

BREAKING ADVANCES

- 5607 | **Highlights from Recent Cancer Literature**

REVIEWS

- 5609 | **Circular RNA and miR-7 in Cancer**
Thomas B. Hansen, Jørgen Kjems, and Christian K. Damgaard
- 5613 | **Antitumor Immunity: Easy as 1, 2, 3 with Monoclonal Bispecific Trifunctional Antibodies?**
John Maher and Antonella A. Adami

PERSPECTIVE

- 5618 | **The Relationship between Tumor Blood Flow, Angiogenesis, Tumor Hypoxia, and Aerobic Glycolysis**
Leif Østergaard, Anna Tietze, Thomas Nielsen, Kim Ryun Drasbek, Kim Mouridsen, Sune Nørhøj Jespersen, and Michael R. Horsman

PRIORITY REPORT

- 5625 | **A Novel Algorithm for Simplification of Complex Gene Classifiers in Cancer**
Raphael A. Wilson, Ling Teng, Karen M. Bachmeyer, Mei Lin Z. Bissonnette, Aliya N. Husain, David M. Parham, Timothy J. Triche, Michele R. Wing, Julie M. Gastier-Foster, Frederic G. Barr, Douglas S. Hawkins, James R. Anderson, Stephen X. Skapek, and Samuel L. Volchenboum
- Précis:* This study presents a computational tool capable of distilling metagenes and other complex classifiers down to as few as two genes, facilitating the use of molecular signatures in clinical testing.

MICROENVIRONMENT AND IMMUNOLOGY

- 5633 | **Infiltrating Macrophages Promote Prostate Tumorigenesis via Modulating Androgen Receptor-Mediated CCL4-STAT3 Signaling**
Lei-Ya Fang, Kouji Izumi, Kuo-Pao Lai, Liang Liang, Lei Li, Hiroshi Miyamoto, Wen-Jye Lin, and Chawnshang Chang
- Précis:* These important findings establish that androgen receptor signaling drives the development of early prostate tumors by modulating the function of infiltrating macrophages in the microenvironment, with attendant effects on downstream inflammatory signaling.

- 5647 | **Interferon- α Suppresses cAMP to Disarm Human Regulatory T Cells**
Nicole Bacher, Verena Raker, Claudia Hofmann, Edith Graulich, Melanie Schwenk, Ria Baumgrass, Tobias Bopp, Ulrich Zechner, Luzie Merten, Christian Becker, and Kerstin Steinbrink

Précis: These findings suggest a new application for IFN- α in cancer treatment by using it to inactivate T-regulatory cells in combination with vaccines as a means to degrade immune escape barriers that limit therapeutic responses.

- 5657 | **Adipocyte-Derived Fibroblasts Promote Tumor Progression and Contribute to the Desmoplastic Reaction in Breast Cancer**
Ludivine Bochet, Camille Lehuédé, Stéphanie Dauvillier, Yuan Yuan Wang, Béatrice Dirat, Victor Laurent, Cédric Dray, Romain Guiet, Isabelle Maridonneau-Parini, Sophie Le Gonidec, Bettina Couderc, Ghislaine Escourrou, Philippe Valet, and Catherine Muller

Précis: This article reports the discovery of a new stromal cell population in the breast tumor microenvironment that may offer unique new opportunities for targeted therapy in breast cancer.

- 5669 | **Tumor Microenvironmental Conversion of Natural Killer Cells into Myeloid-Derived Suppressor Cells**
Young-Jun Park, Boyeong Song, Yun-Sun Kim, Eun-Kyung Kim, Jung-Mi Lee, Ga-Eun Lee, Jae-Ouk Kim, Yeon-Jeong Kim, Woo-Sung Chang, and Chang-Yuil Kang

Précis: Striking findings in this study reveal new insights into how tumor cells hijack their local immune microenvironment to escape immune surveillance.

MOLECULAR AND CELLULAR PATHOBIOLOGY

- 5682 | **Reg3 β Deficiency Impairs Pancreatic Tumor Growth by Skewing Macrophage Polarization**
Meritxell Gironella, Carlos Calvo, Anna Fernández, Daniel Closa, Juan L. Iovanna, Joan Rosello-Catafau, and Emma Folch-Puy
- Précis:* The findings reported in this article may guide further clinical research based on the inhibition of the Reg3 β in the treatment pancreatic cancer.

5695 **Oncogenic Herpesvirus HHV-8 Promotes Androgen-Independent Prostate Cancer Growth**
Justin G. Mygatt, Adit Singhal, Gauthaman Sukumar, Clifton L. Dalgard, and Johnan A.R. Kaleeba
Précis: This provocative study prompts deeper investigations of the relationship between infection with human herpesvirus 8 (HHV-8) and risks of advanced prostate cancer, given findings that HHV-8 infection of primary prostate epithelial cells can drive several features of androgen-independent metastatic disease.

5709 **SOX10 Ablation Arrests Cell Cycle, Induces Senescence, and Suppresses Melanomagenesis**
Julia C. Cronin, Dawn E. Watkins-Chow, Art Incao, Joanne H. Hasskamp, Nicola Schönewolf, Lauren G. Aoude, Nicholas K. Hayward, Boris C. Bastian, Reinhard Dummer, Stacie K. Loftus, and William J. Pavan
Précis: Definition of a core determining factor for cell-cycle control in melanoma suggests a rational new direction for targeted treatment or prevention of this disease.

5719 **Epimorphin Is a Novel Regulator of the Progesterone Receptor Isoform-A**
Jamie L. Bascom, Derek C. Radisky, Eileen Koh, Jimmie E. Fata, Alvin Lo, Hidetoshi Mori, Neda Roosta, Yohei Hirai, and Mina J. Bissell
Précis: This study offers new insights into control of the expression of the progesterone receptor, a key driver and prognostic determinant in hormone-dependent breast cancers.

5730 **Rapid Induction of Lung Adenocarcinoma by Fibroblast Growth Factor 9 Signaling through FGF Receptor 3**
Yongjun Yin, Tomoko Betsuyaku, Joel R. Garbow, Jinbai Miao, Ramaswamy Govindan, and David M. Ornitz
Précis: These findings highlight a mouse model of lung adenocarcinomas that form near the bronchioalveolar duct junction that may be useful to evaluate a growing number of experimental anticancer drugs that interfere with FGF signaling.

5742 **Akt SUMOylation Regulates Cell Proliferation and Tumorigenesis**
Rong Li, Jie Wei, Cong Jiang, Dongmei Liu, Lu Deng, Kai Zhang, and Ping Wang
Précis: This important study reveals a fundamental feature for controlling the function of Akt, which is broadly activated in many human cancers where it contributes to survival, invasion, and therapeutic resistance.

5754 **c-Kit Is Suppressed in Human Colon Cancer Tissue and Contributes to L1-Mediated Metastasis**
Nancy Gavert, Anna Shvab, Michal Sheffer, Amir Ben-Shmuel, Gal Haase, Eszter Bakos, Eytan Domany, and Avri Ben-Ze'ev
Précis: This report challenges the paradigm of c-Kit as an oncogene in demonstrating the importance of its suppression in colorectal cancer for its metastasis to liver, the most common site for dissemination of this disease.

THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

5764 **Src Family Kinases as Novel Therapeutic Targets to Treat Breast Cancer Brain Metastases**
Siyuan Zhang, Wen-Chien Huang, Lin Zhang, Chenyu Zhang, Frank J. Lowery, Zhaoxi Ding, Hua Guo, Hai Wang, Suyun Huang, Aysegul A. Sahin, Kenneth D. Aldape, Patricia S. Steeg, and Dihua Yu
Précis: Inhibitors of Src family tyrosine kinases that have been examined clinically might have excellent prospects for treatment of brain metastases of breast cancer, a deadly and untreatable step in disease progression occurring in many patients with advanced disease.

5775 **KIT Signaling Governs Differential Sensitivity of Mature and Primitive CML Progenitors to Tyrosine Kinase Inhibitors**
Amie S. Corbin, Thomas O'Hare, Zhimin Gu, Ira L. Kraft, Anna M. Eiring, Jamshid S. Khorashad, Anthony D. Pomicter, Tian Y. Zhang, Christopher A. Eide, Paul W. Manley, Jorge E. Cortes, Brian J. Druker, and Michael W. Deininger
Précis: These findings may explain the limited effects that imatinib (Gleevec) has on CML progenitors, a long-standing question that appears to relate to KIT as a core element for understanding therapeutic responses to this iconic drug.

5787 **Targeting ERBB Receptors Shifts Their Partners and Triggers Persistent ERK Signaling through a Novel ERBB/EFNB1 Complex**
Paola D. Vermeer, Paul L. Colbert, Bryant G. Wiekling, Daniel W. Vermeer, and John H. Lee
Précis: This study provides a mechanistic explanation for why EGFR targeting drugs work poorly in head and neck carcinoma despite common involvement of EGFR in this cancer.

TUMOR AND STEM CELL BIOLOGY

- 5798 **Stem Cell Differentiation and Lumen Formation in Colorectal Cancer Cell Lines and Primary Tumors**
Neil Ashley, Trevor M. Yeung, and Walter F. Bodmer
Précis: An in vitro model for functional characterization of colorectal stem-like cells and their differentiation also offers applications to enable high-throughput screening for novel anticancer compounds.
- 5810 **Breast Tumor Kinase (Brk/PTK6) Is a Mediator of Hypoxia-Associated Breast Cancer Progression**
Tarah M. Regan Anderson, Danielle L. Peacock, Andrea R. Daniel, Gregory K. Hubbard, Kristopher A. Lofgren, Brian J. Girard, Alexandra Schörg, David Hoogewijs, Roland H. Wenger, Tiffany N. Seagroves, and Carol A. Lange
Précis: These findings define a kinase-based mechanism that drives the aggressive behavior of triple-negative breast cancers, which may offer a tractable target for therapy in this challenging disease.
- 5821 **ANTXR1, a Stem Cell-Enriched Functional Biomarker, Connects Collagen Signaling to Cancer Stem-like Cells and Metastasis in Breast Cancer**
Daohong Chen, Poornima Bhat-Nakshatri, Chirayu Goswami, Sunil Badve, and Harikrishna Nakshatri
Précis: These findings illuminate functional links between the tumor microenvironment and stemness functions that contribute to metastatic progression, with potential implications for understanding breast cancer pathophysiology and therapy.

5834



Comparative Expression Analysis Reveals Lineage Relationships between Human and Murine Gliomas and a Dominance of Glial Signatures during Tumor Propagation *In Vitro*

Nico V. Henriquez, Tim Forshew, Ruth Tatevossian, Matthew Ellis, Angela Richard-Loendt, Hazel Rogers, Thomas S. Jacques, Pablo Garcia Reitboeck, Kerra Pearce, Denise Sheer, Richard G. Grundy, and Sebastian Brandner

Précis: The brain tumor microenvironment strongly modifies tumor genetics that initiate disease, ultimately directing the pathway for growth dynamics, histology, and therapeutic responsiveness of brain tumors, with implications for understanding how to properly model and treat disease more effectively.

CORRECTION

5845

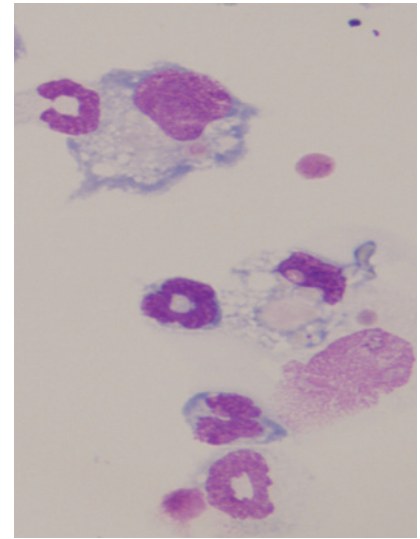
Correction: Quantitative *In Vivo* Characterization of Intracellular and Extracellular pH Profiles in Heterogeneous Tumors: A Novel Method Enabling Multiparametric pH Analysis

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ABOUT THE COVER

The importance of natural killer (NK) cells for eradicating cancer cannot be overemphasized. It was found that the tumor environment impairs the development and function of NK cells and even diminishes the number of NK cells in patients with chronic myelogenous leukemia. Here, Park and colleagues show that a part of $CD11b^{high}CD27^{high}$ NK cells obtained from tumor-bearing mice were converted into $CD11b^{+}Gr1^{+}$ MDSC phenotype by GM-CSF, while the phenotype of NK cells was retained in the presence of IL-2. For details, see article by Park and colleagues on page 5669.



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