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VIEWES In The Spotlight

The GENIE Is Out of the Bottle: Landmark Cancer Genomics Dataset Released 796
K. Litchfield, S. Turajlic, and C. Swanton
See article, p. 818

Refining Targeted Therapy Opportunities for BRAF-Mutant Melanoma 799
R.W. Jenkins and D.A. Barbie
See article, p. 832

Bap1 and Pbrm1: Determinants of Tumor Grade and mTOR Activation in VHL-Deficient Mouse Models of Renal Cell Carcinoma 802
J.Y. Leung and W.Y. Kim
See article, p. 900

REVIEW Tumor Evolution as a Therapeutic Target 805

 N. Amirouchene-Angelozzi, C. Swanton, and A. Bardelli

RESEARCH ARTICLES AACR Project GENIE: Powering Precision Medicine through an International Consortium 818



The AACR Project GENIE Consortium
Précis: AACR Project GENIE is an international consortium that seeks to share integrated clinical and genomic data from patients with cancer to promote cancer precision medicine research.

See commentary, p. 796

Biomarker Accessible and Chemically Addressable Mechanistic Subtypes of BRAF Melanoma 832

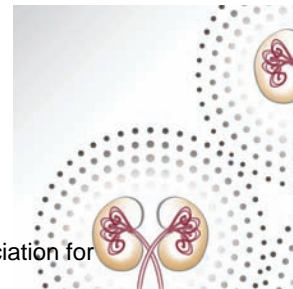
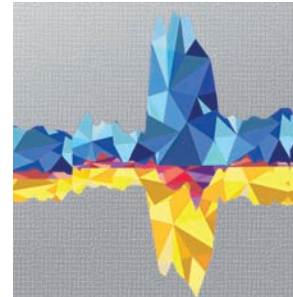
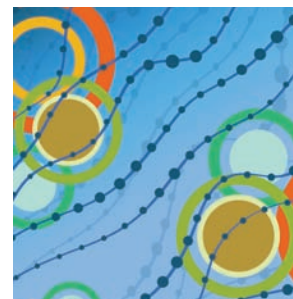
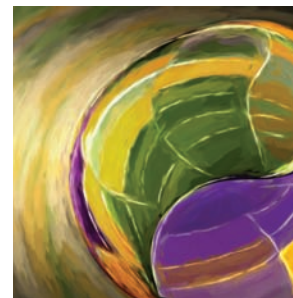
B. Eskiocak, E.A. McMillan, S. Mendiratta, R.K. Kollipara, H. Zhang, C.G. Humphries, C. Wang, J. Garcia-Rodriguez, M. Ding, A. Zaman, T.I. Rosales, U. Eskiocak, M.P. Smith, J. Sudderth, K. Komurov, R.J. Deberardinis, C. Wellbrock, M.A. Davies, J.A. Wargo, Y. Yu, J.K. De Brabander, N.S. Williams, L. Chin, H. Rizos, G.V. Long, R. Kittler, and M.A. White
Précis: Addiction to SOX10 stratifies melanoma into two mechanistic subtypes that are distinguished by sensitivity to either BRAF/MEK inhibitors or TBK1/IKKe inhibitors.

See commentary, p. 799

Synergistic Immunostimulatory Effects and Therapeutic Benefit of Combined Histone Deacetylase and Bromodomain Inhibition in Non-Small Cell Lung Cancer 852

D.O. Adeegbe, Y. Liu, P.H. Lizotte, Y. Kamihara, A.R. Aref, C. Almonte, R. Dries, Y. Li, S. Liu, X. Wang, T. Warner-Hatten, J. Castrillon, G.-C. Yuan, N. Poudel-Neupane, H. Zhang, J.L. Guerriero, S. Han, M.M. Awad, D.A. Barbie, J. Ritz, S.S. Jones, P.S. Hammerman, J. Bradner, S.N. Quayle, and K.-K. Wong

Précis: Combined HDAC6 and BET inhibition promotes T-cell activation and function and suppresses Treg activity to enhance the antitumor immune response and reduce tumor growth in a mouse model of NSCLC.



Epigenetic Identity in AML Depends on Disruption of Nonpromoter Regulatory Elements and Is Affected by Antagonistic Effects of Mutations in Epigenetic Modifiers 868

J.L. Glass, D. Hassane, B.J. Wouters, H. Kunimoto, R. Avellino, F.E. Garrett-Bakelman, O.A. Guryanova, R. Bowman, S. Redlich, A.M. Intlekofer, C. Meydan, T. Qin, M. Fall, A. Alonso, M.L. Guzman, P.J.M. Valk, C.B. Thompson, R. Levine, O. Elemento, R. Delwel, A. Melnick, and M.E. Figueroa

Précis: Comprehensive methylome sequencing of primary AML samples reveals robust changes in cytosine methylation at nonpromoter regulatory elements, such as enhancers, that drive the epigenetic identity in AML.

PAX3-FOXO1 Establishes Myogenic Super Enhancers and Confers BET Bromodomain Vulnerability..... 884



B.E. Gryder, M.E. Yohe, H.-C. Chou, X. Zhang, J. Marques, M. Wachtel, B. Schaefer, N. Sen, Y. Song, A. Gualtieri, S. Pomella, R. Rota, A. Cleveland, X. Wen, S. Sindiri, J.S. Wei, F.G. Barr, S. Das, T. Andresson, R. Guha, M. Lal-Nag, M. Ferrer, J.F. Shern, K. Zhao, C.J. Thomas, and J. Khan

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Précis: PAX3-FOXO1 creates myogenic superenhancers and recruits BRD4, which is essential for its stability and function, suggesting the possibility for using BET inhibitors to treat fusion-positive rhabdomyosarcoma.

Modeling Renal Cell Carcinoma in Mice: Bap1 and Pbrm1 Inactivation Drive Tumor Grade 900

Y.-F. Gu, S. Cohn, A. Christie, T. McKenzie, N. Wolff, Q.N. Do, A.J. Madhuranthakam, I. Pedrosa, T. Wang, A. Dey, M. Busslinger, X.-J. Xie, R.E. Hammer, R.M. McKay, P. Kapur, and J. Brugarolas

Précis: Generation of *Bap1*- and *Pbrm1*-deficient mouse models of clear cell renal cell carcinoma demonstrate that *Bap1* and *Pbrm1* loss determine tumor grade, and suggest that ccRCC arises from Bowman capsule cells.

See commentary, p. 802

Correction

Nods for Atezolizumab and Nivolumab from FDA 918

ON THE COVER

The American Association for Cancer Research (AACR) launched the Genomics, Evidence, Neoplasia, Information, Exchange (GENIE) project in partnership with eight academic institutions to promote sharing of integrated clinical and genomic data from patients with cancer. Data from participating centers include matched clinical and genomic data from a variety of tumor types that are harmonized and made accessible in the cBioPortal for Cancer Genomics. Initial Project GENIE results suggest that more than 30% of tumors harbor potentially clinically actionable mutations. This platform allows for integration of clinical data from electronic health records and increased statistical power to facilitate cancer precision medicine research. The establishment of infrastructure to integrate genomic and clinical data may aid selection of therapeutic targets and biomarkers of treatment and response in patients with cancer to improve patient outcomes. For details, please see the article by The AACR Project GENIE Consortium on page 818.



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7 (8)

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