HIGHLIGHTS FROM THE LITERATURE

249 What We’re Reading

CANCER IMMUNOLOGY AT THE CROSSROADS

250 Designing Late-Stage Randomized Clinical Trials with Cancer Immunotherapy: Can We Make It Simpler?
Tai-Tsang Chen

RESEARCH ARTICLES

255 YAP-Induced PD-L1 Expression Drives Immune Evasion in BRAFi-Resistant Melanoma
Min Hwan Kim, Chang Gon Kim, Sang-Kyum Kim, Sang Joon Shin, Eun Ah Cho, Su-Hyun Park, Eui-Cheol Shin, and Joon Kim
Transcription factor YAP increases PD-L1 expression in BRAF inhibitor-resistant melanoma cells, promoting their direct evasion of T-cell killing. Inhibition of this YAP-orchestrated interplay between inhibitor resistance and immune evasion could improve the treatment of BRAF-mutant melanoma patients.

267 CCL20 Expression by Tumor-Associated Macrophages Predicts Progression of Human Primary Cutaneous Melanoma
Rafael Samaniego, Alejandra Gutiérrez-González, Alba Gutiérrez-Seijo, Sandra Sánchez-Grigorio, Jorge García-Giménez, Enrique Mercader, Iván Márquez-Rodas, José Antonio Avilés, Miguel Relloso, and Paloma Sánchez-Manzanares
Melanoma tumor cells interact synergistically with pro-metastatic macrophages through a CCR6/CCL20 paracrine signaling loop. Stromal expression of CCL20 in primary melanomas may be a useful tool for assessing patient risk, making treatment decisions, and planning clinical trials.

276 Tumor Immunity and Survival as a Function of Alternative Neopeptides in Human Primary Cutaneous Melanoma
Andrew J. Rech, David Balli, Alejandro Mantero, Hernani Ishwaran, Katherine L. Nathanson, Ben Z. Stanger, and Robert H. Vonderheide
Analysis of neopeptides across multiple tumor types revealed that “alternatively defined neopeptides,” derived from tumor-associated mutations, exhibited higher peptide affinity for MHC compared with nonmutant counterparts. These neopeptides were strong predictors of immune phenotype and patient survival.

288 Treatment-Related Adverse Events Predict Improved Clinical Outcome in NSCLC Patients on KEYNOTE-001 at a Single Center
A retrospective analysis of non-small cell lung carcinoma patients treated with pembrolizumab found that treatment-related adverse events predicted improved clinical outcome. This observation could identify the patients most likely to benefit from anti-PD-1 therapy.

295 Prognostic Significance of PD-L1+ and CD8+ Immune Cells in HPV+ Oropharyngeal Squamous Cell Carcinoma
Benjamin Solomon, Richard J. Young, Mathias Bressel, Damien Urban, Shona Hendry, Alesha Thai, Christopher Angel, Afaf Haddad, Marcin Kownatz, Tsien Fua, June Corry, Stephen Fox, and Danny Rischi
Assessment of CD8+ cell infiltration and PD-L1 expression on intratumoral immune cells identified a subgroup of HPV+ OPSCC patients with excellent clinical outcomes. Immunophenotyping tumors provided prognostic information beyond that provided by existing TNM-based staging systems.

305 Integration of Oncogenes via Sleeping Beauty as a Mouse Model of HPV16+ Oral Tumors and Immunologic Control
Yi-Hsin Lin, Ming-Chieh Yang, Suu-Hsueh Tseng, Rosie Jiang, Andrew Yang, Emily Farmer, Shihwen Peng, Tali Henkle, Yung-Nien Chang, Chien-Fu Hung, and T.-C. Wu
A preclinical mouse model of spontaneous, HPV+ oral tumors was generated. Sleeping beauty transposase system-mediated oncogene transfection was assisted by electroporation. This model allowed for the evaluation of disease intervention efficacy and analysis of tumor cell migration.
Combination Gemcitabine and WT1 Peptide Vaccination Improves Progression-Free Survival in Advanced Pancreatic Ductal Adenocarcinoma: A Phase II Randomized Study


Pancreatic ductal adenocarcinoma patients were treated with gemcitabine and a WT1 peptide vaccine in a multi-institutional study. The combination proved synergistic, prolonging progression-free survival that was associated with WT1-specific immune responses. No unexpected toxicities were seen.

Mast Cell–Dependent CD8+ T-cell Recruitment Mediates Immune Surveillance of Intestinal Tumors in ApcMin/+ Mice

Sobha R. Bodduluri, Steven Mathis, Paramahamsa Maturu, Elangovan Krishnan, Shuchismita R. Satpathy, Paula M. Chilton, Thomas C. Mitchell, Sergio Lira, Massimo Locati, Alberto Mantovani, Venkatakrishna R. Jala, and Bodduluri Haribabu

Mast cells, depending on the microenvironment, can promote or suppress tumor progression. Chemokine-mediated recruitment of mast cells was an essential prerequisite for the initiation of LTB4/BLT1-regulated CD8+ T-cell homing and generation of antitumor immunity against intestinal tumors.

NK Cells Control Tumor-Promoting Function of Neutrophils in Mice

Keisuke Ogura, Marimo Sato-Matsushita, Seiji Yamamoto, Takashi Hori, Masakiyo Sasahara, Yoichiro Iwakura, Ikao Saiki, Hideaki Tahara, and Yoshihiro Hayakawa

NK cells control the tumor-promoting function of neutrophils via an IFNγ-mediated mechanism. In mice lacking NK cells, neutrophils promoted tumor growth and angiogenesis. In mice lacking both NK cells and the IL17A-neutrophil axis, tumor progression was reduced.

The Antigen ASB4 on Cancer Stem Cells Serves as a Target for CTL Immunotherapy of Colorectal Cancer

Sho Miyamoto, Vitaly Kochin, Takayuki Kanaseki, Ayumi Hongo, Serina Tokita, Yasuhiro Kikuchi, Akari Takaya, Yoshihiko Hirohashi, Tomohide Tsukahara, Takeshi Terui, Kunihiko Ishitani, Fumitake Hata, Ichiro Takemasa, Akihiro Miyazaki, Hiroyoshi Hiratsuka, Noriyuki Sato, and Toshihiko Torigoe

The ASB4 antigen elicited CTL responses specific to cancer stem cells (CSCs). Adoptive CTL therapy showed that CSCs are the minimal and necessary target to control colorectal cancer and provide a rationale for targeting CSCs as a recurrence-prevention strategy.

Correction: CAR-T Cells Inflict Sequential Killing of Multiple Tumor Target Cells

Keisuke Ogura, Marimo Sato-Matsushita, Seiji Yamamoto, Takashi Hori, Masakiyo Sasahara, Yoichiro Iwakura, Ikao Saiki, Hideaki Tahara, and Yoshihiro Hayakawa

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