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REVIEW Tumor Evolution as a Therapeutic Target805

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RESEARCH ARTICLES AACR Project GENIE: Powering Precision Medicine through an International Consortium818



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.

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Biomarker Accessible and Chemically Addressable Mechanistic Subtypes of BRAF Melanoma832

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

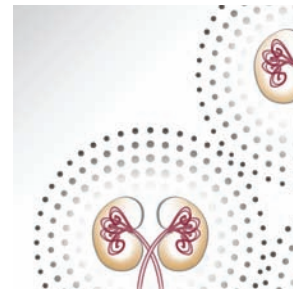
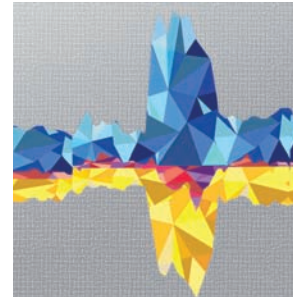
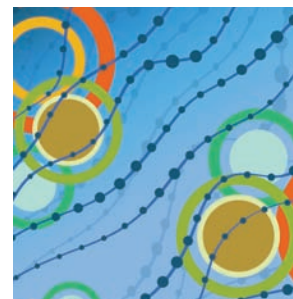
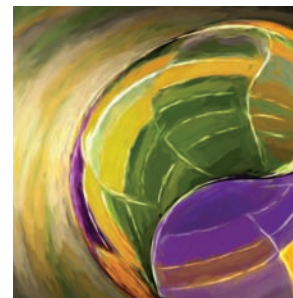
Précis: Addiction to SOX10 stratifies melanoma into two mechanistic subtypes that are distinguished by sensitivity to either BRAF/MEK inhibitors or TBK1/IKKe inhibitors.

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Synergistic Immunostimulatory Effects and Therapeutic Benefit of Combined Histone Deacetylase and Bromodomain Inhibition in Non-Small Cell Lung Cancer852

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.

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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.

