

CANCER RESEARCH

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1229 **Highlights from Recent Cancer Literature**

CANCER RESEARCH HIGHLIGHTS

1231 **Metabolite Imaging at the Margin: Visualizing Metabolic Tumor Gradients Using Mass Spectrometry**
 Ai Wen Tan and Aalim M. Weljie
 See related article, p. 1258

GENOME AND EPIGENOME

1234 **ETV4 Is Necessary for Estrogen Signaling and Growth in Endometrial Cancer Cells**
 Adriana C. Rodriguez, Jeffery M. Vahrenkamp, Kristofer C. Berrett, Kathleen A. Clark, Katrin P. Guillen, Sandra D. Scherer, Chieh-Hsiang Yang, Bryan E. Welm, Margit M. Janát-Amsbury, Barbara J. Graves, and Jason Gertz
 Estrogen receptor alpha (ER) is a key oncogene in endometrial cancer. This study uncovers ETV4 as an important factor in controlling the activity of ER and the growth of endometrial cancer cells.

METABOLISM AND CHEMICAL BIOLOGY

1246 ***In Situ* DESI-MSI Lipidomic Profiles of Breast Cancer Molecular Subtypes and Precursor Lesions**
 Adriana Leandra Santoro, Rodrigo D. Drummond, Israel Tojal Silva, Severino S. Ferreira, Luiz Juliano, Pedro H. Vendramini, Monique Batista da Costa Lemos, Marcos N. Eberlin, and Victor Piana Andrade
 These findings present the first *in situ* metabolomic findings of the four molecular subtypes of breast cancer, DCIS, and normal tissue, and add to the understanding of their pathogenesis.

1258 **Localized Metabolomic Gradients in Patient-Derived Xenograft Models of Glioblastoma**
 Elizabeth C. Randall, Begoña G.C. Lopez, Sen Peng, Michael S. Regan, Walid M. Abdelmoula, Sankha S. Basu, Sandro Santagata, Haejin Yoon, Marcia C. Haigis, Jeffrey N. Agar, Nhan L. Tran, William F. Elmquist, Forest M. White, Jann N. Sarkaria, and Nathalie Y.R. Agar
 GBM tumors exhibit a metabolic gradient that should be taken into consideration when designing therapeutic strategies for treatment.
 See related commentary, p. 1231

1268 **Increased Tumor Penetration of Single-Domain Antibody-Drug Conjugates Improves *In Vivo* Efficacy in Prostate Cancer Models**
 Ian Nessler, Eshita Khera, Steven Vance, Anna Kopp, Qifeng Qiu, Thomas A. Keating, Adnan O. Abu-Yousif, Thomas Sandal, James Legg, Lorraine Thompson, Normann Goodwin, and Greg M. Thurber
 A mechanistic study of protein-drug conjugates demonstrates that a lower potency compound is more effective *in vivo* than other agents with equal tumor uptake due to improved tissue penetration and cellular distribution.

MOLECULAR CELL BIOLOGY

1279 **BACH1 Promotes Pancreatic Cancer Metastasis by Repressing Epithelial Genes and Enhancing Epithelial-Mesenchymal Transition**
 Masaki Sato, Mitsuyo Matsumoto, Yuriko Saiki, Mahabub Alam, Hironari Nishizawa, Masahiro Rokugo, Andrey Brydun, Shinji Yamada, Mika K. Kaneko, Ryo Funayama, Mamoru Ito, Yukinari Kato, Keiko Nakayama, Michiaki Unno, and Kazuhiko Igarashi
 Greater understanding of the gene regulatory network involved in epithelial-to-mesenchymal transition of pancreatic cancer cells will provide novel therapeutic targets and diagnostic markers.

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1293 The MEK5–ERK5 Kinase Axis Controls Lipid Metabolism in Small-Cell Lung Cancer

AC

Sandra Cristea, Garry L. Coles, Daniel Hornburg, Maya Gershkovitz, Julia Arand, Siqi Cao, Triparna Sen, Stuart C. Williamson, Jun W. Kim, Alexandros P. Drinas, Andrew He, Laurent Le Cam, Lauren Averett Byers, Michael P. Snyder, Kévin Contrepois, and Julien Sage

This study is the first to investigate MEK5 and ERK5 in SCLC, linking the activity of these two kinases to the control of cell survival and lipid metabolism.

TUMOR BIOLOGY AND IMMUNOLOGY

1304 Activation of Canonical BMP4-SMAD7 Signaling Suppresses Breast Cancer Metastasis

Bedrich L. Eckhardt, Yuan Cao, Andrew D. Redfern, Lap Hing Chi, Allan D. Burrows, Suraya Roslan, Erica K. Sloan, Belinda S. Parker, Sherene Loi, Naoto T. Ueno, Peter K. H. Lau, Bruce Latham, and Robin L. Anderson

Targeting the BMP4-SMAD7 signaling axis presents a novel therapeutic strategy to combat metastatic breast cancer, a disease that has had no reduction in patient mortality over 20 years.

1316 Lymphoma Angiogenesis Is Orchestrated by Noncanonical Signaling Pathways

Marleen Gloger, Lutz Menzel, Michael Grau, Anne-Clemence Vion, Ioannis Anagnostopoulos, Myroslav Zapukhlyak, Kerstin Gerlach, Thomas Kammertöns, Thomas Hehlhans, Maria Zschummel, Georg Lenz, Holger Gerhardt, Uta E. Höpken, and Armin Rehm

In lymphoma, transcriptomes and morphogenic patterns of the vasculature are distinct from processes in inflammation and solid tumors. Instead, LT β R and VEGFR3 signaling gain leading roles and are targets for lymphomagenesis blockade.

1330 miR-149 Suppresses Breast Cancer Metastasis by Blocking Paracrine Interactions with Macrophages

Ismael Sánchez-González, Anja Bobien, Christian Molnar, Simone Schmid, Michaela Strotbek, Melanie Boerries, Hauke Busch, and Monilola A. Olayoye

These findings contribute to the understanding of tumor-stroma interactions by showing that miR-149 downregulation in TNBC enhances reciprocal growth factor signaling between macrophages and cancer cells, which promotes tumor progression and metastasis.

1342 Breast Cancer Cell-Derived Soluble CD44 Promotes Tumor Progression by Triggering Macrophage IL1 β Production

Jeong-Hoon Jang, Do-Hee Kim, Jae Min Lim, Joon Won Lee, Su Jin Jeong, Kwang Pyo Kim, and Young-Joon Surh

A novel positive feedback loop between IL1 β and CD44 promotes TNBC malignant progression.

POPULATION AND PREVENTION SCIENCE

1357 A Prospective Analysis of Circulating Plasma Metabolites Associated with Ovarian Cancer Risk

AC

Oana A. Zeleznik, A. Heather Eliassen, Peter Kraft, Elizabeth M. Poole, Bernard A. Rosner, Sarah Jeanfavre, Amy A. Deik, Kevin Bullock, Daniel S. Hitchcock, Julian Avila-Pacheco, Clary B. Clish, and Shelley S. Tworoger

Pseudouridine represents a potential novel risk factor for ovarian cancer and triglycerides may be important particularly in rapidly fatal ovarian tumors.

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ABOUT THE COVER

A new, therapeutically actionable molecular pathway that can inhibit distant metastasis has been reported by Eckhardt and colleagues. They report the ability of canonical BMP4-Smad signaling to induce a "stop metastasis" gene signature, with the induction of *Smad7* in breast tumors acting as a critical mediator in the prevention of cancer dissemination. Restored BMP4 expression, or neoadjuvant recombinant BMP4 therapy, inhibited spontaneous metastasis of mammary tumors in a *Smad7*-dependent pathway, linked to the ability of BMP4 and *Smad7* to induce anoikis in disseminating breast cancer cells. Clinically, breast tumors that express BMP4 and/or *Smad7* are linked to good prognostic outcome. The cover art depicts an immunohistochemical stain for BMP4 in a breast cancer sample, false-colored in a homage to "pop art," as BMP4-Smad7 elicits anchorage-independent apoptosis (anoikis). For details, see article by Eckhardt and colleagues on page 1304.

