenbruch, Marina Papin, Meritxell Gironella, Sophie Guelfi, Ramona Nasr, Fanny Grillet, Michel Prudhomme, Jean-Francois Bourgaux, Antoni Castells, Jean-Marc Pascussi, Alexander G. Heriot, Alain Puisieux, Melissa J. Davis, Julie Pannequin, Andrew F. Hill, Erica K. Sloan, and Frédéric Hollande

Significance: Claudin-2-mediated regulation of YAP activity and miR-222-3p expression drives CSC renewal in colorectal cancer, making it a potential target for therapy.

- 2939** I κ B Kinase α Is Required for Development and Progression of KRAS-Mutant Lung Adenocarcinoma

Malamati Vreka, Ioannis Lilis, Maria Papageorgopoulou, Georgia A. Giotopoulou, Marina Lianou, Ioanna Giopanou, Nikolaos I. Kanellakis, Magda Spella, Theodora Agalioti, Vasileios Armenis, Torsten Goldmann, Sebastian Marwitz, Fiona E. Yull, Timothy S. Blackwell, Manolis Pasparakis, Antonia Marazioti, and Georgios T. Stathopoulos

Significance: These findings report a novel requirement for IKK α in mutant KRAS lung tumor formation, with potential therapeutic applications.

- 2952** Transition of Mesenchymal and Epithelial Cancer Cells Depends on α 1-4 Galactosyltransferase-Mediated Glycosphingolipids

Francis Jacob, Shahidul Alam, Martina Konantz, Ching-Yeu Liang, Reto S. Kohler, Arun V. Everest-Dass, Yen-Lin Huang, Natalie Rimmer, Andre Fedier, Andreas Schötzau, Monica Nunez Lopez, Nicolle H. Packer, Claudia Lengerke, and Viola Heinzlmann-Schwarz

Significance: This study highlights the essential role of glycosphingolipids in the maintenance of epithelial cancer cell properties.

- 2966** Mutant IDH1 Cooperates with ATRX Loss to Drive the Alternative Lengthening of Telomere Phenotype in Glioma

Joydeep Mukherjee, Tor-Christian Johannessen, Shigeo Ohba, Tracy T. Chow, Lindsey Jones, Ajay Pandita, and Russell O. Pieper

Significance: Studies show how expression of mutant IDH1 initiates telomeric dysfunction and alters DNA repair pathway preferences at telomeres, cooperating with ATRX loss to defeat a key barrier to gliomagenesis and suggesting new therapeutic options to treat low-grade gliomas.

- 2978** Inhibin Is a Novel Paracrine Factor for Tumor Angiogenesis and Metastasis

Priyanka Singh, Laura M. Jenkins, Ben Horst, Victoria Alers, Shrikant Pradhan, Prabhjot Kaur, Tapasya Srivastava, Nadine Hempel, Balázs Gyórfy, Eugenia V. Broude, Nam Y. Lee, and Karthikeyan Mythreye

Significance: Inhibin is a predictor of poor patient survival in multiple cancers and is a potential target for antiangiogenic therapies.

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2990 Tissue Transglutaminase Regulates Interactions between Ovarian Cancer Stem Cells and the Tumor Niche

Salvatore Condello, Livia Sima, Cristina Ivan, Horacio Cardenas, Gary Schiltz, Rama K. Mishra, and Daniela Matei

Significance: These findings reveal a new mechanism by which ovarian cancer stem cells interact with the tumor microenvironment, promoting cell proliferation and tumor initiation.

3002 Activation of the Receptor Tyrosine Kinase AXL Regulates the Immune Microenvironment in Glioblastoma

Hirokazu Sadahiro, Kyung-Don Kang, Justin T. Gibson, Mutsuko Minata, Hai Yu, Junfeng Shi, Rishi Chhipa, Zhihong Chen, Songjian Lu, Yannick Simoni, Takuya Furuta, Hemragul Sabit, Suojun Zhang, Soniya Bastola, Shinobu Yamaguchi, Hebaallah Alsheikh, Svetlana Komarova, Jun Wang, Sung-Hak Kim, Dolores Hambarzumyan, Xinghua Lu, Evan W. Newell, Biplob DasGupta, Mitsutoshi Nakada, L. James Lee, Burt Nabors, Lyse A. Norian, and Ichiro Nakano

Significance: These findings suggest that development of combination treatments of AXL and immune checkpoint inhibitors may provide benefit to patients with GBM.

3014 Tumor-Derived TGF β Alters the Ability of Plasmacytoid Dendritic Cells to Respond to Innate Immune Signaling



Mariana Terra, Marine Oberkampf, Catherine Fayolle, Pierre Rosenbaum, Camille Guilleray, Gilles Dadaglio, and Claude Leclerc

Significance: These findings highlight the importance of pDCs in the cross-talk between tumor cells and the immune system.

3027 Inhibition of Nr4a Receptors Enhances Antitumor Immunity by Breaking Treg-Mediated Immune Tolerance

Sana Hibino, Shunsuke Chikuma, Taisuke Kondo, Minako Ito, Hiroko Nakatsukasa, Setsuko Omata-Mise, and Akihiko Yoshimura

Significance: This study reveals the role of Nr4a transcription factors in Treg-mediated tolerance to antitumor immunity, with possible therapeutic implications for developing effective anticancer therapies.

3041 Kir2.1 Interaction with Stk38 Promotes Invasion and Metastasis of Human Gastric Cancer by Enhancing MEKK2–MEK1/2–ERK1/2 Signaling

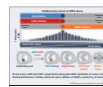


Cheng-Dong Ji, Yan-Xia Wang, Dong-Fang Xiang, Qiang Liu, Zhi-Hua Zhou, Feng Qian, Lang Yang, Yong Ren, Wei Cui, Sen-Lin Xu, Xi-Long Zhao, Xia Zhang, Yan Wang, Peng Zhang, Ji-Ming Wang, You-Hong Cui, and Xiu-Wu Bian

Significance: Kir2.1 contributes to invasion and metastasis by a noncanonical ion permeation-independent signaling pathway and may act as a novel prognostic marker and therapeutic target for gastric cancer.

TRANSLATIONAL SCIENCE

3054 Mechanistic Distinctions between CHK1 and WEE1 Inhibition Guide the Scheduling of Triple Therapy with Gemcitabine



Siang-Boon Koh, Yann Wallez, Charles R. Dunlop, Sandra Bernaldo de Quirós Fernández, Tashinga E. Bapiro, Frances M. Richards, and Duncan I. Jodrell

Significance: Multiple lines of mechanistic insight regarding DNA damage response inhibitors rationally guide the preclinical development of a tolerable multitherapeutic regimen.

3067 Enhanced Lymphodepletion Is Insufficient to Replace Exogenous IL2 or IL15 Therapy in Augmenting the Efficacy of Adoptively Transferred Effector CD8⁺ T Cells

C. Bryce Johnson, Bennett R. May, Brian P. Riesenber, Samantha Suriano, Shikhar Mehrotra, Elizabeth Garrett-Mayer, Mohamed L. Salem, Emily K. Jeng, Hing C. Wong, Chrystal M. Paulos, John M. Wrangle, David J. Cole, and Mark P. Rubinstein

Significance: The relationship between lymphodepletion and cytokine support play a critical role in determining donor T-cell engraftment and antitumor efficacy.

3075 Cotargeting BCL-2 and PI3K Induces BAX-Dependent Mitochondrial Apoptosis in AML Cells

Mohamed Rahmani, Jewel Nkwocha, Elisa Hawkins, Xinyan Pei, Rebecca E. Parker, Maciej Kmiecik, Joel D. Levenson, Deepak Sampath, Andrea Ferreira-Gonzalez, and Steven Grant

Significance: Combined treatment with clinically relevant PI3K and BCL-2 inhibitors may prove effective in the treatment of acute myeloid leukemia.

POPULATION AND PREVENTION SCIENCE

3087 A Large-Scale, Exome-Wide Association Study of Han Chinese Women Identifies Three Novel Loci Predisposing to Breast Cancer



Bo Zhang, Men-Yun Chen, Yu-Jun Shen, Xian-Bo Zhuo, Ping Gao, Fu-Sheng Zhou, Bo Liang, Jun Zu, Qin Zhang, Sufyan Suleman, Yi-Hui Xu, Min-Gui Xu, Jin-Kai Xu, Chen-Cheng Liu, Nikolaos Giannareas, Ji-Han Xia, Yuan Zhao, Zhong-Lian Huang, Zhen Yang, Huai-Dong Cheng, Na Li, Yan-Yan Hong, Wei Li, Min-Jun Zhang, Ke-Da Yu, Guoliang Li, Meng-Hong Sun, Zhen-Dong Chen, Gong-Hong Wei, and Zhi-Min Shao

Significance: Large-scale genetic screening identifies novel missense variants and a noncoding variant as predisposing factors for breast cancer.

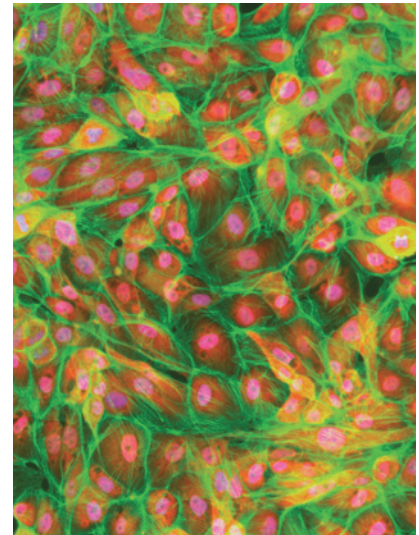
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ABOUT THE COVER

Immunofluorescence imaging of Ser-81 phosphorylated androgen receptor (AR) in human 786-OR renal carcinoma cells treated with sunitinib. Visualization of AR revealed its nuclear localization in renal tumor cells. AR expression and nuclear localization is induced upon chronic treatment with sunitinib and can be impaired by AR antagonists such as enzalutamide. Thus, phosphorylated AR appears to be a novel target for patients with renal cell carcinoma receiving receptor tyrosine kinase inhibitors. For details, see article by Adelaiye-Ogala and colleagues on page 2886.



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