**Cancer Research**

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**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

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**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**  
Fahed Hakim, Yang Wang, Shelley X.L. Zhang, Jiamao 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**  

**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

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**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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Chie Kudo-Saito, Masahiro Yura, Ryusuke Yamamoto, and Yutaka Kawakami

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James Uniacke, J. Kishan Perera, Gabriel Lachance, Camille B. Francisco, and Stephen Lee

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MOLECULAR AND CELLULAR PATHOBIOLOGY

The Transcriptional Regulatory Network of Proneural Glioma Determines the Genetic Alterations Selected during Tumor Progression
Adam M. Sonabend, Mukesh Bansal, Paolo Guarneri, Liang Lei, Benjamin Amendolara, 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 Calitano, and Peter Canoll

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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, Yanmin Xu, Feng Xia, Juanjuan Shan, Junjie Shen, Zhi Yang, Ping Bie, Youhong Cui, Xiu-Wu Bian, Jesus Prieto, Matías A. Avila, and Cheng Qian

Précis: A transcription factor implicated in leukemia cell survival is shown in this report to be an important oncogenic driver in liver cancer, with clinical implications for etiology and treatment.

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

Précis: These results offer explanatory power to understand recent clinical observations in lobular breast cancer, where, despite favorable biomarkers, patients do not necessarily consistently exhibit favorable outcomes.

1475 Molecular Rules Governing De Novo Methylation in Cancer

Deborah Nejman, Ravid Straussman, Israel Steinfeld, Michael Ruvolo, Douglas Roberts, Zohar Yakhini, and Howard Cedar

Précis: This study offers new knowledge into how de novo DNA methylation is controlled at CpG islands in the genome, a process widely altered in human cancer, with implications for how to develop broadly applicable epigenetic therapies for cancer prevention and treatment.

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-Ran H Ahn, Hyelin Ná, Tae-Young Na, Yo Na Kim, Je Kyung Seong, and Mi-Ok Lee

Précis: This study shows how a nucleosome remodeling complex differentially affects ERα positive and ERα negative breast cancer cells, potentially determining their sensitivity to hormone therapy.

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 Mariann Bienz

Précis: These findings suggest that chronic Wnt pathway activation can render cancer cells insensitive to tankyrase inhibitors, a novel class of clinical experimental therapeutics, possibly limiting their potential therapeutic impact in colorectal cancer where Wnt activation is common.

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, Suling Zhou, Lan Liao, Jianming Xu, and Bert W. O’Malley

Précis: Steroid receptor coactivators are key oncogenes and attractive drug targets for cancer therapy that can be effectively inhibited with the small-molecule inhibitor bufalin.

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 Nakashima

Précis: This study suggests that BRCA2 may prevent cancer in part by enforcing checkpoint controls on cytokinesis, the last step in mitosis, where it may be possible to prevent aneuploidy and multinucleation leading to cancer.

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

Andreas Göhrig, Katharina M. Detjen, Georg Hilfenhaus, Jan L. Körner, Martina Welzel, Ruza Arsenic, Rosa Schmuck, Marcus Bahra, Jane Y. Wu, Bertram Wiedenmann, and Christian Fischer

Précis: A cell surface receptor system that guides neuronal migration appears to be dysfuncionally co-opted during development of pancreatic cancer, possibly driving its propensity to metastasize from the pancreas along nerve tracts.
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 Bentes-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, Jinbin 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

CORRECTION
Chemoresistant 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.

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