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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, Wulfran Cacheux, Louis-Bastien Weinswald, Gerald Massonnet, Sophie Chateau-Joubert, André Nicolas, Coletis 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.

MICROENVIRONMENT AND IMMUNOLOGY

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
Debarshi Banerjee, Sonia I. Hernandez, Alejandro Garcia, Thaneel Kangsamaksin, Emily Shiroli, John Andrews, Lynn Ann Forrester, Na Wei, Angela Kadenhe-Chiweshe, Carrie J. Shawber, Jan K. Kitajewski, Jessica J. Kandel, and Darrell J. Yamashiro
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-Petić, Gabriela B. Ferreira, Angelika Muchowicz, Jasper Wouters, Nicole Prada, Shaun Martin, Santeri Kiviluoto, Magdalena Winiarzka, Louis Boon, Chantal Mathieu, Joost van den Oord, Margaerite Stas, Marie-Lise Gougeon, Jakub Golab, Ahihebe 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

MOLECULAR AND CELLULAR PATHOBIOLOGY

High-Mobility Group Box 1 Promotes Hepatocellular Carcinoma Progression through miR-21–Mediated Matrix Metalloproteinase Activity

THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

MyD88-Dependent Signaling Decreases the Antitumor Efficacy of Epidermal Growth Factor Receptor Inhibition in Head and Neck Cancer Cells

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

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

Induction of Vasculogenic Mimicry Overrides VEGF-A Silencing and Enriches Stem-like Cancer Cells in Melanoma

Wnt/β-Catenin Small-Molecule Inhibitor CWP232228 Preferentially Inhibits the Growth of Breast Cancer Stem-like Cells
1703  FOXP3 Controls an miR-146/NF-xB 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-xB Axis and Therapy for Precancerous Lesions in Prostate
Runhua Liu, Bin Yi, Shi Wei, Wei-Hsiung Yang, Karen M. Hart, Priyanka Chauban, 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, Fengqi Cao, Lipeng Bai, Yan Liu, Junling Xie, Wei Wang, Qin Si, Jian Yang, Antao Chang, Dong Liu, DaChuan Liu, Tsung-Hsien Chuang, Rong Xiang, and Yuntao 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 Pianezelo, Ge Wang, Robert J. Maier, Lennart S. Forsberg, Parasito 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.
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.