HIGHLIGHTS FROM THE LITERATURE

515 What We’re Reading

PRIORITY BRIEF

516 Breast Cancer Neoantigens Can Induce CD8\(^+\) T-Cell Responses and Antitumor Immunity

Neoantigens are valuable for immunotherapy, but human breast cancers offer fewer than other cancers. With next-generation sequencing and computerized epitope-prediction, neoantigens in breast cancer were identified. The immune system recognized these neoantigens and protected mice from tumor challenge.

RESEARCH ARTICLES

524 A Four-Factor Immunoscore System That Predicts Clinical Outcome for Stage II/III Gastric Cancer
Ti Wen, Zhenning Wang, Yi Li, Zhi Li, Xiaofang Che, Yibo Fan, Shuo Wang, Jinglei Qu, Xianghong Yang, Kezuo Hou, Wenyang Zhou, Jing Liu, Liqun Chen, Jingdong Zhang, Xiujuan Qu, and Yunpeng Liu

The American Joint Committee on Cancer (AJCC) staging system for gastric cancer is insufficiently prognostic. An immunoscore system based on PD-L1 expression on tumor or immune cells, PD-1 expression, and infiltration of CD8\(^+\) T cells was more prognostic and complements the AJCC system.

535 Depletion of Tumor-Associated Macrophages with a CSF-1R Kinase Inhibitor Enhances Antitumor Immunity and Survival Induced by DC Immunotherapy
Floris Dammeijer, Lysanne A. Lievense, Menno van Nimwegen, Koen Bezemer, Joost P. Hegmans, Thorbald van Hall, Rudi W. Hendriks, and Joachim G. Aerts

Mesothelioma has a poor prognosis and resists conventional therapies. Although tumor-associated macrophage depletion alone cannot restore antitumor immunity, its combination with dendritic cell–based therapy enhanced immune activation and survival in mesothelioma tumor models.

547 All-Trans Retinoic Acid Prevents Osteosarcoma Metastasis by Inhibiting M2 Polarization of Tumor-Associated Macrophages
Qian Zhou, Miao Xian, Senfeng Xiang, Danyan Xiang, Xuejing Shao, Jincheng Wang, Ji Cao, Xiaochun Yang, Bo Yang, Meidan Ying, and Qiaojuan He

Metastasis of osteosarcoma to lung depends on tumor-associated macrophages. All-trans retinoic acid (ATRA) inhibited this metastasis in mice. ATRA downregulated secretion of MMP12, a macrophage-secreted elastase. The results identify ATRA as a possible antimetastasis therapeutic.

560 Converting Lymphoma Cells into Potent Antigen-Presenting Cells for Interferon-Induced Tumor Regression
Jing Liao, Yan Luan, Zhenhua Ren, Xiaojuan Liu, Diyuan Xue, Hairong Xu, Zhichen Sun, Kai ting Yang, Hua Peng, and Yang-Xin Fu

Although mAbs to hCD20 are used therapeutically for B-cell lymphoma, some lymphomas are resistant. In mice, interferon-\(\alpha\) (IFN\(\alpha\)) abolished resistance. Treatment with an anti-CD20–IFN\(\alpha\) fusion protein eradicated B-cell lymphoma by co-opting tumor cells to present antigen.

571 Transgenic Expression of IL15 Improves Antiglioma Activity of IL13R\(\alpha\)2-CAR T Cells but Results in Antigen Loss Variants
Giedre Krenciute, Brooke L. Prinzing, Zhongzhen Yi, Meng-Fen Wu, Hao Liu, Gianpietro Dotti, Irina V. Balyasnikova, and Stephen Gottschalk

Glioblastoma responds imperfectly to immunotherapy. Transgenic expression of IL15 in T cells expressing chimeric antigen receptors improved their proliferative capacity, persistence, and cytokine production. The emergence of antigen-loss variants highlights the need to target multiple tumor antigens.

582 Shifting the Balance of Activating and Inhibitory Natural Killer Receptor Ligands on BRAF\(^{V600E}\) Melanoma Lines with Vemurafenib
Alexandra Frazao, Marina Colombo, Emmanuelle Fourmentaux-Neves, Meriem Messaoudene, Sylvie Rusakiewicz, Laurence Zitvogel, Eric Vivier, Frederic Vely, Florence Faure, Brigitte Dréno, Houssem Benlalam, Fanny Bouquet, Ariel Savina, Eric Pasmart, Antoine Toubert, Marie-Françoise Avril, and Anne Caignard

Vemurafenib-treated melanomas of most patients whose tumors harbor BRAF\(^{V600E}\) mutations regress, but do not durably. Vemurafenib, a Raf kinase-inhibitor, was found to alter expression of natural killer cell–recognized stress-induced ligands, which in turn affected natural killer cell cytotoxicity.
Intravesical BCG Induces CD4\(^+\) T-Cell Expansion in an Immune Competent Model of Bladder Cancer

Intravesical bacillus Calmette–Guérin (BCG) instillations are standard of care for early stage bladder cancer. BCG was found to recruit T cells to the bladder, but their phenotype was unchanged, implying that combining T cell–activating agents with BCG might improve clinical activity.

Antitumor Effects of Epidrug/IFN\(\alpha\) Combination Driven by Modulated Gene Signatures in Both Colorectal Cancer and Dendritic Cells
Alessandra Fragale, Giulia Romagnoli, Valerio Licursi, Maria Buoncervello, Giorgia Del Vecchio, Caterina Giuliani, Stefania Parlato, Celeste Leone, Marta De Angelis, Irene Canini, Elena Toschi, Filippo Belardelli, Rodolfo Negri, Imerio Capone, Carlo Presutti, and Lucia Gabriele

A combination of two epidrugs plus IFN has antitumor effects in colorectal cancer. Epigenetic changes driven by IRF8 in both metastatic colorectal cancer cells and dendritic cells led to increased tumor cell death and increased activity of DCs.

ABOUT THE COVER
Gastric cancer is a common cancer that affects millions of people worldwide. The accurate staging of this cancer is a critical first step upon which a patient’s prognosis and treatment options are based. The conventional staging grid is based on three factors: tumor size, lymphnode involvement, and metastasis (TNM staging). However, the variability of outcomes for patients within the same TNM stage strongly suggests that other key factors need to be included to obtain a more useful classification. Wen et al. examined immunological factors and scored them according to their associations with disease progression. Using only four immune parameters, they identified patients who were in the same stage according to their TNM classification to be at low, medium, or high risk of progressive disease based on their "immunoscore." Read more in this issue of Cancer Immunology Research starting on page 524. The micrograph, from Fig. 5, is a slice of gastric tumor infiltrated by multiple immune cell types in various activation states. Artwork by Lewis Long.
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