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CANCER BIOLOGY

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Active neurons secrete exosomes enriched with miR-184-3p that promote glioblastoma progression and radioresistance by driving the proneural-to-mesenchymal transition in glioma stem cells, which can be reversed by antiepileptic medication levetiracetam.

- 388** **PTEN Lipid Phosphatase Activity Suppresses Melanoma Formation by Opposing an AKT/mTOR/FRA1 Signaling Axis**
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PTEN suppresses melanoma predominantly through its lipid phosphatase function, which when lost, elevates FRA1 levels through AKT/mTOR signaling to promote several aspects of melanomagenesis.

- 405** **RNA Methyltransferase FTSJ3 Regulates the Type I Interferon Pathway to Promote Hepatocellular Carcinoma Immune Evasion**
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Hepatocellular carcinoma cells employ 2'-O-methylation catalyzed by FTSJ3 for immune evasion by suppressing abnormal dsRNA-mediated type I IFN responses, providing a potential target to activate antitumor immunity and enhance immunotherapy efficacy.

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- 419** **PRMT1 Inhibition Activates the Interferon Pathway to Potentiate Antitumor Immunity and Enhance Checkpoint Blockade Efficacy in Melanoma**
Hongru Tao, Chen Jin, Liyuan Zhou, Zhenzhong Deng, Xiao Li, Wenzhen Dang, Shijie Fan, Bing Li, Fei Ye, Junyan Lu, Xiangqian Kong, Chuanpeng Liu, Cheng Luo, and Yuanyuan Zhang
Targeting PRMT1 stimulates interferon signaling by increasing expression of endogenous retroviral elements and double-stranded RNA through repression of DNMT1, which induces antitumor immunity and synergizes with immunotherapy to suppress tumor progression.

CANCER METABOLISM AND MOLECULAR MECHANISMS

- 434** **SUMOylation-Driven mRNA Circularization Enhances Translation and Promotes Lymphatic Metastasis of Bladder Cancer**
Yue Zhao, Jiancheng Chen, Hanhao Zheng, Yuming Luo, Mingjie An, Yan Lin, Mingrui Pang, Yuanlong Li, Yao Kong, Wang He, Tianxin Lin, and Changhao Chen
DHCR24 is a SUMOylation regulator that controls translation initiation complex assembly and orchestrates *TBK1* mRNA circularization to activate Akt/VEGFC signaling, which stimulates lymphangiogenesis and promotes lymph node metastasis in bladder cancer.

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TRANSLATIONAL CANCER BIOLOGY

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Huijuan Fan, Zhanao Xu, Ke Yao, Bingxin Zheng, Yuan Zhang, Xuxiang Wang, Tengjiang Zhang, Xuan Li, Haitian Hu, Bin Yue, Zeping Hu, and Hanqiu Zheng
Metabolic interaction between osteoclasts and tumor cells contributes to resistance to DNA-damaging agents, which can be blocked by combination treatment with PARP and osteoclast inhibitors to reduce bone metastatic burden.
- 468 Serial Circulating Tumor DNA Analysis with a Tumor-Naïve Next-Generation Sequencing Panel Detects Minimal Residual Disease and Predicts Outcome in Ovarian Cancer**
Jinho Heo, Yoo-Na Kim, Saeam Shin, Kyunglim Lee, Ji-Hyun Lee, Yong Jae Lee, Zisun Choi, Jihyang Park, Seungki Min, Sang Wun Kim, Jong Rak Choi, Sunghoon Kim, Seung-Tae Lee, and Jung-Yun Lee
In ovarian cancer, serial circulating tumor DNA testing is a highly predictive marker of patient survival, with a significantly improved recurrence detection lead time compared with conventional monitoring tools.

- 479 Osimertinib Covalently Binds to CD34 and Eliminates Myeloid Leukemia Stem/Progenitor Cells**
Li Xia, Jie-Yang Liu, Meng-Ying Yang, Xue-Hong Zhang, Yue Jiang, Qian-Qian Yin, Chen-Hui Luo, Hong-Chen Liu, Zhi-Jie Kang, Cheng-Tao Zhang, Bei-Bei Gao, Ai-Wu Zhou, Hai-Yan Cai, Edmund K. Waller, Jin-Song Yan, and Ying Lu
Osimertinib binds CD34 and selectively kills CD34⁺ leukemia cells to induce remission in preclinical models and patients with AML with a high percentage of CD34⁺ blasts, providing therapeutic options for myeloid leukemia patients.

COMPUTATIONAL CANCER BIOLOGY AND TECHNOLOGY

- 493 Deep Learning Enables Spatial Mapping of the Mosaic Microenvironment of Myeloma Bone Marrow Trephine Biopsies**
Yeman Brhane Hagos, Catherine S.Y. Lecat, Dominic Patel, Anna Mikolajczak, Simon P. Castillo, Emma J. Lyon, Kane Foster, Thien-An Tran, Lydia S.H. Lee, Manuel Rodriguez-Justo, Kwee L. Yong, and Yinyin Yuan
Spatial analysis of bone marrow trephine biopsies using histology, deep learning, and tailored algorithms reveals the bone marrow architectural heterogeneity and evolution during myeloma progression and treatment.

ABOUT THE COVER

Bone marrow trephine biopsy is crucial for the diagnosis and study of multiple myeloma. To dissect the complex cellular communities and mosaic tissue habitats, the superpixel-inspired deep learning method MoSaicNet (morphological analysis with superpixel-based habitat detection network) was developed, allowing segmentation of blood, bone, cellular tissue, and fat regions. Cell detection and classification can be achieved using AwareNet, a deep learning method that is capable of giving high attention to rarer cell types in a dataset with class imbalance. These machine learning models allow detailed quantitative and spatial analyses of the tumor niche in myeloma bone marrow. For details, see article by Hagos and colleagues on page 493.

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