

CANCER IMMUNOLOGY RESEARCH

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Myeloid-specific HCK activity promotes gastric tumor development by enhancing macrophage polarization and production of STAT3-stimulatory ligands, which enhance STAT3 signaling in tumor epithelial and immune cells. Reduction or inhibition of HCK activity reduces STAT3-dependent tumor growth.

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Lung cancer-derived fibroblasts produce CCL2, which recruits suppressive CCR2⁺ myeloid cells to the tumor microenvironment, where they suppress CD8⁺ T-cell function. Use of various inhibitors shows that this suppression can be reversed, highlighting possible druggable targets.

- 451 **Interferon-Induced IDO1 Mediates Radiation Resistance and Is a Therapeutic Target in Colorectal Cancer**
Baosheng Chen, David M. Alvarado, Micah Iticovici, Nathan S. Kau, Haeseong Park, Parag J. Parikh, Dinesh Thotala, and Matthew A. Ciorba

Inhibition of the immune-metabolic enzyme IDO1 enhances radiation sensitivity in colorectal cancer and is radioprotective to the normal small intestine in mice. IDO1 inhibitors may increase radiation therapy effectiveness in humans with colorectal cancer while reducing intestinal toxicity.

- 465 **CD73 Blockade Promotes Dendritic Cell Infiltration of Irradiated Tumors and Tumor Rejection**

Erik Wennerberg, Sheila Spada, Nils-Petter Rudqvist, Claire Lhuillier, Sylvia Gruber, Qiuying Chen, Fengli Zhang, Xi K. Zhou, Steven S. Gross, Silvia C. Formenti, and Sandra Demaria

Radiation-induced adenosine production is identified as a barrier that limits radiotherapy-induced antitumor immune responses. Antibodies to CD73 that block adenosine generation could be used in combination with radiotherapy and immune checkpoint blockade to improve response to radiation therapy.

- 479 **Fatty Acid Oxidation Controls CD8⁺ Tissue-Resident Memory T-cell Survival in Gastric Adenocarcinoma**

AC Run Lin, Hui Zhang, Yujie Yuan, Qiong He, Jianwen Zhou, Shuhua Li, Yu Sun, Daniel Y. Li, Hai-Bo Qiu, Wei Wang, Zhehong Zhuang, Bin Chen, Yonghui Huang, Chuwei Liu, Yingzhao Wang, Shirong Cai, Zunfu Ke, and Weiling He

Tissue-resident memory T cells (Trm) protect against local infection and tumor formation. In gastric adenocarcinoma, Trm are associated with better patient survival and fatty acid availability, and are crucial for Trm persistence and antitumor effects.

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Metabolomics performed on pancreatic juice from pancreatic ductal adenocarcinoma patients identifies metabolic variables correlating with outcome and immune infiltration of tumors. Obtaining a metabolic profile could aid in the stratification of patients for more tailored immunotherapies.
- 506** **Inhibition of SHP-1 Expands the Repertoire of Antitumor T Cells Available to Respond to Immune Checkpoint Blockade**
Jeremy P. Snook, Ashleigh J. Soedel, H. Atakan Ekiz, Ryan M. O'Connell, and Matthew A. Williams
Checkpoint blockade enhances high-affinity T-cell responses to melanoma, but some patients do not benefit. Targeting SHP-1 expands the repertoire of T cells available to respond to treatment and induces antitumor activity from low-affinity T cells.
- 518** **Improved Antitumor Efficacy of Chimeric Antigen Receptor T Cells that Secrete Single-Domain Antibody Fragments**
Yushu Joy Xie, Michael Dougan, Jessica R. Ingram, Novalia Pishesha, Tao Fang, Noor Momin, and Hidde L. Ploegh
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- 530** **$\gamma\delta$ T-cell Receptors Derived from Breast Cancer-Infiltrating T Lymphocytes Mediate Antitumor Reactivity**
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Proinflammatory $\gamma\delta$ T cells infiltrate triple-negative breast cancers and are positioned in close proximity to tumor cells. T cells engineered to express paired TCR γ /TCR δ chains are tumor reactive against an array of tumor types.
- 544** **Proteogenomics Uncovers a Vast Repertoire of Shared Tumor-Specific Antigens in Ovarian Cancer**
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By exploring all open reading frames of all genomic regions, 103 ovarian cancer-specific antigens are identified. Most would not be detected by traditional methods, highlighting a pipeline that can be used to identify novel target antigens.
- 556** **Immunosuppressive Mediators Impair Proinflammatory Innate Lymphoid Cell Function in Human Malignant Melanoma**
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Innate lymphoid cells (ILCs) reside in epithelial tissues where melanomas arise. ILCs are enriched in melanoma-bearing patients and animals but display impaired cytokine production partially due to adenosine and kynurenine produced by the tumor microenvironment.
- 565** **LncRNA AK036396 Inhibits Maturation and Accelerates Immunosuppression of Polymorphonuclear Myeloid-Derived Suppressor Cells by Enhancing the Stability of Ficolin B**
Xinyu Tian, Yu Zheng, Kai Yin, Jie Ma, Jie Tian, Yue Zhang, Lingxiang Mao, Huaxi Xu, and Shengjun Wang
Knockdown of a lncRNA or its target, ficolin B, inhibits the immunosuppressive capacity of PMN-MDSCs and delays tumor progression in mice. M-ficolin, the human ortholog of ficolin B, is elevated in patients with lung cancer, suggesting clinical relevance.

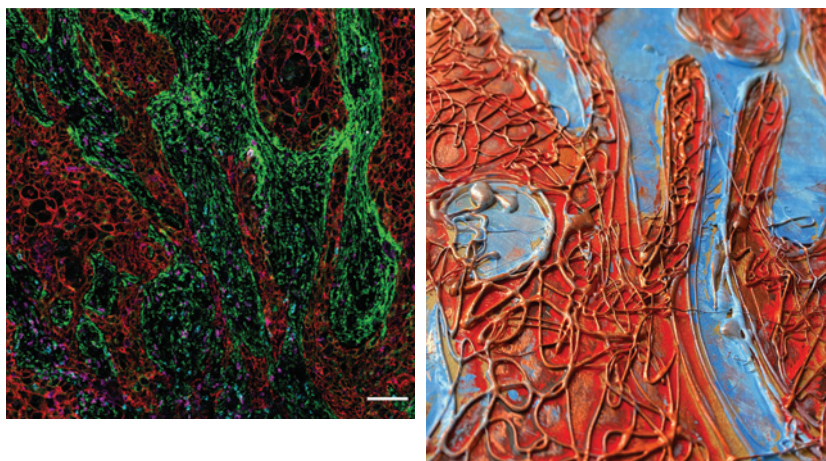
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ABOUT THE COVER

Cancer-associated fibroblasts (CAFs) are a major component of the tumor stroma and can promote tumorigenesis and treatment resistance. However, the mechanisms behind how CAFs do this are not fully understood in lung squamous cell carcinoma (LSCC). By evaluating primary human LSCCs, Xiang et al. demonstrate interactions between CAFs and myeloid cells in the tumor microenvironment (TME). Lung CAFs produce CCL2, which recruits CCR2⁺ myeloid cells to the TME and promotes their polarization into a myeloid-derived suppressor cell (MDSC) phenotype. This results in suppression of CD8⁺ T-cell responses. Reduction of reactive oxygen species in CAF-induced MDSCs reverses the suppression of CD8⁺ T-cell proliferation and function, highlighting possible druggable targets to boost antitumor responses in LSCC. Read more in this issue on page 436. Original image from Fig. 1D. Artwork by Lewis Long.



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