Highlights from Recent Cancer Literature

The MET Oncogene in Glioblastoma Stem Cells: Implications as a Diagnostic Marker and a Therapeutic Target
Carla Boccaccio and Paolo M. Comoglio

Vesicle Trafficking and RNA Transfer Add Complexity and Connectivity to Cell–Cell Communication
Charles T. Roberts Jr and Peter Kurre

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

The Endogenous Tryptophan Metabolite and NAD⁺ Precursor Quinolinic Acid Confers Resistance of Gliomas to Oxidative Stress
Felix Sahm, Iris Oezene, 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.

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

Hypoxia Triggers Hedgehog-Mediated Tumor–Stromal Interactions in Pancreatic Cancer

Précis: These findings provide evidence for a novel molecular mechanism that explains the high levels of hypoxia and desmoplasia that contribute to therapy resistance in pancreatic cancer.

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.
| 3262 | Dachshund Binds p53 to Block the Growth of Lung Adenocarcinoma Cells | 3316 | Inhibition of Tumor Cell Migration by LD22-4, an N-Terminal Fragment of 24-kDa FGFR2, Is Mediated by Neurophilin 1 |
| 3275 | Lineage Relationship of Gleason Patterns in Gleason Score 7 Prostate Cancer | 3326 | DNA Methylation-Mediated Repression of miR-886-3p Predicts Poor Outcome of Human Small Cell Lung Cancer |
| 3285 | Collagen Prolyl Hydroxylases Are Essential for Breast Cancer Metastasis | 3336 | PFI-1, a Highly Selective Protein Interaction Inhibitor, Targeting BET Bromodomains |
| 3297 | Interleukin-1β Promotes Skeletal Colonization and Progression of Metastatic Prostate Cancer Cells with Neuroendocrine Features | 3347 | Bevacizumab-Induced Normalization of Blood Vessels in Tumors Hampers Antibody Uptake |

**PREVENTION AND EPIDEMIOLOGY**

| 3306 | Colorectal Cancer Risk Associated with Hormone Use Varies by Expression of Estrogen Receptor-β | 3316 |

**THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY**

**Précis:** This report identifies a modifier of EGFR signaling and stem cell function as an important new regulator of p53 in the most common type of lung cancer.

**Précis:** This work has important clinical implications because it demonstrates that changes associated with aggressive tumor behavior can be identified prior to the morphologic changes characteristic of aggressive prostate cancer.

**Précis:** Although collagen prolyl hydroxylases have been implicated broadly in cancer pathophysiology, their precise contributions have not been well understood, an important gap in knowledge addressed by this study.

**Précis:** This study suggests that it may be possible to target an important transcriptional regulatory domain that has been implicated in a broad number of aggressive blood cancers, as a generalizable therapeutic approach.

**Précis:** Bevacizumab treatment decreases tumor uptake of antibodies by vessel normalization, and this should be taken into account in the design of clinical trials that combine bevacizumab with other antibodies.

**Précis:** Definition of a cell surface receptor for an inhibitor of cancer cell migration suggests a novel approach to tumor suppression.

**Précis:** These findings identify a little-studied microRNA the epigenetic downregulation of which strongly affects clinical outcomes and malignant cell behaviors in small-cell lung cancer.

**Précis:** This report identifies a modifier of EGFR signaling and stem cell function as an important new regulator of p53 in the most common type of lung cancer.

**Précis:** Bevacizumab treatment decreases tumor uptake of antibodies by vessel normalization, and this should be taken into account in the design of clinical trials that combine bevacizumab with other antibodies.
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**Précis:**
- This study provides the rationale to improve the efficacy of AKT inhibitors for cancer therapy.
- This study offers proof of principle for using antiangiogenic drugs to enhance the efficacy of adoptive T-cell therapies for cancer treatment.
- 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.
- A virus that infects a large proportion of brain tumors in a mouse model.
- 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 Schauf, 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.