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Colonoscopy for Immune-Related Colitis in
Ipilimumab-Treated Advanced Melanoma Patients
Marlene Garcia-Neuer, Melina E. Marmarelis,
Sushrut R. Jangi, Jason J. Luke, Nageatte Ibrahim,
Meredith Davis, Janice Weinberg, Hilary Donahue,
Nancy Bailey, F. Stephen Hodi, Elizabeth L. Buchbinder,
and Patrick A. Ott
Checkpoint blockade is becoming more widespread, so the timely and accurate diagnosis of immune-related colitis is increasingly important. By comparing diagnoses with colonoscopy data, CT scans were a fast, accurate, and non invasive mode of diagnosing ipilimumab-induced immune-related colitis.

292 Clinical Impact of Tumor DNA Repair Expression and T-cell Infiltration in Breast Cancers

Andrew R. Green, Mohammed A. Aleskandarany, Reem Ali, Eleanor Grace Hodgson, Suha Atabani, Karen De Souza, Emad A. Rakha, Ian O. Ellis, and Srinivasan Madhusudan
This study provides clinical evidence that the interplay between DNA repair, CD8⁺ T cells, and expression of PD-L1 and PD-1 can promote aggressive tumor phenotypes. XRCC1-directed personalization of immune checkpoint inhibitor therapy may be feasible in breast cancer.

RESEARCH ARTICLES

300 Induction of NKG2D Ligands on Solid Tumors Requires Tumor-Specific CD8⁺ T Cells and Histone Acetyltransferases

Jiemiao Hu, Chantale Bernatchez, Liangfang Zhang, Xueqing Xia, Eugenie S. Kleinerman, Mien-Chie Hung, Patrick Hwu, and Shulin Li
NKG2D-mediated immune surveillance is crucial for inhibiting tumor growth and metastases, but tumors often downregulate NKG2D ligands. A therapeutic strategy to restore tumor-specific expression of NKG2D ligands on solid tumors was developed that induced tumor regression and increased survival.

312 Comprehensive Meta-analysis of Key Immune-Related Adverse Events from CTLA-4 and PD-1/PD-L1 Inhibitors in Cancer Patients

Guillermo De Velasco, Youjin Je, Dominick Bossé, Mark M. Awad, Patrick A. Ott, Raphael B. Moreira, Fabio Schutz, Joaquim Bellmunt, Guru P. Sonpavde, F. Stephen Hodi, and Toni K. Choueiri
A meta-analysis of immune checkpoint therapies showed a small but significant increase in the risk of developing key immune-related adverse events of any grade, as well as selected high-grade gastrointestinal and liver toxicities.

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319 Serine Proteases Enhance Immunogenic Antigen Presentation on Lung Cancer Cells

Haley L. Peters, Satyendra C. Tripathi, Celine Kerros, Hiroyuki Katayama, Haven R. Garber, Lisa S. St. John, Lorenzo Federico, Ismail M. Meraz, Jack A. Roth, Boris Sepesi, Mourad Majidi, Kathryn Ruisaard, Karen Clise-Dwyer, Jason Roszik, Don L. Gibbons, John V. Heymach, Stephen G. Swisher, Chantale Bernatchez, Cheath Alatrash, Samir Hanash, and Jeffrey J. Mollndrem

Lung cancer cells exposed to granulocyte serine proteases increased the presentation of both endogenous peptides and the exogenous, protease-derived, HLA-A2-restricted PR1 peptide. Circulating CTLs specific for these peptides were identified in lung cancer patients.

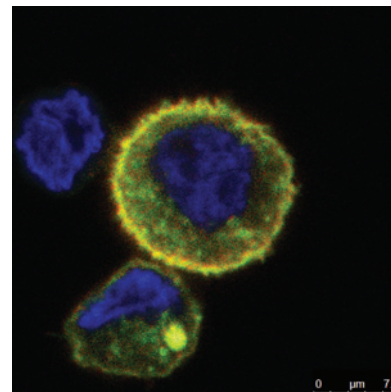
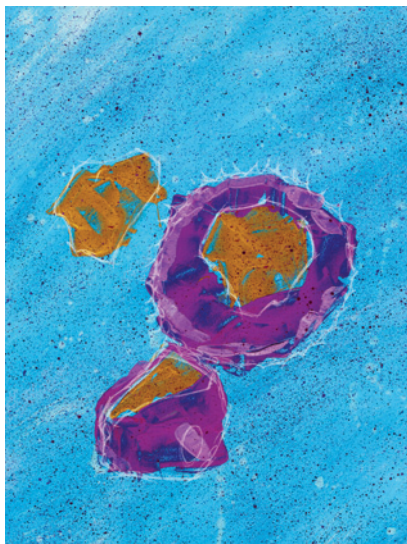
330 Promoter Methylation Modulates Indoleamine 2,3-Dioxygenase 1 Induction by Activated T Cells in Human Breast Cancers

Satish K. Noonepalle, Franklin Gu, Eun-Joon Lee, Jeong-Hyeon Choi, Qimei Han, Jaejik Kim, Maria Ouzounova, Austin Y. Shull, Lirong Pei, Pei-Yin Hsu, Ravindra Kolhe, Fang Shi, Jiseok Choi, Katie Chiou, Tim H.M. Huang, Hasan Korkaya, Libin Deng, Hong-Bo Xin, Shuang Huang, Muthusamy Thangaraju, Arun Sreekumar, Stefan Ambs, Shou-Ching Tang, David H. Munn, and Huidong Shi

Triple-negative breast cancers (TNBCs) are often infiltrated by T cells. These tumors counteracted T-cell activity through hypomethylated IDO1 promoters and increased IDO1 expression in response to IFN γ , providing a rationale for treatment of TNBC with IDO inhibitors.

ABOUT THE COVER

Lung cancer tumors recruit macrophages and granulocytes, which then secrete serine proteases like elastase and proteinase 3. These enzymes are then internalized by the tumor cells, which causes a cascade of events. The proteases both contain a peptide sequence, PR1, that was presented on the lung cancer cell surface HLA-A2 and recognized by antitumor cytotoxic T cells (CTLs). These proteases also induced production of a unique set of endogenous peptides by the tumor cells. CTLs specific for these novel antigens were enriched in lung cancer patients. Read more in the research article by Peters and colleagues on page 319, in this issue of *Cancer Immunology Research*. The confocal micrograph portrays a corona of PR1 peptide-HLA-A2 (yellow) on the surface of lung H2023 cancer cells and nuclei stained blue with DAPI. Micrograph from the laboratory of Dr. J.J. Mollndrem. Artwork by Lewis Long.



Cancer Immunology Research

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