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- 2093** Challenges of Using IFN γ in Clinical Settings
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- 2096** Understanding and Overcoming Immunosuppression Shaped by Cancer Stem Cells
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- 2105** Periostin $^+$ Stromal Cells Guide Lymphovascular Invasion by Cancer Cells
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Highly metastatic breast cancer cells activate a population of periostin-expressing CAFs that remodel the extracellular matrix to promote escape of cancer cells into lymphatic vessels and drive colonization of proximal lymph nodes.

- 2123** β -Catenin-Driven Differentiation Is a Tissue-Specific Epigenetic Vulnerability in Adrenal Cancer
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Oncogenic β -catenin can use tissue-specific partners to regulate cellular differentiation programs that can be reversed by epigenetic therapies, identifying epigenetic control of differentiation as a viable target for β -catenin-driven cancers.

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Genetic Modulation of *BET1L* Confers Colorectal Cancer Susceptibility by Reducing miRNA Binding and m⁶A Modification

Shuwei Li, Mulong Du, Kaili Xu, Shuai Ben, Tianru Zhu, Mengfan Guo, Junyi Xin, Lingjun Zhu, Dongying Gu, Zhengdong Zhang, and Meilin Wang

The integration of miRNA expression profiles and genetic variants identified rs11245997 as a colorectal cancer risk-related variant that reduces miR-140-3p binding and m⁶A modification, leading to *BET1L* upregulation to promote colorectal tumorigenesis.

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A Rare Subset of Primary Tumor Cells with Concomitant Hyperactivation of Extracellular Matrix Remodeling and dsRNA-IFN1 Signaling Metastasizes in Breast Cancer

Niccolò Roda, Andrea Cossa, Roman Hillje, Andrea Tirelli, Federica Ruscitto, Stefano Cheloni, Chiara Priami, Alberto Dalmasso, Valentina Gambino, Giada Blandano, Andrea Polazzi, Paolo Falvo, Elena Gatti, Luca Mazzarella, Lucilla Luzi, Enrica Migliaccio, and Pier Giuseppe Pelicci

Transcriptional lineage tracing coupled with single-cell transcriptomics defined the transcriptional programs underlying metastatic progression in breast cancer, identifying prognostic signatures and prevention strategies.

CANCER IMMUNOLOGY

2171

Attenuation of Sialylation Augments Antitumor Immunity and Improves Response to Immunotherapy in Ovarian Cancer

Kankan Cao, Guodong Zhang, Moran Yang, Yiyi Wang, Mengdi He, Chen Zhang, Yan Huang, Jiaqi Lu, and Haiou Liu

Blocking sialylation augments antitumor immunity and enhances response to immune checkpoint blockade therapy, highlighting a potential therapeutic approach for treating patients with high-grade serous ovarian cancer.

CANCER METABOLISM AND MOLECULAR MECHANISMS

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Metabolic Reprogramming Driven by IGF2BP3 Promotes Acquired Resistance to EGFR Inhibitors in Non-Small Cell Lung Cancer

Ziyou Lin, Jingwei Li, Jian Zhang, Weineng Feng, Jiaye Lu, Xiaofan Ma, Wen Ding, Shumin Ouyang, Jinjian Lu, Peibin Yue, Guohui Wan, Peiqing Liu, and Xiaolei Zhang
IGF2BP3 stabilizes COX6B2 to increase oxidative phosphorylation and to drive resistance to EGFR inhibitors in lung cancer, which provides a therapeutic strategy to overcome acquired resistance by targeting metabolic transitions.

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2208	<i>N⁶-Methyladenosine Promotes Translation of VEGFA to Accelerate Angiogenesis in Lung Cancer</i>	TRANSLATIONAL CANCER BIOLOGY
	Haisheng Zhang, Jiawang Zhou, Jixin Li, Zhaotong Wang, Zhuojia Chen, Ziyan Lv, Lichen Ge, Guoyou Xie, Guoming Deng, Yalan Rui, Hongbing Huang, Likun Chen, and Hongsheng Wang Methylation of the 5'UTR IRES of VEGFA mRNA increases cap-independent translation via recruitment of the YTHDC2/eIF4GI complex, which stimulates angiogenesis to promote lung tumor growth.	2248 Caffeine Supplementation and FOXM1 Inhibition Enhance the Antitumor Effect of Statins in Neuroblastoma Gia-Buu Tran, Jane Ding, Bingwei Ye, Mengling Liu, Yajie Yu, Yunhong Zha, Zheng Dong, Kebin Liu, Sunil Sudarshan, and Han-Fei Ding Caffeine treatment and FOXM1 inhibition can both enhance the antitumor effect of statins by blocking the molecular and metabolic processes that confer statin resistance, indicating potential combination therapeutic strategies for neuroblastoma. See related commentary, p. 2091
2226	<i>MEN1 Degradation Induced by Neddylation and the CUL4B-DCAF7 Axis Promotes Pancreatic Neuroendocrine Tumor Progression</i>	2262 TGFβ Antagonizes IFNγ-Mediated Adaptive Immune Evasion via Activation of the AKT-Smad3-SHP1 Axis in Lung Adenocarcinoma Fan Ye, Zihao Cai, Boyu Wang, Chenxi Zeng, Yu Xi, Shaojie Hu, Rirong Qu, Zhiwei Yuan, Jiaqi Yue, Yitao Tian, Xue Wang, Xiangning Fu, and Lequn Li Blocking TGF β facilitates IFN γ -mediated resistance to anti-PD-L1 therapy due to the role of TGF β in inhibiting IFN γ -induced immuno-evasion by increasing SHP1 phosphatase activity in tumor cells.

ABOUT THE COVER

Periostin lineage tracing in mice revealed a population of perivascular and periductal stromal cells that are activated by highly metastatic cancer cells. These cells comprise a small portion of the naïve mammary gland but expand within the tumor microenvironment of highly metastatic mammary tumors where they remodel the extracellular matrix and promote collagen-mediated lymphovascular invasion and lymphatic metastasis. The cover image shows perivascular periostin-expressing cells, genetically labeled with ZSGreen, surrounding a CD31 $^+$ blood vessel (purple) in a tumor-naïve murine mammary gland that has been stained with DAPI (blue). For details, see article by Null and colleagues on page 2105.

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