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- 3074** **p300-Mediated Acetylation of Histone Demethylase JMJD1A Prevents Its Degradation by Ubiquitin Ligase STUB1 and Enhances Its Activity in Prostate Cancer**
Songhui Xu, Lingling Fan, Hee-Young Jeon, Fengbo Zhang, Xiaolu Cui, McKayla B. Mickle, Guihong Peng, Arif Hussain, Ladan Fazli, Martin E. Gleave, Xuesen Dong, and Jianfei Qi
Identification of mechanisms regulating JMJD1A protein stability reveals new strategies to destabilize JMJD1A and concomitantly inhibit AR activities as potential prostate cancer therapy.

TUMOR BIOLOGY AND IMMUNOLOGY

- 3088** **IL26, a Noncanonical Mediator of DNA Inflammatory Stimulation, Promotes TNBC Engraftment and Progression in Association with Neutrophils**
Timothy N. Trotter, Casey W. Shuptrine, Li-Chung Tsao, Robert D. Marek, Chaitanya Acharya, Jun-Ping Wei, Xiao-Yi Yang, Gangjun Lei, Tao Wang, Herbert Kim Lyerly, and Zachary C. Hartman
These findings identify IL26 as a unique, clinically relevant, inflammatory amplifier that enhances TNBC engraftment and dissemination in association with neutrophils, which has potential as a therapeutic target.
- 3101** **Long-Term Gemcitabine Treatment Reshapes the Pancreatic Tumor Microenvironment and Sensitizes Murine Carcinoma to Combination Immunotherapy**
A C Daniel R. Principe, Matthew Narbutis, Sandeep Kumar, Alex Park, Navin Viswakarma, Matthew J. Dorman, Suneel D. Kamath, Paul J. Grippo, Melissa L. Fishel, Rosa F. Hwang, Dinesh Thummuri, Patrick W. Underwood, Hidayatullah G. Munshi, Jose G. Trevino, and Ajay Rana
These data suggest that long-term treatment with gemcitabine leads to extensive reprogramming of the pancreatic tumor microenvironment and that patients who progress on gemcitabine-based regimens may benefit from multidrug immunotherapy.
See related commentary, p. 3070
- 3116** **Oncogenic Herpesvirus Engages Endothelial Transcription Factors SOX18 and PROX1 to Increase Viral Genome Copies and Virus Production**
A C Silvia Gramolelli, Endrit Elbasani, Krista Tuohinto, Veijo Nurminen, Thomas Günther, Riikka E. Kallinen, Seppo P. Kaijalainen, Raquel Diaz, Adam Grundhoff, Caj Haglund, Joseph M. Ziegelbauer, Teijo Pellinen, Mark Bower, Mathias Francois, and Päivi M. Ojala
SOX18 and PROX1, central regulators of lymphatic development, are key factors for KSHV genome maintenance and lytic cycle in lymphatic endothelial cells, supporting Kaposi sarcoma tumorigenesis and representing attractive therapeutic targets.

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3130 The Lymphatic Cell Environment Promotes Kaposi Sarcoma Development by Prox1-Enhanced Productive Lytic Replication of Kaposi Sarcoma Herpes Virus

Dongwon Choi, Eunkyung Park, Kyu Eui Kim, Eunson Jung, Young Jin Seong, Luping Zhao, Shrimika Madhavan, George Daghlian, Hansuh H. Lee, Patill T. Daghlian, Saren Daghlian, Khoa Bui, Chester J. Koh, Alex K. Wong, Il-Taeg Cho, and Young-Kwon Hong

This study defines the mechanism by which Kaposi's sarcoma could be maintained by virus constantly produced by lymphatic cells in HIV-positive individuals.

3145 Autocrine IL6-Mediated Activation of the STAT3-DNMT Axis Silences the TNF α -RIP1 Necroptosis Pathway to Sustain Survival and Accumulation of Myeloid-Derived Suppressor Cells

Alyssa D. Smith, Chunwan Lu, Daniela Payne, Amy V. Paschall, John D. Klement, Priscilla S. Redd, Mohammed L. Ibrahim, Dafeng Yang, Qimei Han, Zhuoqi Liu, Huidong Shi, Thomas J. Hartney, Asha Nayak-Kapoor, and Kebin Liu

These findings demonstrate that targeting IL6 expression or function represents potentially effective approaches to suppress MDSC survival and accumulation in the tumor microenvironment.

CONVERGENCE AND TECHNOLOGIES

3157 State-Transition Analysis of Time-Sequential Gene Expression Identifies Critical Points That Predict Development of Acute Myeloid Leukemia

AC

Russell C. Rockne, Sergio Branciamore, Jing Qi, David E. Frankhouser, Denis O'Meally, Wei-Kai Hua, Guerry Cook, Emily Carnahan, Lianjun Zhang, Ayelet Marom, Herman Wu, Davide Maestrini, Xiwei Wu, Yate-Ching Yuan, Zheng Liu, Leo D. Wang, Stephen Forman, Nadia Carlesso, Ya-Huei Kuo, and Guido Marcucci

These findings apply the theory of state transitions to model the initiation and development of acute myeloid leukemia, identifying transcriptomic perturbations that accurately predict time to disease development.

See related commentary, 3072

RESOURCE REPORT

3170 Comprehensive Analysis of Radiomic Datasets by RadAR

Matteo Benelli, Andrea Barucci, Nicola Zoppetti, Silvia Calusi, Laura Redapi, Giuseppe Della Gala, Stefano Piffer, Luca Bernardi, Franco Fusi, and Stefania Pallotta

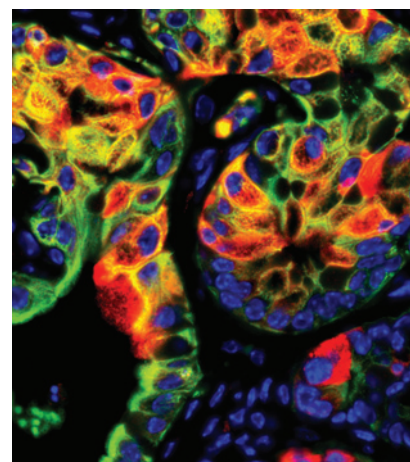
A new computational tool performs comprehensive analysis of high-dimensional radiomic datasets, recapitulating expected results in the analysis of radiomic profiles of >850 patients with cancer from independent datasets.

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ABOUT THE COVER

In this issue, Principe and colleagues explored gemcitabine-induced alterations to the pancreatic tumor microenvironment (TME) in order to identify potential treatment strategies for patients who progress on cytotoxic chemotherapy. They found that gemcitabine leads to extensive reprogramming of the pancreatic TME, sensitizing mice to a multidrug immunotherapy regimen. In the cover image, they examined the pancreas of a tumor-bearing mouse treated with gemcitabine in the setting of TGF β and PD-1 signal inhibition. Tissues were stained for the duct marker CK19 (green) and the cytotoxic immune surrogate granzyme B (red). This affirmed the restoration of a functional antitumor immune response and suggests that this approach may warrant consideration in the treatment of gemcitabine-refractory pancreatic ductal adenocarcinoma. For details, see article by Principe and colleagues on page 3101.



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