BREAKING ADVANCES

1539  Highlights from Recent Cancer Literature

REVIEWS

1541  Accuracy of Molecular Data Generated with FFPE Biospecimens: Lessons from the Literature
Sarah R. Greytak, Kelly B. Engel, B. Paige Bass, and Helen M. Moore

1548  Mesoscopic and Macroscopic Optoacoustic Imaging of Cancer
Adrian Taruttis, Gooitzen M. van Dam, and Vasilis Ntziachristos

PRIORITY REPORT

1560  Evaluating Patient-Derived Colorectal Cancer Xenografts as Preclinical Models by Comparison with Patient Clinical Data
Manoel Nunes, Patricia Vrignaud, Sophie Vacher, Sophie Richon, Astrid Lièvre, Wulfian Cacheux, Louis-Bastien Weiswold, Gerald Massonnet, Sophie Chateau-Joubert, André Nicolas, Coletic Dib, Weidong Zhang, James Watters, Donald Bergstrom, Sergio Roman-Roman, Ivan Bieche, and Virginie Dangles-Marie
Précis: This study highlights the translational relevancy of patient-derived colorectal cancer xenografts in both therapeutic response and genomic profiles.

INTEGRATED SYSTEMS AND TECHNOLOGIES

1567  Impact of Metabolic Heterogeneity on Tumor Growth, Invasion, and Treatment Outcomes
Mark Robertson-Tessi, Robert J. Gillies, Robert A. Gatenby, and Alexander R.A. Anderson
Précis: Models that incorporate tumor heterogeneity highlight the risks of cytotoxic and antiangiogenic treatment due to their potential to select for cell populations with more aggressive behaviors, reinforcing “watchful-waiting” clinical attitudes toward more indolent early-stage cancers such as breast and prostate cancer.

1580  Chaperone Hsp47 Drives Malignant Growth and Invasion by Modulating an ECM Gene Network
Jieqing Zhu, Gaofeng Xiong, Hanjiang Fu, B. Mark Evers, Binhua P. Zhou, and Ren Xu
Précis: These findings define a microRNA-controlled nodal hub that regulates expression and deposition of extracellular matrix proteins needed to drive malignant growth and invasion of breast cancer cells, with potential implications for therapy and prevention in this disease.

1592  Notch Suppresses Angiogenesis and Progression of Hepatic Metastases
Précis: This important preclinical study suggests a new perspective on the clinical risks of Notch inhibitors in development for cancer treatment based on evidence that these agents may facilitate formation of metastatic lesions in the liver.

1603  Antitumor Immunity Triggered by Melphalan Is Potentiated by Melanoma Cell Surface–Associated Calreticulin
Aleksandra M. Dudek-Perić, Gabriela B. Ferreira, Angelika Muchowicz, Jasper Wouters, Nicole Prada, Shaun Martin, Santeri Kiviluoto, Magdalena Winiarska, Louis Boon, Chantal Mathieu, Joost van den Oord, Margaertie Stas, Marie-Lise Gougeon, Jakub Golab, Abhishek D. Carg, and Patrizia Agostinis
Précis: Immunogenic effects of a limb-perfused chemotherapeutic used for locoregional treatment of melanoma can be leveraged by coadministration of a sterile danger signal that can heighten antitumor immunity.

1615  MDSC and TGFβ Are Required for Facilitation of Tumor Growth in the Lungs of Mice Exposed to Carbon Nanotubes
Précis: Studies in a mouse model of nanomaterial-induced pulmonary inflammation show how myeloid-derived suppressor cells act to condition a local tissue niche to support growth of lung cancer.
Interleukin-5 Facilitates Lung Metastasis by Modulating the Immune Microenvironment

These results establish a network of allergic inflammatory circuitry that can be co-opted by metastatic cancer cells to facilitate lung colonization, suggesting new therapeutic interventions to target this pathway as an antimetastatic strategy.

IL10 and PD-1 Cooperate to Limit the Activity of Tumor-Specific CD8+ T Cells
Zhaojun Sun, Julien Fourcade, Ornella Pagliano, Joe-Marc Chauvin, Cindy Sander, John M. Kirkwood, and Hassane M. Zarour

This study shows that IL10 blockade cooperates with PD-1 antibodies to more effectively counteract T-cell immunosuppression in melanoma, with immediate implications for the use of IL10 neutralizing antibodies to improve immune checkpoint therapy in patients with advanced melanoma.

High-Mobility Group Box 1 Promotes Hepatocellular Carcinoma Progression through miR-21–Mediated Matrix Metalloproteinase Activity
Man Chen, Yao Liu, Patrick Varley, Ying Chang, Xing-xing He, Hai Huang, Daolin Tang, Michael T. Lotze, Jusheng Lin, and Allan Tsourou

This study examines a pathway of chronic sterile inflammatory signaling in the liver that may be sufficient to drive malignant progression in the absence of viral infections such as HBV and HCV, which are widely but not universally involved in liver cancer development.

MyD88-Dependent Signaling Decreases the Antitumor Efficacy of Epidermal Growth Factor Receptor Inhibition in Head and Neck Cancer Cells
Adam T. Koch, Laurie Love-Homan, Madelyn Espinosa-Cotton, Aditya Stanam, and Andrea L. Simons

These findings suggest mechanism-based approaches to improve the efficacy of EGFR inhibitors used to treat head and neck cancer.

Genetic and Pharmacological Screens Converge in Identifying FLIP, BCL2, and IAP Proteins as Key Regulators of Sensitivity to the TRAIL-Inducing Anticancer Agent ONC201/TIC10
Joshua E. Allen, Vanun V. Prabhul, Mala Taleskar, A. Pieter J. van den Heuvel, Boza Lim, David T. Dicker, Jennifer L. Fritz, Adam Beck, and Wafik S. El-Deiry

This preclinical study identifies and mechanistically rationalizes the use of a set of predictive biomarkers that may help advance phase Ib/II clinical evaluations of a novel TRAIL-inducing cancer drug.

Ibrutinib Exerts Potent Antifibrotic and Antitumor Activities in Mouse Models of Pancreatic Adenocarcinoma

The results of this important study provide a preclinical rationale for evaluation of the clinical efficacy of the recently approved Bruton tyrosine kinase inhibitor ibrutinib in patients with pancreatic cancer.

Wnt/b-Catenin Small-Molecule Inhibitor CWP232228 Preferentially Inhibits the Growth of Breast Cancer Stem-like Cells
Gyu-Beom Jang, In-Sun Hong, Ran-Ju Kim, Su-Youn Lee, Se-Jin Park, Eun-Sook Lee, Jung Hyuck Park, Chi-Ho Yun, Jae-Uk Chung, Kyoung-June Lee, Hwa-Yong Lee, and Jeong-Seok Nam

These findings highlight a candidate therapeutic agent that may target stem-like cells as well as bulk tumor cells and lead to more effective treatment of breast cancer.
1703 FOXP3 Controls an miR-146/NF-κB Negative Feedback Loop That Inhibits Apoptosis in Breast Cancer Cells
Runhua Liu, Cong Liu, Dongquan Chen, Wei-Hsiung Yang, Xiuping Liu, Chang-Gong Liu, Courtney M. Dugas, Fei Tang, Pan Zheng, Yang Liu, and Lihong Wang
Précis: FOXP3 is a master regulator of regulatory T cells that limit antitumor immunity, but it also functions as an X-linked tumor suppressor gene in breast cancer, where the pathways it controls may offer direct therapeutic targets.

1714 FOXP3–miR-146–NF-κB Axis and Therapy for Precancerous Lesions in Prostate
Runhua Liu, Bin Yi, Shi Wei, Wei-Hsiung Yang, Karen M. Hart, Priyanka Chauhan, Wei Zhang, Xicheng Mao, Xiuping Liu, Chang-Gong Liu, and Lihong Wang
Précis: FOXP3 is best known as an expression biomarker for regulatory T cells that promote immune escape in cancer, but it can be altered in prostate tumor cells themselves, where it directly participates in tumorigenesis.

1725 IKKβ Enforces a LIN28B/TCF7L2 Positive Feedback Loop That Promotes Cancer Cell Stemness and Metastasis
Chong Chen, Fengji Cao, Lipeng Bai, Yan Liu, Junling Xie, Wei Wang, Qin St, Jian Yang, Antao Chang, Dong Liu, Dachuan Liu, Tsung-Hsien Chuang, Rong Xiang, and Yunping Luo
Précis: This important study defines a nodal positive feedback loop that reinforces cancer stemness driven by pro-inflammatory processes, with important implications for understanding progression and metastasis and for conceptualizing a novel generalized intervention in advanced cancers.

1736 RIP1 Kinase Is an Oncogenic Driver in Melanoma
Précis: These findings reveal a well-established regulator of cell death to be an oncogenic driver, with potential implications for its candidacy as a therapeutic target in melanoma.

1749 Modification of Helicobacter pylori Peptidoglycan Enhances NOD1 Activation and Promotes Cancer of the Stomach
Giovanni Suarez, Judith Romero-Gallo, M. Blanca Pianzelio, Ge Wang, Robert J. Maier, Lennart S. Forsberg, Parastoo Azadi, Martin A. Gomez, Pelayo Correa, and Richard M. Peek, Jr.
Précis: This study provides mechanistic insights into how chronic infections of the stomach with the bacteria H. pylori increase risks of developing gastric cancer.

1760 Hyperthermia Sensitizes Glioma Stem-like Cells to Radiation by Inhibiting AKT Signaling
Précis: These preclinical findings show how hyperthermia treatments can reduce the inherent radioresistance of glioma stem cells, with clinical implications for improving the treatment of glioblastoma.

CORRECTIONS

1770 Correction: Fearful Symmetry: Subversion of Asymmetric Division in Cancer Development and Progression

1771 Correction: Autophagic Survival in Resistance to Histone Deacetylase Inhibitors: Novel Strategies to Treat Malignant Peripheral Nerve Sheath Tumors
ABOUT THE COVER

Bruton’s tyrosine kinase inhibitor ibrutinib triggers reduction of collagen content (red staining) in tumors from a transgenic mouse model of pancreatic ductal adenocarcinoma (PDAC). This dramatic reduction in fibrosis is accompanied by a decrease in Ki-67-positive proliferating cells, CD11b⁺ leukocytes, and F4/80⁺ macrophages. Overall, ibrutinib extends survival of PDAC-bearing mice as monotherapy or in combination with the standard of care chemotherapy gemcitabine. For details, see article by Massó-Vallès and colleagues on page 1675.