MASTERS OF IMMUNOLOGY

1109 Innate Lymphoid Cells in Cancer
Blandine Vallentin, Vincent Barlogis,
Christelle Pipieroglou, Sophie Cypowyj, Nicolas Zucchini,
Matthieu Chené, Florent Navarro, Catherine Farmarier,
Eric Vivier, and Frédéric Vely

CANCER IMMUNOLOGY AT THE CROSSROADS: EXPERIMENTAL IMMUNOTHERAPIES

1115 T-cell–based Immunotherapy: Adoptive Cell Transfer and Checkpoint Inhibition
Roch Houot, Liora Michal Schultz, Aurélien Marabelle,
and Holbrook Kohrt

CANCER IMMUNOLOGY MINIATURES

1123 Epithelial PD-L2 Expression Marks Barrett’s Esophagus and Esophageal Adenocarcinoma
Sarah Derks, Katie S. Nason, Xiaoyun Liao,
Matthew D. Stachler, Kevin X. Liu, Jie Bin Liu,
Ewa Scinska, Michael S. Goldberg, Gordon J. Freeman,
Scott J. Rodig, Jon M. Davison, and Adam J. Bass

PRIORITY BRIEF

1130 Follicle-Stimulating Hormone Receptor as a Target in the Redirected T-cell Therapy for Cancer
Katarzyna Urbanska, Caitlin Stashwick, Mathilde Poussin,
and Daniel J. Powell Jr
Synopsis: Ovarian cancers, and possibly tumor-associated vasculature, express follicle-stimulating hormone receptors (FSHRs), a potential target for antitumor immunity. T cells expressing anti-FSHR receptors killed tumors expressing the FSHR in vitro and reduced tumor growth in mouse models.

RESEARCH ARTICLES

1138 Human Leukocyte Antigen (HLA) A*1101-Restricted Epstein-Barr Virus–Specific T-cell Receptor Gene Transfer to Target Nasopharyngeal Carcinoma
Yong Zheng, Greg Parsonage, Xiaodong Zhuang,
Lee R. Machado, Christine H. James, Asmaa Salman,
Peter F. Searle, Edwin P. Hui, Anthony T.C. Chan, and
Steven P. Lee
Synopsis: Nasopharyngeal carcinomas contain Epstein-Barr virus, with potentially immunogenic target epitopes. An HLA A*1101–restricted T-cell receptor (TCR) with specificity for LMP2 was cloned, could activate both CD4+ and CD8+ T cells, and inhibited tumor growth in a mouse model.

1148 Antibody-Dependent Cellular Cytotoxicity Activity of a Novel Anti–PD-L1 Antibody Avelumab (MSB0010718C) on Human Tumor Cells
Benjamin Boyerinas, Caroline Jochems, Massimo Fantini,
Christopher R. Heery, James L. Gulley, Kwong Yok Tsang,
and Jeffrey Schlim
Synopsis: Inhibition of PD-L1 interferes with an immunosuppressive signal, thereby prolonging antitumor responses. A novel monoclonal antibody to PD-L1 also mediated antibody-dependent cell-mediated cytotoxicity (ADCC) of tumor cells, an additional mode of action for checkpoint inhibitors.

1158 Differential Expression of PD-L1 between Primary and Metastatic Sites in Clear-Cell Renal Cell Carcinoma
Marcella Callea, Laurence Albige, Mamta Gupta,
Su-Chun Cheng, Elizabeth M. Genega, André P. Fay,
Jiaxi Song, Ingrid Carvo, Rupal S. Bhatt, Michael B. Atkins,
F. Stephen Hodi, Toni K. Choueiri, David F. McDermott,
Gordon J. Freeman, and Sabina Signoretti
Synopsis: Response to PD-L1 inhibition depends on its expression. Primary ccRCC tumors and their matching metastases were compared, and because PD-L1 was mostly in high nuclear-grade areas, these should be specifically selected for assessment to limit false negatives.
Interleukin-6/STAT3 Pathway Signaling Drives an Inflammatory Phenotype in Group A Ependymoma

Andrea M. Griesinger, Rebeca J. Josephson, Andrew M. Donson, Jean M. Mulcahy Levy, Vladimir Amani, Diane K. Birks, Lindsey M. Hoffman, Steffanie L. Furtek, Phillip Reigan, Michael H. Handler, Rajeev Vibhakar, and Nicholas K. Foreman

Synopsis: Subgroup A ependymomas are brain tumors with a poor prognosis. Tumors were found to be IL6/STAT3-dependent and infiltrated with polarized myeloid cells. Targeting this pathway to relieve immunosuppression could be an important approach for this tumor type.

A Paracrine Role for IL6 in Prostate Cancer Patients: Lack of Production by Primary or Metastatic Tumor Cells

Shu-Han Yu, Qizhi Zheng, David Esopi, Anne Macgregor-Das, Jun Luo, Emmanuel S. Antonarakis, Charles G. Drake, Robert Vessella, Colm Morrissey, Angelo M. De Marzo, and Karen S. Sfanos

Synopsis: The source of the IL6 production in prostate cancer was found to be tumor vasculature, not primary or metastatic tumor cells. This paracrine source may explain the low clinical activity of monoclonal antibodies targeting IL6 in prostate cancer.

Radiographic Profiling of Immune-Related Adverse Events in Advanced Melanoma Patients Treated with Ipilimumab


Synopsis: As more melanoma patients are treated with CTLA-4 antibodies, immune-related adverse effects (irAEs) need elucidation. Radiographic imaging identified irAEs in 31% of patients, with colitis being most common. Most irAEs developed within 3 months of therapy.
ABOUT THE COVER

Innate lymphoid cells (ILCs) are a newly discovered type of lymphocyte, the study of which is an emerging field in immunology having a major impact on our understanding of immune responses. This artistic rendition is based on a frozen-section image of an immature isolated lymphoid follicle in the small intestine. Intestinal microvilli can be seen as multiple blue rings of cells, forming a backdrop for the isolated lymphoid follicle. The red cells express RORγt and are mostly ILC3s, including lymphoid tissue inducer-like cells and other NCR-ILC3s. Bright green marks NKP46. Cells with red nuclei surrounded by bright green are NCR−ILC3s. The blue cells within the follicle are B cells. For more details on the various types of ILCs, their development, functions, and possible roles in the antitumor immune response, see the Masters of Immunology article by Vivier and colleagues on page 1109 of this issue. This illustration (by Lewis Long) is based on Figure 1C from a paper originally published by these authors: Reynders A, Essaad N, Vu Manh TP, Dalod M, Fenis A, Aubry C, Nikitas G, et al. Differential function of NKP46+RORγt and NKP46−RORγt gut lymphoid cells. EMBO J 2011;30:2934–47A, with permission of the authors.

ABOUT THE MASTER

Eric Vivier, DVM, PhD, is a professor of immunology at Aix-Marseille University who was born in Clamart, France. He graduated with the highest honors (silver medal) from the Ecole Nationale Vétérinaire de Maisons-Alfort and received his doctoral degree in immunology from Paris XI University. He began his postdoctoral training as a Fogarty International Center Research Fellow at Harvard Medical School with Paul J. Anderson and Stuart F. Schlossman (the Dana-Farber Cancer Institute). He joined Aix-Marseille University as a professor at the Centre d’Immunologie de Marseille-Luminy (CIML) in 1993 and became its director in 2008. In 1999, Dr. Vivier cofounded the biotech company Innate-Pharma. In 2014, he was one of the founders of the Marseille-Immunopole, an immunology cluster linking fundamental research, therapeutic innovation, and industrial development in the Aix-Marseille region.

Dr. Vivier has made seminal contributions to our understanding of the molecular basis of the ontogeny, function, and therapeutic manipulation of natural killer (NK) cells, and the identification of innate lymphoid cells (ILCs) in mice and humans. His research has had a profound influence on the field of innate immunity. His early work determined the mode of action of the inhibitory MHC class I receptors expressed on NK cells and extended the concept of ITIM-bearing molecules to multiple cell types and multiple biologic functions. In parallel, his group identified the ITAM-bearing polypeptide, KARAP/DAP12. The Vivier laboratory has since been a world leader in the generation of transgenic mouse models for the dissection of NK-cell function in vivo. Building on these basic research results, the Vivier laboratory has also been involved in the development of innovative treatments for cancer. This translation of basic research discoveries into clinical applications led to the development, in 2009, of a first-in-class therapeutic monoclonal antibody to KIR (lirilumab), the efficacy of which against various cancers is currently being assessed. These studies on NK cells led to the involvement of the Vivier laboratory in the discovery of ILCs through the detection and characterization of the ILC3 cell subset in human and mouse intestine.

Dr. Vivier has published more than 270 scientific articles and is on the editorial boards of leading peer-reviewed journals. He serves on the expert panel of the European Research Council and on the committees of pharmaceutical and biotechnology companies. In recognition of his scientific achievements, Dr. Vivier has received awards from the French National League against Cancer (1996, 2004, and 2013), the National Award and Tremplins Rhône-Poulenc Award for Biotech start-ups (1999), the Lucien Tartois Award from the Fondation pour la Recherche Médicale (1999), the Jacques Oudin Award from the French Society for Immunology (2003), the Deutsche Gesellschaft für Immunologie/EFIS Award (2004), the Grand Prix Turpin in Oncology (2008), and the Grand Prix Charles Oberling in Oncology (2010). In 2007, Dr. Vivier became a senior fellow of the Institut Universitaire de France, and, in 2013, he was elected to the French National Academy of Medicine.
Cancer Immunology Research

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