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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 Chandrashekhara, Quang-Dé Nguyen, Roberta Sala, 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
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

1349 Novel Bispecific Antibodies Increase γδ T-Cell Cytotoxicity against Pancreatic Cancer Cells
Hans-Heinrich Ober, Matthias Peipp, Christian Kellner, Susanne Sebens, Sarah Krause, Domantas Petrick, Sabine Adam-Klages, Christoph Röcken, Thomas Becker, Ilka Vogel, Dietrich Weisner, 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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**Molecular and Cellular Pathobiology**

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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
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-Rahn Ahn, Hyelin Nà, Tae-Young Na, Yo Na Kim, Je Kyung Seong, and Mi-Ock 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 Miesczczanek, 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, Suding 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, Yosho 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 Gohrig, Katharina M. Detjen, Georg Hilfenzhaus, 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 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, Jimin 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.

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

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.
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.