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Katie Teng, Matthew J. Ford, Keerthana Harwalkar, YuQi Li, Alain S. Pacis, David Farnell, Nobuko Yamanaka, Yu-Chang Wang, Dunarel Badescu, Tuyet Nhung Ton Nu, Jiannis Ragoussis, David G. Huntsman, Jocelyne Arseneau, and Yojiro Yamanaka  
This study unveils a new strategy to generate genetic mouse models of ovarian cancer with high flexibility in selecting mutation combinations and targeting areas.

5161 **Novel Mouse Models of Bladder Cancer Identify a Prognostic Signature Associated with Risk of Disease Progression**

Soonbum Park, Lijie Rong, Tomasz B. Owczarek, Matteo Di Bernardo, Rivka L. Shoulson, Chee-Wai Chua, Jaime Y. Kim, Amir Lankarani, Prithi Chakrapani, Talal Syed, James M. McKiernan, David B. Solit, Michael M. Shen, Hikmat A. Al-Ahmadie, and Cory Abate-Shen

Analysis of bladder cancer progression in a new series of genetically engineered mouse models has identified a gene signature of poor prognosis in human bladder cancer.

## GENOME AND EPIGENOME

5176 **Epigenetic Therapies in Ovarian Cancer Alter Repetitive Element Expression in a *TP53*-Dependent Manner**  
James I. McDonald, Noor Diab, Elisa Arthofer, Melissa Hadley, Tomas Kanholm, Uzma Rentia, Stephanie Gomez, Angela Yu, Erin E. Grundy, Olivia Cox, Michael J. Topper, Xiaoyun Xing, Pamela L. Strissel, Reiner Strick, Ting Wang, Stephen B. Baylin, and Katherine B. Chiappinelli  
This study identifies the repetitive element targets of epigenetic therapies in ovarian carcinoma and indicates a role for p53 in this process.

5190 **miR-766-5p Targets Super-Enhancers by Downregulating CBP and BRD4**  
Yasuyuki Gen, Tomoki Muramatsu, Jun Inoue, and Johji Inazawa  
This study demonstrates that *miR-766-5p* targets CBP and BRD4, which can mitigate the protumorigenic consequences of SEs and oncogenic fusion proteins.

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## METABOLISM AND CHEMICAL BIOLOGY

- 5202** **Oncogenic HSP90 Facilitates Metabolic Alterations in Aggressive B-cell Lymphomas**  
M. Nieves Calvo-Vidal, Nahuel Zamponi, Jan Krumsiek, Max A. Stockslager, Maria V. Revuelta, Jude M. Phillip, Rossella Marullo, Ekaterina Tikhonova, Nikita Kotlov, Jayeshkumar Patel, Shao Ning Yang, Lucy Yang, Tony Taldone, Catherine Thieblemont, John P. Leonard, Peter Martin, Giorgio Inghirami, Gabriela Chiosis, Scott R. Manalis, and Leandro Cerchietti
- The oncogenic form of HSP90 organizes and maintains functional multienzymatic metabolic hubs in cancer cells, suggesting the potential of repurposing oncogenic HSP90 selective inhibitors to disrupt metabolism in lymphoma cells.

## MOLECULAR CELL BIOLOGY

- 5217** **Stem Cell Factor SOX2 Confers Ferroptosis Resistance in Lung Cancer via Upregulation of SLC7A11**  
Xinbo Wang, Yueqing Chen, Xudong Wang, Hongling Tian, Yanjin Wang, Jiali Jin, Zezhi Shan, Yu'e Liu, Zhenyu Cai, Xinyuan Tong, Yi Luan, Xiao Tan, Bing Luan, Xin Ge, Hongbin Ji, Xuejun Jiang, and Ping Wang
- This study uncovers a SOX2-SLC7A11 regulatory axis that confers resistance to ferroptosis in lung cancer stem-like cells.
- 5230** **Neural Crest-Like Stem Cell Transcriptome Analysis Identifies LPAR1 in Melanoma Progression and Therapy Resistance**  
Jianglan Liu, Vito W. Rebecca, Andrew V. Kossenkov, Thomas Connelly, Qin Liu, Alexis Gutierrez, Min Xiao, Ling Li, Gao Zhang, Anastasia Samarkina, Delaine Zayasbazan, Jie Zhang, Chaoran Cheng, Zhi Wei, Gretchen M. Alicea, Mizuho Fukunaga-Kalabis, Clemens Krepler, Pedro Aza-Blanc, Chih-Cheng Yang, Bela Delvadia, Cynthia Tong, Ye Huang, Maya Delvadia, Alice S. Morias, Katrin Sproesser, Patricia Brafford, Joshua X. Wang, Marilda Beqiri, Rajasekharan Somasundaram, Adina Vultur, Denitsa M. Hristova, Lawrence W. Wu, Yiling Lu, Gordon B. Mills, Wei Xu, Giorgos C. Karakousis, Xiaowei Xu, Lynn M. Schuchter, Tara C. Mitchell, Ravi K. Amaravadi, Lawrence N. Kwong, Dennie T. Frederick, Genevieve M. Boland, Joseph M. Salvino, David W. Speicher, Keith T. Flaherty, Ze'ev A. Ronai, and Meenhard Herlyn
- This study identifies an LPAR1-axis critical for melanoma invasion and intrinsic/acquired therapy resistance.
- 5242** **Fam20C Regulates Bone Resorption and Breast Cancer Bone Metastasis through Osteopontin and BMP4**  
Hao Zuo, Dengbao Yang, and Yihong Wan
- Osteoclastogenesis and bone metastasis are suppressed by myeloid-derived Fam20C, but enhanced by breast cancer-associated Fam20C, uncovering novel Fam20C functions and new therapeutic strategies via targeting Fam20C substrates OPN and BMP4.

## TUMOR BIOLOGY AND IMMUNOLOGY

- 5255** **Slit2 Inhibits Breast Cancer Metastasis by Activating M1-Like Phagocytic and Antifibrotic Macrophages**  
Dinesh K. Ahirwar, Manish Charan, Sanjay Mishra, Ajeet K. Verma, Konstantin Shilo, Bhuvanewari Ramaswamy, and Ramesh K. Ganju
- This study provides evidence that the antitumor effect of Slit2 in breast cancer occurs by activating the phagocytic activity of M1-like tumor-associated macrophages against tumor cells and diminishing fibrosis.
- 5268** **N<sup>6</sup>-methyladenosine-Mediated Upregulation of WTAPP1 Promotes WTAP Translation and Wnt Signaling to Facilitate Pancreatic Cancer Progression**  
Junge Deng, Jialiang Zhang, Ying Ye, Kaijing Liu, Lingxing Zeng, Jingyi Huang, Ling Pan, Mei Li, Ruihong Bai, Lisha Zhuang, Xudong Huang, Guandi Wu, Lusheng Wei, Yanfen Zheng, Jiachun Su, Shaoping Zhang, Rufu Chen, Dongxin Lin, and Jian Zheng
- This study reveals how aberrant m<sup>6</sup>A modification of the *WTAPP1* pseudogene results in increased translation of its protein-coding counterpart to promote Wnt signaling, which contributes to pancreatic cancer progression.
- 5284** **Characterizing Macrophage Diversity in Metastasis-Bearing Lungs Reveals a Lipid-Associated Macrophage Subset**  
Danielle N. Huggins, Rebecca S. LaRue, Ying Wang, Todd P. Knutson, Yingzheng Xu, Jesse W. Williams, and Kathryn L. Schwertfeger
- scRNA-seq of macrophages isolated from lung metastases reveals extensive macrophage heterogeneity and identifies a novel subpopulation enriched for genes involved in lipid metabolism, extracellular matrix remodeling, and immunosuppression.
- 5296** **Dietary Fats High in Linoleic Acids Impair Antitumor T-cell Responses by Inducing E-FABP-Mediated Mitochondrial Dysfunction**  
Rong Jin, Jiaqing Hao, Yanmei Yi, Di Yin, Yuan Hua, Xiaohong Li, Hanmei Bao, Xianlin Han, Nejat K. Egilmez, Edward R. Sauter, and Bing Li
- These findings suggest that modulation of dietary oil composition and inhibition of E-FABP activity may represent novel strategies to enhance T-cell function in the prevention and treatment of obesity-associated cancers.

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## TRANSLATIONAL SCIENCE

**5311 Targeting *HER2* Exon 20 Insertion–Mutant Lung Adenocarcinoma with a Novel Tyrosine Kinase Inhibitor Mobocertinib**

Han Han, Shuai Li, Ting Chen, Michael Fitzgerald, Shengwu Liu, Chengwei Peng, Kwan Ho Tang, Shougen Cao, Johara Chouitar, Jiansheng Wu, David Peng, Jiehui Deng, Zhendong Gao, Theresa E. Baker, Fei Li, Hua Zhang, Yuanwang Pan, Hailin Ding, Hai Hu, Val Pyon, Cassandra Thakurdin, Eleni Papadopoulou, Sittinon Tang, Francois Gonzalez, Haiquan Chen, Victor M. Rivera, Rachael Brake, Sylvie Vincent, and Kwok-Kin Wong

This study elucidates the potent inhibitory activity of mobocertinib against *HER2* exon 20 insertion–mutant lung cancer and the synergic effect of combined mobocertinib and T-DM1, providing a strong rationale for clinical investigation.

**5325 Targeting the *IRE1α*/*XBP1* Endoplasmic Reticulum Stress Response Pathway in *ARID1A*-Mutant Ovarian Cancers**

Joseph A. Zundell, Takeshi Fukumoto, Jianhuang Lin, Nail Fatkhudinov, Timothy Nacarelli, Andrew V. Kossenkov, Qin Liu, Joel Cassel, Chih-Chi Andrew Hu, Shuai Wu, and Rugang Zhang

These findings indicate that pharmacological inhibition of the *IRE1α*-*XBP1* pathway alone or in combination with HDAC6 inhibition represents an urgently needed therapeutic strategy for *ARID1A*-mutant ovarian cancers.

**5336 Oncostatin M Receptor–Targeted Antibodies Suppress *STAT3* Signaling and Inhibit Ovarian Cancer Growth**

Anjali Geethadevi, Ajay Nair, Deepak Parashar, Zhiqiang Ku, Wei Xiong, Hui Deng, Yongsheng Li, Jasmine George, Donna M. McAllister, Yunguang Sun, Ishaque P. Kadamberi, Prachi Gupta, Michael B. Dwinell, William H. Bradley, Janet S. Rader, Hallgeir Rui, Robert F. Schwabe, Ningyan Zhang, Sunila Pradeep, Zhiqiang An, and Pradeep Chaluvally-Raghavan

This study uncovers a role for OSMR in promoting ovarian cancer cell proliferation and metastasis by activating *STAT3* signaling and demonstrates the preclinical efficacy of antibody-based OSMR targeting for ovarian cancer treatment.

**5353 Psychologic Stress Drives Progression of Malignant Tumors via *DRD2*/*HIF1α* Signaling**

Huijuan Liu, Jiahuan Yang, Yang Zhang, Jingxia Han, Yuyan Yang, Zihan Zhao, Xintong Dai, Hongqi Wang, Xiujuan Ding, Yanrong Liu, Weilong Zhong, Wenqing Gao, and Tao Sun

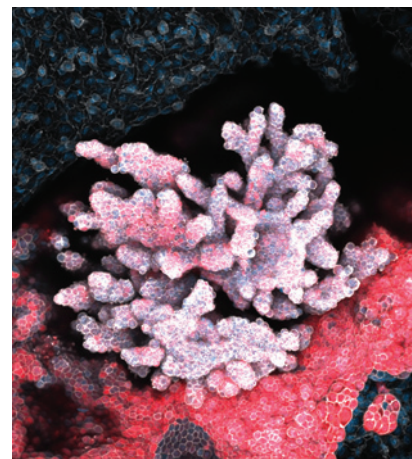
This work identifies *DRD2* regulation of *HIF1α* as a mechanism underlying the progression of malignant tumors stimulated by psychological stress and suggests that *DRD2* inhibition can mitigate these stress conditions in patients.

See related commentary, p. 5144

## ABOUT THE COVER

High-grade serous ovarian carcinoma (HGSOC) accounts for the majority of ovarian cancer cases, and it is most frequently diagnosed at advanced stages. The cover image captures a peritoneal micrometastasis formed in a new somatic HGSOC mouse model generated using a combination of *in vivo* electroporation and CRISPR-Cas9–mediated genome editing (red, RFP marking cancer cells; cyan, nucleus; white, F-actin). For details, see the article by Teng and colleagues on page 5147.

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