

PRIORITY BRIEFS

- 563** **Molecular Drivers of the Non-T-cell-Inflamed Tumor Microenvironment in Urothelial Bladder Cancer**
Randy F. Sweis, Stefani Spranger, Riyue Bao, Gladell P. Paner, Walter M. Stadler, Gary Steinberg, and Thomas F. Gajewski
Immunotherapy resistance is a reality for many cancer patients. Three tumor-intrinsic molecular pathways, β -catenin, PPAR γ , and FGFR3, were identified and linked to the exclusion of T cells from urothelial tumors. Targeting these pathways may enhance immune checkpoint efficacy.

- 569** **Prolonged Benefit from Ipilimumab Correlates with Improved Outcomes from Subsequent Pembrolizumab**
Amanda Shreders, Richard Joseph, Chengwei Peng, Fei Ye, Shilin Zhao, Igor Puzanov, Jeffrey A. Sosman, and Douglas B. Johnson
Anti-PD-1 therapies are becoming first-line treatments for metastatic melanoma, but how prior immune therapy affects anti-PD-1 efficacy is unknown. Prior ipilimumab was found to predict response to anti-PD-1, which could help select patients for therapy.

RESEARCH ARTICLES

- 574** **Expanded and Activated Natural Killer Cells for Immunotherapy of Hepatocellular Carcinoma**
Takahiro Kamiya, Yu-Hsiang Chang, and Dario Campana
Hepatocellular carcinoma (HCC) is often incurable. Human NK cells with enhanced cytotoxicity against HCC were expanded in vitro, generating efficient killers of HCC in culture and in mice, supporting the infusion of such cells for treatment of HCC.

- 582** **Immune-Derived PD-L1 Gene Expression Defines a Subgroup of Stage II/III Colorectal Cancer Patients with Favorable Prognosis Who May Be Harmed by Adjuvant Chemotherapy**
Philip D. Dunne, Darragh G. McArt, Paul G. O'Reilly, Helen G. Coleman, Wendy L. Allen, Maurice Loughrey, Sandra Van Schaeybroeck, Simon McDade, Manuel Salto-Tellez, Daniel B. Longley, Mark Lawler, and Patrick G. Johnston
A subgroup of patients with colorectal cancer was defined by high PD-L1 gene expression on their tumor-infiltrating immune cells. These patients may be harmed by standard chemotherapy and may benefit from immunotherapy that targets the PD-1 immune checkpoint.

- 592** **Pretreatment Immune Status Correlates with Progression-Free Survival in Chemotherapy-Treated Metastatic Colorectal Cancer Patients**
Kohei Tada, Shigehisa Kitano, Hirokazu Shoji, Takashi Nishimura, Yasuhiro Shimada, Kengo Nagashima, Kazunori Aoki, Nobuyoshi Hiraoka, Yoshitaka Honma, Satoru Iwasa, Natsuko Okita, Atsuo Takashima, Ken Kato, Yasuhide Yamada, Naoyuki Katayama, Narikazu Boku, Yuji Heike, and Tetsuya Hamaguchi
It was not clear whether immune cell subsets in peripheral blood have prognostic value for patients about to undergo first-line chemotherapy. This prospective study reveals an immune signature that correlates with significantly longer progression-free survival.

- 600** **Immunogenic Subtypes of Breast Cancer Delineated by Gene Classifiers of Immune Responsiveness**
Lance D. Miller, Jeff A. Chou, Michael A. Black, Cristin Print, Julia Chifman, Angela Alistar, Thomas Putti, Xiaobo Zhou, Davide Bedognetti, Wouter Hendrickx, Ashok Pullikuth, Jonathan Rennhack, Eran R. Andrechek, Sandra Demaria, Ena Wang, and Francesco M. Marincola
Assessment of expression profiles and clinical data from many breast tumors enabled classifications having prognostic value. Tumors comprising molecularly distinct subtypes differed in potential for metastasis-protective immune responsiveness, perhaps reflecting a differential activation of immunomodulatory pathways.

- 611** **Enhanced Tumor Control with Combination mTOR and PD-L1 Inhibition in Syngeneic Oral Cavity Cancers**
Ellen C. Moore, Harrison A. Cash, Andria M. Caruso, Ravindra Uppaluri, James W. Hodge, Carter Van Waes, and Clint T. Allen
Inhibition of mTOR is felt to be systemically immunosuppressive. However, the antitumor immunity induced by checkpoint inhibition in an immunogenic model of oral cavity cancer was enhanced by the mTOR inhibitor rapamycin via a T cell-dependent mechanism.

- 621** **Antitumor Efficacy of Radiation plus Immunotherapy Depends upon Dendritic Cell Activation of Effector CD8⁺ T Cells**
Simon J. Dovedi, Grazyna Lipowska-Bhalla, Stephen A. Beers, Eleanor J. Cheadle, Lijun Mu, Martin J. Glennie, Timothy M. Illidge, and Jamie Honeychurch
Radiotherapy plus CD40 or TLR7 stimulation leads to long-term clearance of B- and T-cell lymphomas. These curative responses after combining radiotherapy with an immunomodulatory agent depended upon the priming of tumor-specific CD8⁺ T cells by dendritic cells.

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631 Antitumor Efficacy of Anti-GD2 IgG1 Is Enhanced by Fc Glyco-Engineering

Hong Xu, Hongfen Guo, Irene Y. Cheung, and Nai-Kong V. Cheung

Most effective antibody immunotherapy relies on ADCC. A potent ADCC-enhanced antibody is described that, in comparison with Abs with altered affinities for Fc receptors, significantly improved the growth control of tumors expressing cancer-antigen GD2.

ADDENDUM

639 ADDENDUM: T Cells Expressing CD19/CD20 Bispecific Chimeric Antigen Receptors Prevent Antigen Escape by Malignant B Cells

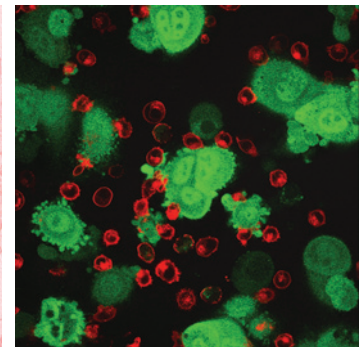
Eugenia Zah, Meng-Yin Lin, Anne Silva-Benedict, Michael C. Jensen, and Yvonne Y. Chen

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ABOUT THE COVER

Patients with advanced hepatocellular carcinoma (liver cancer) have a median life expectancy of 8 to 11 months. These tumors are frequently associated with viral hepatitis. Natural killer (NK) cells recognize virally infected cells and malignant cells, so to develop an immunotherapy, the authors expanded and activated NK cells *ex vivo*. These cells, when reinfused into immunodeficient mice hosting human tumors, enabled many mice to survive and efficiently killed tumor cells. The cover is based on a fluorescence confocal image (far right) of PLC/PRF/5 hepatocarcinoma cells (green) surrounded by expanded, activated human NK cells (red). Cover by Lewis Long; image captured by T. Kamiya. Read more starting on page 574 in this issue of *Cancer Immunology Research*.



Cancer Immunology Research

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