MILESTONES IN CANCER IMMUNOLOGY

1291 The 2015 William B. Coley Awards

RESEARCH ARTICLES

1316 Simultaneous Targeting of FcγRs and FcζRI Enhances Tumor Cell Killing
The efficacy of anticancer monoclonal antibodies (mAbs) is limited by the exhaustion of cellular effector mechanisms. The combination of IgG and IgA to two different tumor targets leads to enhanced cytotoxicity, providing a basis for therapeutic mAb improvements.

1325 Complement Factor H Antibodies from Lung Cancer Patients Induce Complement-Dependent Lysis of Tumor Cells, Suggesting a Novel Immunotherapeutic Strategy
Michael J. Campa, Elizabeth B. Gottlin, Ryan T. Bushey, and Edward F. Patz Jr
Select early-stage lung cancer patients never develop metastasis. Some of these patients have antibodies that inactivate a protein that protects tumor cells from complement lysis, thus making tumor cells more susceptible to being killed.

1333 Efficacy of a Cancer Vaccine against ALK-Rearranged Lung Tumors
Claudia Voena, Matteo Menotti, Cristina Mastini, Filomena Di Giacomo, Dario Livio Longa, Barbara Castella, Maria Elena Boggio Merlo, Chiara Ambrogio, Qi Wang, Valerio Giacomo Minero, Teresa Poggio, Cinzia Martinengo, Lucia D’Amico, Elena Panizza, Luca Mologni, Federica Cavallo, Fiorella Altruda, Mohit Butaney, Marzia Capelletti, Giorgio Inghirami, Pasi A. Jänne, and Roberto Chiarello
Lung cancers harboring ALK translocations are treated with protein kinase inhibitors, which can extend survival. A cancer vaccine against ALK induced strong immune responses and enhanced survival when used alone, or in combination with kinase inhibitors or checkpoint inhibitors.

1344 Progression of Lung Cancer Is Associated with Increased Dysfunction of T Cells Defined by Coexpression of Multiple Inhibitory Receptors
Daniela S. Thommen, Jens Schreiner, Philipp Müller, Petra Herzig, Andreas Roller, Anton Belousov, Pablo Urmana, Pavel Pisa, Christian Klein, Marina Bacac, Ozana S. Fischer, Wolfgang Moersig, Spasenija Savic Prince, Victor Levitsky, Vaics Karanikas, Didier Landinois, and Alfréd Zippelius
T cells within non–small cell lung cancer tumors acquire greater numbers, and more diversity, of inhibitory receptors as tumors progress, correlating with a loss in function as well as in their ability to be reactivated after anti-checkpoint treatment.
Prognostic Significance of CD169+ Lymph Node Sinus Macrophages in Patients with Malignant Melanoma
Yoichi Saito, Koji Ohnishi, Azusa Miyashita, Satoshi Nakahara, Yukio Fujiwara, Hasita Horlad, Takanobu Motoshima, Satoshi Fukushima, Masatoshi Jinnin, Hitonobu Ihn, Motohiro Takeya, and Yoshihiro Komohara

Prognostic indicators are needed for malignant melanoma. The presence of high densities of CD169+ macrophages in the draining lymph nodes of patients significantly correlates with CTL infiltration and longer overall survival, providing a potentially useful biomarker.

Effector CD8+ T-cell Engraftment and Antitumor Immunity in Lymphodepleted Hosts Is IL7Ra Dependent
C. Bryce Johnson, Brian P. Riesenberg, Bennett R. May, Stuart C. Gilreath, Guangfu Li, Kevin F. Staveley-O’Carroll, Elizabeth Garrett-Mayer, Shikhar Mehrotra, David J. Cole, and Mark P. Rubinstein

Adoptive cellular immunotherapy requires donor cells to survive and accumulate, which this study shows requires an IL12/IL7 axis in activated CD8+ T cells. IL12 leads to enhanced IL7Ra expression and IL7 responsiveness, which maximizes antitumor efficacy.

HDAC Inhibition Upregulates PD-1 Ligands in Melanoma and Augments Immunotherapy with PD-1 Blockade

Combining other agents with immune-based approaches can enhance treatment for melanoma. PDL-1 gene expression was increased after inhibition of histone deacetylases. Combining PD-1-blockade immunotherapy with histone deacetylase inhibition increased responses in a mouse model of melanoma.

Acknowledgment to Reviewers

ABOUT THE COVER

Some patients with early stage non–small cell lung cancer never develop metastatic disease. Autoantibodies isolated from these individuals bind to a cryptic epitope of a complement-blocking protein called complement factor H (CFH). In the presence of CFH, cells are protected from complement killing. Given that the CFH epitope to which the autoantibodies bind is not normally exposed, these autoantibodies may be interfering with CFH only within tumors, relieving the block to complement, and making it possible to kill cancer cells that would otherwise be protected. The cover art (left) was inspired by the micrograph (right) of autoantibodies to CFH binding to the lung cancer cell line A549, and detected with AlexaFluor 647–conjugated anti-human IgG. Fluorescence micrograph image taken by Rebekah Dumm (Duke University Medical Center); artwork by Lewis Long. Read more about these autoantibodies in Campa et al., page 1325 in this issue of Cancer Immunology Research.