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### Priority Briefs

- **136** Combined BRAF, MEK, and CDK4/6 Inhibition Depletes Intratumoral Immune-Potentiating Myeloid Populations in Melanoma
  
  
  
  
  
  - Emily J. Lelliott, Stefano Mangiola, Kelly M. Ramsbottom, Magnus Zethoven, Lydia Lim, Peter K.H. Lau, Amanda J. Oliver, Luciano G. Martelotto, Laura Kirby, Claire Martin, Riyaben P. Patel, Alison Slater, Carleen Cullinan, Anthony T. Papenfuss, Nicole M. Haynes, Grant A. McArthur, Jane Oliaro, and Karen E. Sheppard
  
  
  
  
  
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- **147** Kindlin3-Dependent CD11b/CD18-Integrin Activation Is Required for Potentiation of Neutrophil Cytotoxicity by CD47–SIRPα Checkpoint Disruption
  
  
  
  
  
  - Panagioti Bouti, Xi Wen Zhao, Paul J.J.H. Verkuijlen, Anton T.J. Tool, Michel van Houdt, Nezihe Köker, Mustafa Yavuz Köker, Özlem Keskin, Sinan Akbayram, Robin van Bruggen, Taco W. Kuijpers, Hanke L. Matlung, and Timo K. van den Berg
  
  
  
  
  
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### Research Articles

- **156** KIR3DL3 Is an Inhibitory Receptor for HHLA2 that Mediates an Alternative Immunoinhibitory Pathway to PD1
  
  
  
  
  
  
  
  
  
  
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- **170** Nutlin-3a Enhances Natural Killer Cell–Mediated Killing of Neuroblastoma by Restoring p53-Dependent Expression of Ligands for NKG2D and DNAM-1 Receptors
  
  
  
  
  
  - Irene Veneziani, Paola Infante, Elisa Ferretti, Ombretta Melaui, Cecilia Battistelli, Valeriu Lucarini, Mirco Compagnone, Carmine Nicoletti, Aurora Castellano, Stefania Petrini, Marzia Ognibene, Annalisa Pezzolo, Lucia Di Marcotullio, Roberto Bei, Lorenzo Moretta, Vito Pistoia, Dorianna Fruci, Vincenzo Barnaba, Franco Locatelli, and Loredana Cifaldi
  
  
  
  
  
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- **184** Pharmacologic Screening Identifies Metabolic Vulnerabilities of CD8⁺ T Cells
  
  
  
  
  
  - Jefte M. Drijvers, Jacob E. Gillis, Tara Muylwijk, Thao H. Nguyen, Emily F. Gaudiano, Isaac S. Harris, Martin W. LaFleur, Alison E. Ringel, Cong-Hui Yao, Kiran Kurmi, Vikram R. Juneja, Justin D. Trombley, Marcia C. Haigis, and Arlene H. Sharpe
  
  
  
  
  
  It is challenging to develop metabolism-targeted therapeutics because T cells and cancer cells have similar metabolic properties. The authors develop an in vitro pharmacologic screening platform and highlight ferroptosis as a metabolic vulnerability of CD8⁺ T cells.
Targeted Deletion of CXCR2 in Myeloid Cells Alters the Tumor Immune Environment to Improve Antitumor Immunity

Jinming Yang, Chi Yan, Anna E. Vilgelm, Sheau-Chiann Chen, Gregory D. Ayers, Christopher A. Johnson, and Ann Richmond

Myeloid cell CXCR2 affects not only suppressive MDSCs but also B cells, especially the B1b subset. CXCL11-producing B cells are key and impact infiltration and activation of effector CD8+ T cells in the tumor microenvironment.

Oxidized Lipoproteins Promote Resistance to Cancer Immunotherapy Independent of Patient Obesity


The influence of obesity on cancer immunotherapy is not clear. This study shows oxidized LDL promotes resistance to immunotherapy by suppressing T-cell function and driving tumor cytoprotection mediated by heme oxygenase-1 (HO-1), suggesting HO-1 is a promising therapeutic target.

Fructose Promotes Cytoprotection in Melanoma Tumors and Resistance to Immunotherapy


Dietary fructose can be utilized by tumor cells and promotes cytoprotection by inducing HO-1 expression, thereby impacting TIL responses and immunotherapy outcomes. The data highlight a novel immune evasion mechanism and a potential therapeutic target.

Therapy of Established Tumors with Rationally Designed Multiple Agents Targeting Diverse Immune–Tumor Interactions: Engage, Expand, Enable

Kellsye P. Fabian, Anthony S. Malamas, Michelle R. Padget, Kristen Solocinski, Benjamin Wolfson, Rika Fuji, Houssein Abdul Sater, Jeffrey Schlom, and James W. Hodge

Treatment of established tumors with a combination “pentatherapy” regimen leads to T-cell activation while decreasing Treg suppression. The data highlight how the combination of multimodal immunotherapy agents can engage, enhance, and enable adaptive antitumor responses.