BREAKING ADVANCES

1285  Highlights from Recent Cancer Literature

REVIEWS

1287  Monocyte Subpopulations in Angiogenesis
Heather J. Dalton, Guillermo N. Armaiz-Pena,
Vianey Gonzalez-Villasana, Gabriel Lopez-Berestein,
Menashe Bar-Eli, and Anil K. Sood

1294  Ganetespib and HSP90: Translating Preclinical
Hypotheses into Clinical Promise
David A. Proia and Richard C. Bates

1301  RNA Editome Imbalance in Hepatocellular
Carcinoma
Lihua Qi, Tim Hon Man Chan, Daniel G. Tenen, and
Leilei Chen

MEETING REPORT

1307  Future Opportunities in Cancer Nanotechnology—NCI Strategic Workshop
Report
Piotr Grodzinski and Dorothy Farrell

CLINICAL STUDIES

1311  Fusobacterium in Colonic Flora and Molecular
Features of Colorectal Carcinoma
Tomomitsu Tahara, Eiichiro Yamamoto,
Hiromu Suzuki, Reo Maruyama, Woonbok Chung,
Judith Garriga, Jaroslav Jelinek, Hiro-o Yamano,
Tamotsu Sugai, Byonggu An, Imad Shureiqi,
Minoru Toyota, Yutaka Kondo, Marcos R.H. Estévez,
and Jean-Pierre J. Issa
Précis: Particular alterations of the bacterial species in the
gut microbiome are linked to molecular features of colon
cancer, highlighting the potential utility of those species as
biomarkers and prevention targets.

INTEGRATED SYSTEMS AND TECHNOLOGIES

1319  A Novel Radiotracer to Image Glycogen
Metabolism in Tumors by Positron Emission
Tomography
Timothy H. Witney, Laurence Carroll, Israt S. Alam,
Anil Chandrashekar, Shuang-Dé Nguyen,
Robert A.  Shum, Robert Harris, Ralph J. DeBerardinis,
Roshan Agarwal, and Eric O. Aboagye
Précis: By exploiting the little-studied process of glycogen
synthesis in tumors, a novel radiotracer for PET scans was
developed in this study to evaluate tumoral quiescence.

1329  Fragmented Sleep Accelerates Tumor Growth
and Progression through Recruitment of
Tumor-Associated Macrophages and TLR4
Signaling
Alaa Elissa, Yang Wang, Shelley X.L. Zhang,
Jia Mao Zheng, Esma S. Yolcu, Alba Carreras,
Abdelnaby Khalyfa, Haval Shirwan,
Isaac Almendros, and David Gozal
Précis: Sleep apnea caused by breathing difficulties in obese
individuals may be a contributing factor in how obesity
promotes cancer, given links between sleep disruption and a
higher incidence of cancer prevalence and mortality.

1338  Genetic and Phenotypic Diversity in Breast
Tumor Metastases
Vanessa Almendros, Hee Jung Kim, Yu-Kang Cheng,
Mithat Gonen, Shalev Itzkovitz, Pedram Argani,
Alexander van Oudenaarden, Saraswati Sukumar,
Franziska Michor, and Kornelia Polyak
Précis: Understanding changes in cancer cell populations
during malignant progression is a critical first step toward
the design of improved therapies for advanced cancers.

MICROENVIRONMENT AND IMMUNOLOGY

1349  Novel Bispecific Antibodies Increase γδ T-Cell
Cytotoxicity against Pancreatic Cancer Cells
Hans-Heinrich Oberg, Matthias Peipp,
Christian Kellner, Susanne Sebens, Sarah Krause,
Domantas Petrick, Sabine Adam-Klages,
Christoph Röcken, Thomas Becker, Ilka Vogel,
Dietrich Weisnerg, Sandra Freitag-Wolf,
Martin Gramatzki, Dieter Kabelitz, and
Daniela Wesch
Précis: These results show how bispecific antibodies that
selectively recruit γδ T cells to pancreatic tumors can exploit
the immunotherapeutic potential of this type of T cell from
pancreatic cancer patients.
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1361 Induction of Immunoregulatory CD271+ Cells by Metastatic Tumor Cells That Express Human Endogenous Retrovirus H
Chie Kudo-Saito, Masahiro Yura, Ryusuke Yamamoto, and Yutaka Kawakami

Précis: An expressed endogenous retrovirus present in the human genome is found to be a critical determinant of immune escape and metastasis, acting to organize immunosuppressive mesenchymal stem cells and myeloid-derived suppressor cells in the tumor microenvironment.

1371 P14ARF Suppresses Tumor-Induced Thrombosis by Regulating the Tissue Factor Pathway
Abdessamad Zerrouqi, Beata Pyrzynska, Daniel J. Brat, and Erwin G. Van Meir

Précis: This study links an important suppressor pathway to the vascular microenvironment of tumors, suggesting how necrotic areas that promote progression can develop.

1379 Cancer Cells Exploit eIF4E2-Directed Synthesis of Hypoxia Response Proteins to Drive Tumor Progression
James Uniacke, J. Kishan Perera, Gabriel Lachance, Camille B. Francisco, and Stephen Lee

Précis: Cancer cells shift their use of translation initiation factors to adapt to hypoxic microenvironments where aggressive characters are selected, with implications for understanding and preventing the malignant progression of subclinical lesions.

MOLECULAR AND CELLULAR PATHOBIOLOGY

1390 LIMD2 Is a Small LIM-Only Protein Overexpressed in Metastatic Lesions That Regulates Cell Motility and Tumor Progression by Directly Binding to and Activating the Integrin-Linked Kinase
Hongzhuang Peng, Mehdi Talebzadeh-Farrooji, Michael J. Osborne, Jeremy W. Prokop, Paul C. McDonald, Jayashree Karar, Zhaoyuan Hou, Mei He, Electron Kebebew, Torben Orntoft, Meenhard Herlyn, Andrew J. Caton, Craig Soderquist, Richard Leung, Jonathan Yun, Benjamin Kennedy, Julia Sisti, Samuel Bruce, Rachel Bruce, Reena Shakya, Thomas Ludwig, Steven Rosenfeld, Peter A. Sims, Jeffrey N. Bruce, Andrea Califano, and Peter Canoll

Précis: Perturbing a transcriptional network associated with glial progenitor transformation alters the course of glioma progression and prevents the selection of proneural-specific genetic alterations, demonstrating a functional interplay between tumor phenotype and genotype.
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1452 Overexpression of the Transcription Factor MEF2D in Hepatocellular Carcinoma Sustains Malignant Character by Suppressing G2–M Transition Genes
Leina Ma, Jia Liu, Limei Liu, Guangjie Duan, Qingliang Wang, Yannin Xu, Feng Xia, Juanjuan Shan, Junjie Shen, Zhi Yang, Ping Bie, Youhong Cui, Xiu-Wu Bian, Jesus Prieto, Matías A. Avila, and Cheng Qian

1463 Invasive Lobular Carcinoma Cell Lines Are Characterized by Unique Estrogen-Mediated Gene Expression Patterns and Altered Tamoxifen Response
Matthew J. Sikora, Kristine L. Cooper, Amir Bahreini, Soumya Luthra, Guoying Wang, Uma R. Chandran, Nancy E. Davidson, David J. Dabbs, Alana L. Welm, and Steffi Oesterreich

1475 Molecular Rules Governing De Novo Methylation in Cancer
Deborah Nejman, Ravid Straussman, Israel Steinfeld, Michael Ruvolo, Douglas Roberts, Zohar Yakhini, and Howard Cedar

1484 Differential Regulation of Estrogen Receptor α Expression in Breast Cancer Cells by Metastasis-Associated Protein 1
Hyun-Jin Kang, Min-Ho Lee, Hae-Lim Kang, Sung-Hye Kim, Jung-Ranh Ahn, Hyelin Nā, Tae-Young Na, Yo Na Kim, Je Kyun Seong, and Mi-Ock Lee

1495 LEF1 and B9L Shield β-Catenin from Inactivation by Axin, Desensitizing Colorectal Cancer Cells to Tankyrase Inhibitors
Marc de la Roche, Ashraf E.K. Ibrahim, Juliusz Mieszczanek, and Mariiann Bienz

1506 Bufalin Is a Potent Small-Molecule Inhibitor of the Steroid Receptor Coactivators SRC-3 and SRC-1
Ying Wang, David M. Lonard, Yang Yu, Dar-Chone Chow, Timothy G. Falzkill, Jin Wang, Ruogu Qi, Alexander J. Matzuk, Xianzhou Song, Franck Madoux, Peter Hodder, Peter Chase, Patrick R. Griffin, Suding Zhou, Lan Liao, Jinanning Xu, and Bert W. O’Malley

TUMOR AND STEM CELL BIOLOGY

1518 BRCA2 Phosphorylated by PLK1 Moves to the Midbody to Regulate Cytokinesis Mediated by Nonmuscle Myosin IIC
Miho Takaoka, Hiroko Saito, Katsuya Takenaka, Yoshio Miki, and Akira Nakashiki

1529 Axon Guidance Factor SLIT2 Inhibits Neural Invasion and Metastasis in Pancreatic Cancer
Andreas Gohrig, Katharina M. Detjen, Georg Hilfenhaus, Jan L. Körner, Martina Welzel, Ruza Arsenic, Rosa Schmuck, Marcus Bahra, Jane Y. Wu, Bertram Wiedenmann, and Christian Fischer

Therapeutics, Targets, and Chemical Biology

1452 Overexpression of the Transcription Factor MEF2D in Hepatocellular Carcinoma Sustains Malignant Character by Suppressing G2–M Transition Genes

1463 Invasive Lobular Carcinoma Cell Lines Are Characterized by Unique Estrogen-Mediated Gene Expression Patterns and Altered Tamoxifen Response

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1484 Differential Regulation of Estrogen Receptor α Expression in Breast Cancer Cells by Metastasis-Associated Protein 1

1495 LEF1 and B9L Shield β-Catenin from Inactivation by Axin, Desensitizing Colorectal Cancer Cells to Tankyrase Inhibitors

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1529 Axon Guidance Factor SLIT2 Inhibits Neural Invasion and Metastasis in Pancreatic Cancer

Therapeutics, Targets, and Chemical Biology

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Therapeutics, Targets, and Chemical Biology
microRNA-148a Is a Prognostic oncomiR That Targets MIG6 and BIM to Regulate EGFR and Apoptosis in Glioblastoma
Jungeun Kim, Ying Zhang, Michael Skalski, Josie Hayes, Benjamin Kefas, David Schiff, Benjamin Purrow, Sarah Parsons, Sean Lawler, and Roger Abounader

Précis: These findings provide a comprehensive analysis of the prognostic value and oncogenic function of a microRNA in aggressive brain cancer, with further implications as a potential target for therapy.

CD133+ Cancer Stem-like Cells in Small Cell Lung Cancer Are Highly Tumorigenic and Chemoresistant but Sensitive to a Novel Neuropeptide Antagonist
Sana Sarvi, Alison C. Mackinnon, Nicolaos Avlonitis, Mark Bradley, Robert C. Rintoul, Doris M. Rassl, Wei Wang, Stuart J. Forbes, Christopher D. Gregory, and Tariq Sethi

Précis: Small-cell lung cancer has neuroendocrine features that suggest its targeting by neuropeptide antagonists, an idea that is strongly reinforced by the findings of this study.

VEGF-Mediated Angiogenesis Links EMT-Induced Cancer Stemness to Tumor Initiation
Anna Fantozzi, Dorothea C. Gruber, Laura Pisarsky, Chantal Heck, Akiko Kunita, Mahmut Yilmaz, Nathalie Meyer-Schaller, Karen Cornille, Ulrike Hopfer, Mohamed Bentires-Alj, and Gerhard Christofori

Précis: This study offers provocative findings suggesting that the ability of cancer stem-like cells to initiate cancer relies on their ability to promote angiogenesis.

Mesenchymal Stem Cells Use IDO to Regulate Immunity in Tumor Microenvironment
Weifang Ling, Jinning Zhang, Zengrong Yuan, Guangwen Ren, Liying Zhang, Xiaodong Chen, Arnold B. Rabson, Arthur I. Roberts, Ying Wang, and Yufang Shi

Précis: This study corroborates the concept that IDO offers a pivotal mediator of immune escape in human cancer by showing that IDO expression in mesenchymal stem cells in the tumor microenvironment is sufficient to drive tumor formation.

Sequential Gene Targeting to Make Chimeric Tumor Models with De Novo Chromosomal Abnormalities

Précis: This study describes a rapid method to generate mouse models of cancer, providing a flexible platform to tag cancer-initiating cells and a means to learn how chromosomal abnormalities interact with other mutations.

Integrin αvβ6 Promotes an Osteolytic Program in Cancer Cells by Upregulating MMP2

Précis: This study shows how expression of a single integrin can contribute to osteolysis by cancer cells by triggering matrix degradation in bone.

Interactions between MUC1 and p120 Catenin Regulate Dynamic Features of Cell Adhesion, Motility, and Metastasis
Xiang Liu, Chunhui Yi, Yunfei Wen, Prakash Radakrishnan, Jarrod R. Tremayne, Thongtan Dao, Keith R. Johnson, and Michael A. Hollingsworth

Précis: These findings provide new functional insights into the dynamic interplay between cell adhesion and motility and their relationship to metastasis.

Correction: Circadian Regulation of mTOR by the Ubiquitin Pathway in Renal Cell Carcinoma

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ABOUT THE COVER

Chemosensitive small cell lung cancer (SCLC) tumors demonstrate increased expression of CD133, a known marker for cancer stem cells. The CD133 positive SCLC cells coexpress gastrin releasing peptide receptor (GRPR), which facilitates signaling and growth in response to GRP while rendering cells more sensitive to neuropeptide antagonists. Confocal microscopic analysis of chemoresistant human SCLC xenografts show clusters of CD133 positive cells (green) within the tumor that were shown to coexpress GRPR (red). Antagonists such as the one described by Sarvi and colleagues may provide a new avenue for the treatment of chemoresistant SCLC tumors. For details, see article by Sarvi and colleagues on page 1554.