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  Zhengjia Chen, Chao Zhang, Jianhong Chen, Dongsheng Wang, Jieqiu Tu, Carter Van Waes, Nabil F. Saba, Zhuo G. Chen, and Zhong Chen  
  Integrative bioinformatics and statistical analyses reveal a panel of genes and proteins associated with *FAF1* mutation in HNSCC, providing important insights into prospective clinical investigations with targeted therapies.

## Metabolism and Chemical Biology
- **4417** Metabolic Enzyme DLST Promotes Tumor Aggression and Reveals a Vulnerability to OXPHOS Inhibition in High-Risk Neuroblastoma  
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  These findings demonstrate a novel role for DLST in neuroblastoma aggression and identify the OXPHOS inhibitor IACS-010759 as a potential therapeutic strategy for this deadly disease.
- **4431** PPARα Agonist Fenofibrate Enhances Cancer Vaccine Efficacy  
  Arezki Chekaoui and Hildegund C.J. Ertl  
  These findings suggest that metabolic manipulations using already approved drugs may offer an easy pathway to increase the efficacy of vaccines against solid tumors.

## Molecular Cell Biology
- **4441** A Wnt-Independent LGR4–EGFR Signaling Axis in Cancer Metastasis  
  Fei Yue, Weiyou Jiang, Amy T. Ku, Adelaide I.J. Young, Weijie Zhang, Eric P. Souto, Yankun Gao, Zihan Yu, Yi Wang, Chad J. Creighton, Chandandeep Nagi, Tao Wang, Susan G. Hilsenbeck, Xin-Hua Feng, Shixia Huang, Cristian Coarfa, Xiang H.-F. Zhang, Qingsyun Liu, Xia Lin, and Yi Li  
  This work demonstrates a Wnt-independent mechanism by which LGR4 promotes cancer metastasis.  
  See related commentary, p. 4397
AP-2α-Mediated Activation of E2F and EZH2 Drives Melanoma Metastasis

Jeffrey R. White, Dakota T. Thompson, Kelsey E. Koch, Boris S. Kiriazov, Anna C. Beck, Dana M. van der Heide, Benjamin G. Grimm, Mikhail V. Kulak, and Ronald J. Weigel

AP-2α drives melanoma metastasis by upregulating E2F pathway genes including EZH2 through inhibition of the NuRD repression complex, serving as a biomarker to predict responsiveness to EZH2 inhibitors.

MAP3K7-IKK Inflammatory Signaling Modulates AR Protein Degradation and Prostate Cancer Progression

Zhenlin Huang, Bo Tang, Yinhui Yang, Zhaogang Yang, Lei Shi, Yang Bai, Binyuan Yan, R. Jeffrey Karnes, Jun Zhang, Rafael Jimenez, Liguo Wang, Qiang Wei, Jinjian Yang, Wanhai Xu, Zhankui Jia, and Haojie Huang

This study identifies that MAP3K7-IKK signaling plays a tumor suppressive role in prostate cancer by degrading AR, revealing potential prognostic and therapeutic strategies for MAP3K7-deficient tumors.

Fusobacterium Nucleatum Promotes the Development of Colorectal Cancer by Activating a Cytochrome P450/Epoxyoctadecenoic Acid Axis via TLR4/Keap1/NRF2 Signaling

Cheng Kong, Xuebing Yan, Yefei Zhu, Huiyuan Zhu, Ying Luo, Peipei Liu, Sylvain Ferrandon, Matthew F. Kalady, Renyuan Gao, Jide He, Fang Yin, Xiao Qs, Jiayi Zheng, Yaohui Gao, Jianli Ma, Jun-Yan Liu, and Huanlong Qin

This study uncovers a mechanism by which Fusobacterium nucleatum regulates colorectal cancer metabolism to drive metastasis, suggesting this axis as a potential target for cancer immunotherapy.

Nonsense-Mediated RNA Decay Is a Unique Vulnerability of Cancer Cells Harboring SF3B1 or U2AF1 Mutations

Abigail Cheruiyot, Shan Li, Sridhar Nonavinkere Srivatsan, Tanzir Ahmed, Yuhao Chen, Delphine S. Lemacon, Ying Li, Zheng Yang, Brian A. Wadugu, Wayne A. Warner, Shondra M. Pruett-Miller, Esther A. Obeng, Daniel C. Link, Dalin He, Fei Xiao, Xiaowei Wang, Julie M. Bailis, Matthew J. Walter, and Zhongsheng You

This study has developed a novel NMD reporter system and identified a potential therapeutic approach of targeting the NMD pathway to treat cancer with spliceosome gene mutations.

Development of a Novel Mouse Model of Spontaneous High-Risk HPV E6/E7-Expressing Carcinoma in the Cervicovaginal Tract

Talia R. Henkle, Brandon Lam, Yu Jui Kung, John Lin, Ssu-Hsueh Tseng, Louise Ferrall, Deyin Xing, Chien-Fu Hung, and T.-C. Wu

This study describes the development of a clinically relevant mouse model of cervicovaginal carcinoma that progresses from high-grade lesions and recapitulates key features of human HPV+ cervical cancer.
Quantitative In Vivo Analyses Reveal a Complex Pharmacogenomic Landscape in Lung Adenocarcinoma

Chuan Li, Wen-Yang Lin, Hira Rizvi, Hongchen Cai, Christopher D. McFarland, Zoe N. Rogers, Maryam Yousefi, Ian P. Winters, Charles M. Rudin, Dmitri A. Petrov, and Monte M. Winslow

An experimental and analytical framework to generate in vivo pharmacogenomic maps that relate tumor genotypes to therapeutic responses reveals a surprisingly complex map of genotype-specific resistance and sensitivity.

Treatment with HIV-Protease Inhibitor Nelfinavir Identifies Membrane Lipid Composition and Fluidity as a Therapeutic Target in Advanced Multiple Myeloma

Lenka Besse, Andrej Besse, Sara C. Stolze, Amin Sobh, Esther A. Zaal, Alwin J. van der Ham, Mario Ruiz, Santosh Phuyal, Lorina Büchler, Marc Sathianathan, Bogdan I. Florea, Jan Borén, Marcus Stahlman, Julia Huber, Arnold Bolomsky, Heinz Ludwig, J. Thomas Hannich, Alex Loguinov, Bart Everts, Celia R. Berkers, Marc Pilon, Herman S. Overkleeft, and Christoph Driessen

Nelfinavir induces lipid bilayer stress in cellular organelles that disrupts mitochondrial respiration and transmembrane protein transport, resulting in broad anticancer activity via metabolic rewiring and activation of the unfolded protein response.

Interventional Optical Imaging Permits Instant Visualization of Pathological Zones of Ablated Tumor Periphery and Residual Tumor Detection

Xuefeng Kan, Guanhui Zhou, Feng Zhang, Hongxiu Ji, Hui Zheng, Jeffrey Forris Beecham Chick, Karim Valji, Chuansheng Zheng, and Xiaoming Yang

Interventional optical imaging can instantly visualize pathologic zones of ablated tumor peripheries to detect residual tumors, which could revolutionize current image-guided interventional oncologic ablation techniques.
ABOUT THE COVER

LGR4/5/6 proteins play critical roles in development and cancer. The biological functions of these proteins have been primarily attributed to their roles in potentiating Wnt signaling. The mosaic photo illustrates widespread lung metastases in mice xenografted with green fluorescence–labeled human breast cancer cells expressing LGR4 mutants that cannot potentiate Wnt signaling, revealing that LGR4 promotes metastasis even when disengaged from Wnt signaling. For details, see article by Yue and colleagues on page 4441.