HIGHLIGHTS FROM THE LITERATURE

717 What We’re Reading

RESEARCH ARTICLES

718 Development of Aggressive Pancreatic Ductal Adenocarcinomas Depends on Granulocyte Colony Stimulating Factor Secretion in Carcinoma Cells
Michael W. Pickup, Philip Owens, Agnieszka E. Gorska, Anna Chytil, Fei Ye, Chanjuan Shi, Valerie M. Weaver, Raghu Kalluri, Harold L. Moses, and Sergey V. Novitskiy

Aggressive PDAC correlates with increased G-CSF production and accumulation of immunosuppressive cells. Treatment of mouse models with gemcitabine and anti–G-CSF was efficacious. Analysis of clinical data indicates a subset of patients for whom this treatment might be effective.

730 Using Antigen-Specific B Cells to Combine Antibody and T Cell–Based Cancer Immunotherapy
Kerstin Wennhold, Martin Thelen, Hans Anton Schlößer, Natalie Haustein, Sabrina Reuter, Maria Garcia-Marquez, Axel Lechner, Sebastian Kobold, Felicitas Rataj, Olaf Utermöhlen, Geothy Chakupurakal, Sebastian Theurich, Michael Hallek, Hinrich Abken, Alexander Shimabukuro-Vornhagen, and Michael von Bergwelt-Baildon

B-cell effector functions could be exploited for cancer immunotherapy. A two-pronged approach in mice, combining antigen-specific CD40-activated B cells with antigen-specific plasma cells, induced a successful T-cell antitumor immune response, demonstrating potential for translation.

744 Clonal Expansion and Interrelatedness of Distinct B-Lineage Compartments in Multiple Myeloma
Leo Hansmann, Arnold Han, Livius Penter, Michaela Liedtke, and Mark M. Davis

Only some multiple myeloma patients benefit from cellular immunotherapies. A single-cell, high-throughput methodology was developed that determines the phenotypic range of a given B- or plasma cell clone, which could aid identification of those most likely to respond.

755 Concurrent PD-1 Blockade Negates the Effects of OX40 Agonist Antibody in Combination Immunotherapy through Inducing T-cell Apoptosis

Simultaneous treatment of mice with checkpoint inhibitor anti–PD-1 and agonist anti-OX40 negated the benefits of anti-OX40 alone, due to increased apoptosis of CD8+ T cells. Thus, for clinical success, sequencing optimization for combination immunotherapy is crucial.

767 The Tumor Microenvironment Regulates Sensitivity of Murine Lung Tumors to PD-1/PD-L1 Antibody Blockade
Howard Y. Li, Maria McSharry, Bonnie Bulllock, Teresa T. Nguyen, Jeff Kwak, Joanna M. Poczobutt, Trisha R. Sippel, Lynn E. Heasley, Mary C. Weiser-Evans, Eric T. Clambey, and Raphael A. Nemenoff

In several mouse lung cancer models, response to PD-1/PD-L1 inhibitors depended on the cancer cells as well as the tumor microenvironment. Blocking PD-L1 expression in either the cancer cells or the host limited tumor growth.

778 MICA-Expressing Monocytes Enhance Natural Killer Cell Fc Receptor-Mediated Antitumor Functions
Amanda R. Campbell, Megan C. Duggan, Lorena P. Suarez-Kelly, Neela Bhave, Kallan S. Opheim, Elizabeth L. McMichael, Prashant Trikha, John C. Byrd, Michael A. Caligiuri, and William E. Carson III

Natural killer (NK) cells secrete immunostimulatory factors like IFNγ in response to tumors. Engagement of monocyte MICA and NK cell NKG2D promoted and enhanced the NK response to HER2+ breast tumors treated with mAb to HER2 in a murine model.

790 A Multikinase and DNA-PK Inhibitor Combination Immunomodulates Melanomas, Suppresses Tumor Progression, and Enhances Immunotherapies
Alexander K. Tsai, Asra Y. Khan, Christina E. Worgo, Lucy L. Wang, Yuanyuan Liang, and Eduardo Davila

Regorafenib and NU7441 are targeted therapies that immunomodulated a heterogeneous panel of melanomas. The compounds favorably altered T-cell phenotype and function, and cooperated with existing immunotherapies to suppress melanoma progression in a murine tumor model.
Role of NOX2-Derived Reactive Oxygen Species in NK Cell–Mediated Control of Murine Melanoma Metastasis

Ebru Aydin, Junko Johansson, Faisal Hayat Nazir, Kristoffer Hellstrand, and Anna Martner

Inhibition of NOX2 in mice reduced melanoma metastasis through a natural killer cell and interferon-γ–based mechanism. Pharmacological inhibition of NOX2, alone or combined with immunostimulatory strategies, could provide an approach to preventing hematogenous dissemination of melanoma cells.

Primary Tumors Limit Metastasis Formation through Induction of IL15-Mediated Cross-Talk between Patrolling Monocytes and NK Cells

Hiroshi Kubo, Sofia Mensurado, Natacha Gonçalves-Sousa, Karine Serre, and Bruno Silva-Santos

This study identifies an IL15-dependent immune network against cancer metastasis, with the use of a model that delineated tumor establishment from metastasis formation. IL15 produced by patrolling monocytes was found to activate NK cells that then inhibited metastasis.