The Endogenous Tryptophan Metabolite and NAD+ Precursor Quinolinic Acid Confers Resistance of Gliomas to Oxidative Stress
Felix Sahm, Iris Oezen, Christiane A. Opitz, Bernhard Radlwimmer, Andreas von Deimling, Tilman Ahrendt, Seray Adams, Helge B. Bode, Gilles J. Guillemim, Wolfgang Wick, and Michael Platten

Précis: A downstream catabolite of the tryptophan degradation pathway of IDO- and TDO-dependent immune escape, which is elevated in the majority of human cancers, is found to be a key element in their therapeutic resistance, with implications to improve treatment.

Application of Raman Spectroscopy to Identify Microcalcifications and Underlying Breast Lesions at Stereotactic Core Needle Biopsy
Ishan Barman, Narahara Chari Dingari, Anushree Saha, Sasha McGee, Luis H. Galindo, Wendy Liu, Donna Plecha, Nina Klein, Ramachandra Rao Dasari, and Maryann Fitzmaurice

Précis: These findings illustrate a powerful noninvasive spectroscopic approach to detect microcalcifications and other cancer-associated lesions that offers real-time feedback to radiologists during biopsy procedures and thus could reduce nondiagnostic and false-negative biopsies.

Manganese-Enhanced MRI Reveals Early-Phase Radiation-Induced Cell Alterations In Vivo
Shigeyoshi Saito, Sumitaka Hasegawa, Aiko Sekita, Rumiana Bakalova, Takako Furukawa, Kenya Murase, Tsume Saga, and Ichio Aoki

Précis: This study reports a noninvasive method to monitor cell-cycle alterations in tumors based on manganese uptake and MRI, offering a potentially useful tool for longitudinal studies to optimize radiotherapy.

Single Copies of Mutant KRAS and Mutant PIK3CA Cooperate in Immortalized Human Epithelial Cells to Induce Tumor Formation

Précis: These findings suggest a paradigm that helps to explain how a single mutant KRAS allele can cooperate with mutant PIK3CA to impart a transformed phenotype.
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<td>Dachshund Binds p53 to Block the Growth of Lung Adenocarcinoma Cells</td>
<td>Ke Chen, Kongming Wu, Shaoxin Cai, Wei Zhang, Jie Zhou, Jing Wang, Adam Ertel, Zhiping Li, Hallgeir Rui, Andrew Quong, Michael P. Lisanti, Aydin Tozeren, Ceylan Tanes, Sankar Addya, Michael Gormley, Chenguang Wang, Steven B. McMahon, and Richard G. Pestell</td>
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<td>Lineage Relationship of Gleason Patterns in Gleason Score 7 Prostate Cancer</td>
<td>Irina V. Kovtun, John C. Cherille, Stephen J. Murphy, Sarah H. Johnson, Shabnam Zarei, Farhad Kosari, William R. Sukov, R. Jeffrey Karnes, and George Vasmatzis</td>
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<td>Collagen Prolyl Hydroxylases Are Essential for Breast Cancer Metastasis</td>
<td>Danieile M. Gilkes, Pallavi Chaturvedi, Saumendra Bajpai, Carmen C. Wong, Hong Wei, Stephen Pitcairn, Alain Monnier, Eulalia Hui, Denis Wirtz, and Gregor L. Semenza</td>
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<td>Interleukin-1β Promotes Skeletal Colonization and Progression of Metastatic Prostate Cancer Cells with Neuroendocrine Features</td>
<td>Qingxin Liu, Mike R. Russell, Kristina Shahriri, Daniell E. Lernagan, Mercedes J. Lioni, Fernando U. Garcia, and Alessandro Fatatis</td>
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<td>DNA Methylation-Mediated Repression of miR-886-3p Predicts Poor Outcome of Human Small Cell Lung Cancer</td>
<td>Jianzhong Cao, Yongmei Song, Nan Bi, Jie Shen, Wenyang Liu, Jing Fan, Guoqi Sun, Tong Tong, Jie He, Yuankai Shi, Xin Zhang, Ning Lu, Yinghua He, Hongyu Zhang, Kelong Ma, Xiaoying Luo, Lei Ly, Hui Deng, Jing Cheng, Jingde Zhu, Luhua Wang, and Qimin Zhan</td>
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<td>Inhibition of Tumor Cell Migration by LD22-4, an N-Terminal Fragment of 24-kDa FGFR2, Is Mediated by Neurophilin 1</td>
<td>Ling Zhang, Graham C. Parry, and Eugene G. Levin</td>
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<td>Collagen Prolyl Hydroxylases Are Essential for Breast Cancer Metastasis</td>
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Threshold Levels of ABL Tyrosine Kinase Inhibitors Retained in Chronic Myeloid Leukemia Cells Determine Their Commitment to Apoptosis


Précis: By providing deeper insights into the pharmacodynamic requirements for the cytotoxic effects of the paradigm kinase inhibitor imatinib, this study may more broadly assist the development of maximally effective kinase inhibitors for cancer treatment.

Simultaneous Targeting of Tumor Antigens and the Tumor Vasculature Using T Lymphocyte Transfer Synergize to Induce Regression of Established Tumors in Mice

Dhanalakshmi Chinnasamy, Eric Tran, Zhiya Yu, Richard A. Morgan, Nicholas P. Restifo, and Steven A. Rosenberg

Précis: This study offers proof of principle for using antiangiogenic drugs to enhance the efficacy of adoptive T-cell therapies for cancer treatment.

Hedgehog Signaling Alters Reliance on EGF Receptor Signaling and Mediates Anti-EGFR Therapeutic Resistance in Head and Neck Cancer


Précis: Preclinical results show that resistance to the widely used EGFR targeting drug cetuximab, which occurs widely in the clinic, could be prevented by administration of inhibitors of the hedgehog pathway, which appears to be emerging as a major factor in cancer drug resistance more broadly.

Regulation of FANCD2 by the mTOR Pathway Contributes to the Resistance of Cancer Cells to DNA Double-Strand Breaks

Changxian Shen, Duane Oswald, Doris Phelpis, Hakari Cam, Christopher E. Pello斯基, Qishen Pang, and Peter J. Houghton

Précis: This study provides the basis for the sensitization of cancer cells to DNA damaging agents by targeting the mTOR pathway and gives insight into potential strategies that may enhance therapeutic activity or reduce sequelae from high-dose therapies, particularly in children.

Elevation of Receptor Tyrosine Kinases by Small Molecule AKT Inhibitors in Prostate Cancer Is Mediated by Pim-1

Bo Cen, Sandeep Mahajan, Wenzhe Wang, and Andrew S. Kraft

Précis: This study provides a rationale to improve the efficacy of AKT inhibitors for cancer therapy.

CIP4 Controls CCL19-Driven Cell Steering and Chemotaxis in Chronic Lymphocytic Leukemia

Gema Malet-Engra, Julien Vial, Loïc Ysebaert, Manon Farcé, Fanny Lafouresse, Guy Laurent, Frédérique Gaits-Iacovoni, Giorgio Scita, and Loïc Dupré

Précis: This study offers important new mechanistic insights into how leukemia cells migrate, with potentially important implications for understanding how to block invasive growth by these cells.

miR145 Targets the S0X9/ADAM17 Axis to Inhibit Tumor-Initiating Cells and IL-6–Mediated Paracrine Effects in Head and Neck Cancer

Cheng-Chia Yu, Lo-Lin Tsai, Mong-Lien Wang, Chuan-Hang Yu, Wen-Liang Lo, Yun-Ching Chang, Guang-Yuh Chiu, Ming-Tung Chou, and Shi-Hwa Chiu

Précis: This mechanistically extensive study reveals a core pathway of support for cancer stem-like cells in head and neck squamous carcinomas, with implications for new treatment strategies in this setting.

Cytomegalovirus Contributes to Glioblastoma in the Context of Tumor Suppressor Mutations


Précis: A virus that infects a large proportion of brain tumors in a mouse model.

Notch3 Functions as a Tumor Suppressor by Controlling Cellular Senescence

Hang Cui, Yahui Kong, Mei Xu, and Hong Zhang

Précis: These findings offer a novel mechanism to enhance our understanding of the tumor-suppressive function of Notch signaling in cancer, with implications in many solid tumor settings.
Dual Role of the Antioxidant Enzyme Peroxiredoxin 6 in Skin Carcinogenesis
Frank Rolfs, Marcel Huber, Florian Gruber, Friederike Böhm, Herbert J. Pfister, Valery N. Bochkov, Erwin Tschachler, Reinhard Dummer, Daniel Hohl, Matthias Schäfer, and Sabine Werner

Précis: Antioxidant functions do not contribute exclusively to tumor suppression, as widely believed, but can also promote tumor development depending on the stage of the disease.

Growth of Triple-Negative Breast Cancer Cells Relies upon Coordinate Autocrine Expression of the Proinflammatory Cytokines IL-6 and IL-8

Précis: Findings offer a preclinical proof of principle to improve therapy of triple-negative breast cancer, a particularly aggressive disease subtype lacking effective mechanism-based interventions.

ABOUT THE COVER

In gliomas, constitutive metabolism of the essential amino acid tryptophan leads to the accumulation of the tryptophan metabolite quinolinic acid. Quinolinic acid is used by tumor cells to generate NAD⁺, thus contributing to the resistance towards radiotherapy and chemotherapy by replenishing depleted intracellular NAD pools. Using Western blot analyses and immunohistochemistry, it was found that the key enzyme leading to accumulation of quinolinic acid, 3-hydroxyanthranilate oxygenate (3-HAO), is expressed by tumor-infiltrating monocytes. Thus, infiltrating monocytes contribute to resistance to cytotoxic therapies in malignant gliomas. For details, see article by Sahm and colleagues on page 3225.
Cancer Research

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