WHAT WE'RE READING

527  A Sampling of Highlights from the Literature

CANCER IMMUNOLOGY AT THE CROSSROADS

528  Adoptive Immunotherapy with Antigen-Specific T Cells Expressing a Native TCR
Wingchi Leung and Helen E. Heslop

CANCER IMMUNOLOGY MINIATURE

534  Immunologic Recognition of a Shared p53 Mutated Neoantigen in a Patient with Metastatic Colorectal Cancer
Winifred Lo, Maria Parkhurst, Paul F. Robbins, Eric Tran, Yong-Chen Lu, Li Jia, Jared J. Gattner, Anna Pasetto, Drew Deniger, Parisa Malekzadeh, Thomas E. Shelton, Todd Prickett, Satyajit Ray, Scott Kivitz, Biman C. Paria, Isaac Kriley, David S. Schrump, and Steven A. Rosenberg

A patient with metastatic colon cancer had T-cell receptors reactive with a mutation in the tumor suppressor gene TP53. The TCRs were neoantigen-specific and HLA-A*0201-restricted and could be used to treat others with tumors sharing the same parameters.

PRIORITY BRIEFS

544  Early-Life Microbiota Exposure Restricts Myeloid-Derived Suppressor Cell–Driven Colonic Tumorigenesis
Akihito Harusato, Emilie Viennois, Lucie Etienne-Mesmin, Shingo Matsuyama, Hirohito Abo, Satoshi Osuka, Nicholas W. Lukacs, Yuji Naito, Yoshito Itoh, Jian-Dong Li, Didier Merlin, Andrew T. Gewirtz, and Timothy L. Denning

Mice with altered colon microbiota early in life exhibit augmented inflammatory cytokine and chemokine expression in the colon. This led to an increased susceptibility to colitis-associated cancer later in adulthood, demonstrating the microbiota’s impact on colon homeostasis.

552  Broad Cytotoxic Targeting of Acute Myeloid Leukemia by Polyclonal Delta One T Cells
Biagio Di Lorenzo, André E. Simões, Francisco Caiado, Paola Tierppo, Daniel V. Correia, Tânia Carvalho, Maria Comes da Silva, Julie Déchanel-Merville, Ton N. Schumacher, Immo Prinz, Haakan Norell, Sarina Ravens, David Vermijlen, and Bruno Silva-Santos

This study provides preclinical in vitro and in vivo proof-of-concept for use of Delta One T (DOT) cells as immunotherapy to treat acute myeloid leukemia.

RESEARCH ARTICLES

559  CD96 Is an Immune Checkpoint That Regulates CD8+ T-cell Antitumor Function

The antitumor activity of anti-CD96 monotherapy depends on several host factors, including CD8+ T cells and immune signaling. Inhibition of CD96 in combination with other immune checkpoint inhibitors showed superior antitumor activity over single or dual agent therapy.

572  Targeted Delivery of IL2 to the Tumor Stroma Potentiates the Action of Immune Checkpoint Inhibitors by Preferential Activation of NK and CD8+ T Cells
Cornelia Huttmacher, Nicolás Gonzalo Núñez, Anna Rita Liuzzi, Burkhard Becher, and Dario Neri

Treatment of murine tumors with combination checkpoint blockade and an antibody-IL2 fusion protein reduces tumor growth, an effect dependent on CD8+ T cells and NK cells. These data support the use of engineered IL2 products for anti-cancer therapy.

600  Regulatory T Cells in an Endogenous Mouse Lymphoma Recognize Specific Antigen Peptides and Contribute to Immune Escape
Fatima Ahmedić, Tanja Riedel, Nadine Hönig, Vera Bauer, Nico Trautwein, Albert Geishauser, Tim Sparwasser, Stefan Stelvanović, Martin Röcken, and Ralph Mocikat

In a mouse model of B-cell lymphoma, regulatory T cells suppressed antitumor responses. Treg cells recognized unmethylated self epitopes, which were characteristic of lymphoma and which were related to malignancy.
### Table of Contents

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>609</td>
<td>Automated Analysis of Lymphocytic Infiltration, Tumor Budding, and Their Spatial Relationship Improves Prognostic Accuracy in Colorectal Cancer</td>
<td>Ines P. Nearchou, Kate Lillard, Christos G. Gavriel, Hideki Ueno, David J. Harrison, and Peter D. Caie</td>
</tr>
<tr>
<td>621</td>
<td>Intravesical Ty21a Vaccine Promotes Dendritic Cells and T Cell–Mediated Tumor Regression in the MB49 Bladder Cancer Model</td>
<td>Sonia Domingos-Pereira, Karthik Sathiyanadan, Stefano La Rosa, Lenka Poláková, Mathieu F. Chevalier, Paul Martel, Rim Hojej, Laurent Derré, Jacques-Antoine Haefligger, Patrice Jichlinski, and Denise Nardelli-Haefliger</td>
</tr>
<tr>
<td>630</td>
<td>Low-Dose Apatinib Optimizes Tumor Microenvironment and Potentiates Antitumor Effect of PD-1/PD-L1 Blockade in Lung Cancer</td>
<td>Sha Zhao, Shengxiang Ren, Tao Jiang, Bo Zhu, Xuèfèi Li, Chao Zhao, Yijun Jia, Jingpeng Shi, Limin Zhang, Xiaozhen Liu, Meng Qiao, Xiaoxia Chen, Chuxia Su, Hui Yu, Caicun Zhou, Jun Zhang, D. Ross Camidge, and Fred R. Hirsch</td>
</tr>
<tr>
<td>644</td>
<td>Immune Profiling and Quantitative Analysis Decipher the Clinical Role of Immune-Checkpoint Expression in the Tumor Immune Microenvironment of DLBCL</td>
<td>Ziju Y. Xu-Monette, Min Xiao, Qingyan Au, Raghav Padmanabhan, Bing Xu, Nicholas Hoe, Sandra Rodriguez-Perales, Raul Torres-Ruiz, Ganiiju C. Manyam, Carlo Visco, Yi Miao, Xiaohong Tan, Hongwei Zhang, Alexandar Tzanov, Jing Wang, Karen Dybkær, Wayne Tam, Hua You, Govind Bhagat, Eric D. Hsi, Maurilio Ponzozi, Andrés J.M. Ferreri, Michael B. Møller, Miguel A. Piris, J. Han van Krieken, Jane N. Winter, Jason R. Westin, Lan V. Pham, L. Jeffrey Medeiros, George Z. Rassidakis, Yong Li, Gordon J. Freeman, and Ken H. Young</td>
</tr>
<tr>
<td>663</td>
<td>Radiotherapy and Cisplatin Increase Immunotherapy Efficacy by Enabling Local and Systemic Intratumoral T-cell Activity</td>
<td>Paula Kroon, Elselen Frijlink, Victoria Iglesias-Guiranais, Andriy Volkov, Martí M. van Buuren, Tom N. Schumacher, Marcel Verheij, Janierce Borst, and Inge Verbrugge</td>
</tr>
<tr>
<td>670</td>
<td>T-cell Activity against AML Improved by Dual-Targeted T Cells Stimulated through T-cell and IL7 Receptors</td>
<td>Eric Krawczyk, Sergey N. Zolov, Kevin Huang, and Challice L. Bonifant</td>
</tr>
<tr>
<td>683</td>
<td>Correction: Collapse of the Plasmacytoid Dendritic Cell Compartment in Advanced Cutaneous Melanomas by Components of the Tumor Cell Secretome</td>
<td>AC icon indicates AuthorChoice</td>
</tr>
</tbody>
</table>
CD96 is an immune checkpoint and is known to suppress T-cell and NK cell effector functions. Thus, CD96 can impair antitumor responses in the tumor microenvironment. Mittal et al. demonstrate that CD96 blockade can inhibit primary tumor growth in multiple tumor models. The effects of anti-CD96 are dependent on several host factors, including CD8^+^ T cells, cytokines, and DNAM-1/CD226 signaling. Because CD96 is co-expressed with other immune checkpoints, especially PD-1, dual and triple blockade protocols were tested. Dual blockade of CD96 and other immune checkpoints is more effective than anti-CD96 monotherapy, and an optimal triple combination blocking CD96, PD-1, and TIGIT is superior over dual combinations. These treatments increase T-cell infiltration and enhance antitumor responses, highlighting that combining the targeting of CD96 with other immune checkpoints could be a strategy for augmenting T-cell responses that suppress tumor growth. Read more in this issue on page 559. Original image from Fig. 3A. Artwork by Lewis Long.