BREAKING ADVANCES

3129 Highlights from Recent Cancer Literature

REVIEWS


3135 FOXM1 in Cancer: Interactions and Vulnerabilities Andrei L. Gartel

PERSPECTIVE

3140 Human Subjects Protection and Cancer Surveillance Research: Revised Regulations, Expanded Opportunities Robert H. McLaughlin, Scarlett Lin Gomez, Dennis Deapen, and Marta Induni

PRIORITY REPORTS

3144 Interaction between Tumor Cell Surface Receptor RAGE and Proteinase 3 Mediates Prostate Cancer Metastasis to Bone Mikhail G. Kolonin, Anna Sergeeva, Daniela I. Staquicini, Tracey L. Smith, Christy A. Tarleton, Jeffrey J. Molldrem, Richard L. Sidman, Serena Marchiò, Renata Pasqualini, and Wadih Arap

3151 Merkel Cell Polyomavirus Small T Antigen Initiates Merkel Cell Carcinoma-like Tumor Development in Mice Monique E. Verhaegen, Doris Mangelberger, Paul W. Harms, Markus Eberl, Dawn M. Wilbert, Julia Meireles, Christopher K. Bichakjian, Thomas L. Saunders, Sunny Y. Wong, and Andrzej A. Dlugosz

3158 Increased T-cell Infiltration Elicited by Erk5 Deletion in a Pten-Deficient Mouse Model of Prostate Carcinogenesis Carolyn J. Loveridge, Ernest J. Mui, Rachana Patel, Ee Hong Tan, Imran Ahmad, Michelle Welsh, Julie Galbraith, Ann Hedley, Colin Nixon, Karen Blyth, Owen Sansom, and Hing Y. Leung

3169 Plk1 Phosphorylation of Mre11 Antagonizes the DNA Damage Response Zhiguo Li, Jie Li, Yifan Kong, Shan Yan, Nihal Ahmad, and Xiaoqi Liu


3194 tRF/miR-1280 Suppresses Stem Cell–like Cells and Metastasis in Colorectal Cancer Bingqing Huang, Huijing Yang, Xiuxi Cheng, Dan Wang, Shuyi Fu, Wencui Shen, Qi Zhang, Lijuan Zhang, Zhenyi Xue, Yan Li, Yurong Da, Qing Yang, Zesong Li, Li Liu, Liang Qiao, Ying Kong, Zhi Yao, Peng Zhao, Min Li, and Rongxin Zhang

MOLECULAR AND CELLULAR PATHOBIOLOGY

3158 Increased T-cell Infiltration Elicited by Erk5 Deletion in a Pten-Deficient Mouse Model of Prostate Carcinogenesis

3169 Plk1 Phosphorylation of Mre11 Antagonizes the DNA Damage Response

3181 TWIST1-WDR5-Hottip Regulates Hoxa9 Chromatin to Facilitate Prostate Cancer Metastasis

3194 tRF/miR-1280 Suppresses Stem Cell–like Cells and Metastasis in Colorectal Cancer

Precis: This provocative study shows that functional miRNA can be derived from tRNA fragments, acting here to mediate a tumor suppressor signaling cascade in human colorectal cancer.
Assessing Prostate Cancer Aggressiveness with Hyperpolarized Dual-Agent 3D Dynamic Imaging of Metabolism and Perfusion
Hsin-Yu Chen, Peder E.Z. Larson, Robert A. Bok, Cornelius von Morze, Renika Sritam, Romelyn Delos Santos, Justin Delos Santos, Jeremy W. Gordon, Naeim Bahrami, Marcus Ferrone, John Kurhanewicz, and Daniel B. Vigneron

Pyruvate Kinase Inhibits Proliferation during Postnatal Cerebellar Neurogenesis and Suppresses Medulloblastoma Formation
Katherine Tech, Andrey P. Tikunov, Hamza Farooq, A. Sorana Morrissy, Jessica Meidinger, Taylor Fish, Sarah C. Green, Hedi Liu, Yisu Li, Andrew J. Mungall, Richard A. Moore, Yussanne Ma, Steven J.M. Jones, Marcus A. Marra, Matthew G. Vander Heiden, Michael D. Taylor, Jeffrey M. Macdonald, and Timothy R. Gershon

Activation of NOTCH Signaling by Tenascin-C Promotes Growth of Human Brain Tumor-Initiating Cells
Susobhan Sarkar, Reza Mirzazai, Franz J. Zemp, Wu Wei, Donna L. Senger, Stephen M. Robbins, and V. Wee Yong

Micellar Delivery of miR-34a Modulator Rubone and Paclitaxel in Resistant Prostate Cancer
Di Wen, Yang Peng, Feng Lin, Rakesh K. Singh, and Ram I. Mahato

Table of Contents

3207 Assessing Prostate Cancer Aggressiveness with Hyperpolarized Dual-Agent 3D Dynamic Imaging of Metabolism and Perfusion
Hsin-Yu Chen, Peder E.Z. Larson, Robert A. Bok, Cornelius von Morze, Renika Sritam, Romelyn Delos Santos, Justin Delos Santos, Jeremy W. Gordon, Naeim Bahrami, Marcus Ferrone, John Kurhanewicz, and Daniel B. Vigneron

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3244 Micellar Delivery of miR-34a Modulator Rubone and Paclitaxel in Resistant Prostate Cancer
Di Wen, Yang Peng, Feng Lin, Rakesh K. Singh, and Ram I. Mahato

3255 p62/SQSTM1 Cooperates with Hyperactive mTORC1 to Regulate Glutathione Production, Maintain Mitochondrial Integrity, and Promote Tumorigenesis

3268 IL4 Primed the Dynamics of Breast Cancer Progression via DUSP4 Inhibition
Miriam Gaggianesi, Alice Turdo, Aurora Chinnici, Elisa Lipari, Tiziana Apuzzo, Antonina Benfante, Isabella Sperduti, Simone Di Franco, Serena Meraviglia, Elena Lo Presti, Francesco Dieli, Valentina Caputo, Gabriella Miliello, Salvatore Vienni, Giorgio Stassi, and Matilde Todaro

3280 Extracellular Matrix/Integrin Signaling Promotes Resistance to Combined Inhibition of HER2 and PI3K in HER2+ Breast Cancer
Ariella B. Hanker, Mónica Valeria Estrada, Giampaolo Bianchini, Preston D. Moore, Junfei Zhao, Feixiong Cheng, James P. Koch, Luca Gianni, Darren R. Tyson, Violeta Sánchez, Brent N. Reser, Melinda E. Sanders, Zhongming Zhao, Thomas P. Stricker, and Carlos L. Arteaga

3293 Multifunctional Telodendrimer Nanocarriers Restore Synergy of Bortezomib and Doxorubicin in Ovarian Cancer Treatment
Lili Wang, Changying Shi, Forrest A. Wright, Dandan Guo, Xu Wang, Dongliang Wang, Richard J.H. Wojcikiewicz, and Juntao Luo

TUMOR AND STEM CELL BIOLOGY

THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

Extracellular Matrix/Integrin Signaling Promotes Resistance to Combined Inhibition of HER2 and PI3K in HER2+ Breast Cancer
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Précis: Drug synergy in solid tumor treatments can be optimized by novel nanocarriers that can coordinate drug pharmacokinetics and biodistribution of codelivered drugs.
3306 Oncogenic Role of SND1 in Development and Progression of Hepatocellular Carcinoma
Nidhi Jariwala, Devaraja Rajasekaran, Rachel G. Mendoza, Xue-Ning Shen, Ayeesha Siddiq, Maaged A. Akiel, Chuda L. Robertson, Mark A. Subler, Jolene J. Windle, Paul B. Fisher, Arun J. Sanyal, and Devanand Sarkar

Précis: A small-molecule inhibitor of the liver cancer oncogene SND1 shows preclinical efficacy by abrogating tumor-initiating cell formation, suggesting its development as a novel therapy.

MICROENVIRONMENT AND IMMUNOLOGY
3317 Immune Gene Expression Is Associated with Genomic Aberrations in Breast Cancer
Anton Safonov, Tingting Jiang, Giampaolo Bianchini, Balázs Győrffy, Thomas Karn, Christos Hatzis, and Lajos Pusztai

Précis: Analysis of 1025 breast cancers revealed that higher expression of immune-associated genes associates with lower clonal heterogeneity in all breast cancer subtypes, suggesting immune escape is enabled by genomic diversification.

INTEGRATED SYSTEMS AND TECHNOLOGIES
3325 Personalized Management of Pancreatic Ductal Adenocarcinoma Patients through Computational Modeling
Kimiyo N. Yamamoto, Shinichi Yachida, Akira Nakamura, Atsushi Niida, Minoru Oshima, Subhajyoti De, Lauren M. Rosati, Joseph M. Herman, Christine A. Iacobuzio-Donahue, and Hiroshi Haeno

Précis: A new mathematical model identifies pancreatic cancer patients with a lower propensity to develop metastatic disease and shows this subpopulation benefits from locally intensive therapies such as surgery and radiation therapy.

3336 An Ex Vivo Platform for the Prediction of Clinical Response in Multiple Myeloma

Précis: These findings describe a novel tool to quickly predict the clinical response to a large number of drugs used to treat multiple myeloma using fresh bone marrow aspirates, a digital image analysis algorithm, mathematical models, and pharmacokinetic data.

3352 Western Diet Deregulates Bile Acid Homeostasis, Cell Proliferation, and Tumorigenesis in Colon
Denis Dermadi, Satu Valo, Saara Ollila, Rabah Soliymani, Nina Sipari, Marjaana Pussila, Laura Sarantaus, Jere Linden, Marc Baumann, and Minna Nystöm

Précis: These findings establish a comprehensive deep proteomics resource for the colon cancer community and observes changes in normal mucosa caused by Western-style diet preceding colon cancer development.

3364 Drug Resistance Mechanisms in Colorectal Cancer Dissected with Cell Type–Specific Dynamic Logic Models
Federica Eduati, Victoria Doldán-Martelli, Bertram Klinger, Thomas Cokelaer, Anja Sieber, Fiona Kogera, Mathurin Dorel, Mathew J. Garnett, Nils Blüthgen, and Julio Saez-Rodriguez

Précis: Dynamic logic models of signaling pathways based on perturbation data provide biomarkers of efficacy for drugs for which no genomic marker exist and suggest strategies to overcome drug resistance.

LETTER TO THE EDITOR
3376 TLR-3/9 Agonists Synergize with Anti-ErbB2 mAb—Letter
Anna H. Turaj, Lekh N. Dahal, Stephen A. Beers, Mark S. Cragg, and Sean H. Lim

CORRECTION
3379 Correction: TALEN-Mediated Inactivation of PD-1 in Tumor-Reactive Lymphocytes Promotes Intratumoral T-cell Persistence and Rejection of Established Tumors

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ABOUT THE COVER

Human prostate cancer selectively metastasizes to the bone with mechanisms that are partially unknown. RAGE is a receptor overexpressed by prostate cancer cells whose expression correlates with the capacity of colonizing the bone marrow microenvironment. Proteinase 3 (PR3) is a serine protease produced and released by myeloid cells, and has been identified as a RAGE-interacting protein. Using high resolution confocal microscopy, it was found that soluble PR3 (red) accumulates at the surface of prostate cancer cells overexpressing RAGE (green). This result supports further evidence of heterotypic cell-cell interactions between prostate cancer cells expressing RAGE and hematopoietic cells expressing PR3. For more details, see article by Kolonin and colleagues on page 3144.