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- **5459** Chromatin Looping Shapes KLFS-Dependent Transcriptional Programs in Human Epithelial Cancers
  - An integrative 3D genomics methodology delineates mechanisms underlying the function of KLFS in multiple epithelial cancers and suggests potential strategies to target cancers with aberrantly activated KLFS.
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5515  **Loss of Fbxw7 Impairs Development of and Induces Heterogeneous Tumor Formation in the Mouse Mammary Gland**  
Ichiro Onoyama, Shogo Nakayama, Hideyuki Shimizu, and Keiichi I. Nakayama  
Mammary gland-specific ablation of Fbxw7 in mice results in defective gland development and spontaneous mammary tumor formation reminiscent of human basal-like carcinoma with intratumoral heterogeneity.

5531  **Transient Activation of the Hedgehog-Gli Pathway Rescues Radiotherapy-Induced Dry Mouth via Recovering Salivary Gland Resident Macrophages**  
Qingguo Zhao, Linying Zhang, Bo Hai, Jun Wang, Courtney L. Baetge, Michael A. Deveau, Geoffrey M. Kapler, Jian Q. Feng, and Fei Liu  
These findings illuminate a novel direction for developing effective treatment of irreversible dry mouth, which is common after radiotherapy for head and neck cancer and for which no effective treatments are available.

5543  **Transcriptional Activation of MYC-Induced Genes by GCN5 Promotes B-cell Lymphomagenesis**  
Aimee T. Farria, Joshua B. Plummer, Andrew P. Salinger, Jianjun Shen, Kevin Lin, Yue Lu, Kevin M. McBride, Evangelia Koutelou, and Sharon Y.R. Dent  
Our results provide important proof of principle for Gcn5 functions in formation and progression of Myc-driven cancers, suggesting that GCN5 may be a viable target for development of new cancer therapies.

### TRANSLATIONAL SCIENCE

5597  **Inhibition of IL1β by Canakinumab May Be Effective against Diverse Molecular Subtypes of Lung Cancer: An Exploratory Analysis of the CANTOS Trial**  
Connie C. Wong, Jason Baum, Angela Silvestro, Michael T. Beste, Bharani Bharani-Dharan, Siyan Xu, Ying A. Wang, Xiaoshan Wang, Margaret F. Prescott, Lynne Krajkovich, Margaret Dugan, Paul M. Ridker, Anne-Marie Martin, and Eric C. Svensson  
These findings suggest that targeting the IL1β inflammatory pathway might be critical in reducing tumor-promoting inflammation and lung cancer incidence.

5606  **Cancers from Novel Pole-Mutant Mouse Models Provide Insights into Polymerase-Mediated Hypermutagenesis and Immune Checkpoint Blockade**  
Two mouse models of polymerase exonuclease deficiency shed light on mechanisms of mutation accumulation and considerations for immunotherapy.

### TUMOR BIOLOGY AND IMMUNOLOGY

5554  **Peritoneal Spread of Ovarian Cancer Harbors Therapeutic Vulnerabilities Regulated by FOXM1 and EGFR/ERBB2 Signaling**  
Deepak Parashar, Bindu Nair, Anjali Geethadevi, Jasmine George, Ajay Nair, Shring-Wen Tsaih, Ishaque P. Kadambare, Gopa Kumar Gopinadhan Nair, Yiling Lu, Ramani Ramchandran, Denise S. Uyar, Janet S. Rader, Prahlad T. Ram, Gordon B. Mills, Sunila Pradeep, and Pradeep Chaluvally-Raghavan  
This study describes the mechanism exhibited by ovarian cancer cells required for adherent cell transition to nonadherent form during peritoneal spread and metastasis.

5569  **A Wnt-Induced Phenotypic Switch in Cancer-Associated Fibroblasts Inhibits EMT in Colorectal Cancer**  
Mohammed H. Mosa, Birgitta E. Michels, Constantin Menche, Adele M. Nicolas, Tahmineh Darvishi, Florian R. Greten, and Henner F. Farin  
This study provides evidence for Wnt-induced functional diversity of colorectal cancer-associated fibroblasts, representing a non-cell autonomous mechanism for colon cancer progression.

5583  **Tumor Fibroblast-Derived FGF2 Regulates Expression of SPRY1 in Esophageal Tumor-Infiltrating T Cells and Plays a Role in T-cell Exhaustion**  
Qing-yun Chen, Yi-ni Li, Xin-yue Wang, Xu Zhang, Yi Hu, Lei Li, Da-qin Suo, Ke Ni, Zhuo Li, Jia-rong Zhan, Ting-ting Zeng, Ying-hui Zhu, Yan Li, Li-jia Ma, and Xin-Yuan Guan  
These findings reveal FGF2 as an important regulator of SPRY1 expression involved in establishing the dysfunctional state of CD8+ T cells and suggest that inhibition of FGF2 has potential clinical value in ESCC.

5593  **Inhibition of IL1β by Canakinumab May Be Effective against Diverse Molecular Subtypes of Lung Cancer: An Exploratory Analysis of the CANTOS Trial**  
Connie C. Wong, Jason Baum, Angela Silvestro, Michael T. Beste, Bharani Bharani-Dharan, Siyan Xu, Ying A. Wang, Xiaoshan Wang, Margaret F. Prescott, Lynne Krajkovich, Margaret Dugan, Paul M. Ridker, Anne-Marie Martin, and Eric C. Svensson  
These findings suggest that targeting the IL1β inflammatory pathway might be critical in reducing tumor-promoting inflammation and lung cancer incidence.

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Two mouse models of polymerase exonuclease deficiency shed light on mechanisms of mutation accumulation and considerations for immunotherapy.

See related commentary, p. 5459

5619  **The Functional Landscape of Patient-Derived RNF43 Mutations Predicts Sensitivity to Wnt Inhibition**  
Jia Yu, Permeen A. Mohammed Yusoff, Danielle T.J. Woutersen, Pamela Goh, Nathan Harmanston, Ron Smits, David M. Epstein, David M. Virshup, and Babita Madan  
Systematic examination of patient-derived RNF43 mutations identifies rules to guide patient selection, including that truncation or point mutations in well-defined functional domains sensitize cancers to PORCN inhibitors.
RIG-I–Like Receptor LGP2 Is Required for Tumor Control by Radiotherapy
Wenxin Zheng, Diana Rose E. Ranoa, Xiaona Huang, Yuzhu Hou, Kaiting Yang, Elizabeth C. Poli, Michael A. Beckett, Yang-Xin Fu, and Ralph R. Weichselbaum
These findings reveal an essential role of LGP2 in promoting antitumor immunity after radiotherapy and provides a new strategy to enhance radiotherapy.

STAT3–Mediated Astrocyte Reactivity Associated with Brain Metastasis Contributes to Neurovascular Dysfunction
Manuel Sarmiento Soto, James R. Larkin, Chris Martin, Alexandre A. Khrapitchev, Melissa Maczka, Vasiliki Economopoulos, Helen Scott, Carole Escartin, Gilles Bonvento, Sébastien Serres, and Nicola R. Sibson
These findings demonstrate that selectively targeting STAT3–mediated astrocyte reactivity ameliorates the cerebrovascular dysfunction associated with brain metastasis, providing a potential therapeutic avenue for improved patient outcome.

ABOUT THE COVER
Ovarian cancer cells rely on differential signaling of EGFR/ERBB2- or FOXM1-activated pathways when cancer cells become spheroids or when they attach to the mesothelium on distant organs, respectively. Using immunofluorescence, the authors photographed GFP-labeled ovarian cancer cells (green) that were grown on the RFP-labeled mesothelial cells (red). Ovarian cancer cells were then sorted, and gene expression signatures for both adherent and nonadherent cells were determined. The authors further identified that ZEB1 is an important regulator of EGFR, ERBB2, and FOXM1, which are critical for the transition between adherent and nonadherent forms of cells. For details, see the article by Parashar and colleagues on page 5554.