BREAKING ADVANCES
4209  Highlights from Recent Cancer Literature

REVIEWS
4211  Immunogenetic Studies of Chronic Lymphocytic Leukemia: Revelations and Speculations about Ontogeny and Clinical Evolution
Anna Vardi, Andreas Agathangelidis, Lesley-Ann Sutton, Paolo Ghia, Richard Rosenquist, and Kostas Stamatopoulos

4217  Harnessing the Intestinal Microbiome for Optimal Therapeutic Immunomodulation

PRIORITY REPORT
4222  MYC Synergizes with Activated BRAFV600E in Mouse Lung Tumor Development by Suppressing Senescence
Vedrana Tabor, Matteo Bocci, Nyosha Alikhani, Raoul Kuiper, and Lars-Gunnar Larsson

PRécis: This study suggests a route through which senescence can be defeated to blunt a fail-safe mechanism that can restrain the powerful oncogenic effects of deregulated MYC, which underpins the malignant development of most human tumors.

CLINICAL STUDIES
4230  Pentraxin 3: A Novel Biomarker for Predicting Progression from Prostatic Inflammation to Prostate Cancer
Giovanni Stallone, Luigi Cormio, Giuseppe Stefano Netti, Barbara Infante, Oscar Selvaggio, Giuseppe Di Fino, Elena Ranieri, Francesca Bruno, Clelia Prattichizzo, Francesca Sanguedolce, Simona Tortorella, Pantaleo Bufo, Giuseppe Grandaliano, and Giuseppe Carrié

PRécis: These findings encourage further evaluation of an innate immune regulator as a noninvasive biomarker that discriminates cancer from benign hyperplasia in the prostate, perhaps reducing the need for a biopsy to diagnose prostate cancer in the primary care setting.

INTEGRATED SYSTEMS AND TECHNOLOGIES
4239  Capillary-Wall Collagen as a Biophysical Marker of Nanotherapeutic Permeability into the Tumor Microenvironment
Kenji Yokoi, Milos Kojic, Miljan Milosevic, Tomonori Tanei, Mauro Ferrari, and Arturas Ziemys

PRécis: Determining the level of blood vessel collagen in different tumor types may help guide efforts to optimize the delivery routes for nanotherapeutics.


PRécis: This study describes a novel noninvasive imaging method that can inform the status of metabolic reprogramming in tumors.

MICROENVIRONMENT AND IMMUNOLOGY
4258  Transient Ablation of Regulatory T cells Improves Antitumor Immunity in Colitis-Associated Colon Cancer
Eva Pastille, Katrin Bardini, Diana Freissner, Alexandra Adamczyk, Annika Frede, Munisch Wadwa, Dorthe von Smolinski, Stefan Kasper, Tim Sparwasser, Achim D. Gruber, Martin Schuler, Shimon Sakaguchi, Axel Roers, Werner Müller, Wiebke Hansen, Jan Buer, and Astrid M. Westendorf

PRécis: This study addresses the controversy concerning whether T-regulatory cells promote or retard the formation of colon cancers driven by chronic intestinal inflammation, with implications for how to use cancer immunotherapies that ablate T-regulatory cells in this setting.

MOLECULAR AND CELLULAR PATHOBIOLOGY
4270  Cancer Affects microRNA Expression, Release, and Function in Cardiac and Skeletal Muscle
Daohong Chen, Chirayu P. Goswami, Riesa M. Burnett, Manjushree Anjanappa, Poornima Bhat-Nakshatri, William Muller, and Harikrishna Nakshatri

PRécis: This study offers evidence that a circulating microRNA could serve as a surrogate of the effects of cancer on microRNA expression in distant organs.
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<td>Germline Mutations in BAP1 Impair Its Function in DNA Double-Strand Break Repair</td>
<td>Ismail Hassan Ismail, Riley Davidson, Jean-Philippe Gagné, Zhi Zhong Xu, Guy G. Poirier, and Michael J. Hendzel</td>
<td>Précis: This study provides a missing link in the DNA damage response and provides a mechanistic explanation for how BAP1 functions as a tumor suppressor gene.</td>
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<td>PME-1 Modulates Protein Phosphatase 2A Activity to Promote the Malignant Phenotype of Endometrial Cancer Cells</td>
<td>Ewa Wandzioch, Michelle Pusey, Amy Werda, Sophie Bail, Aishwarya Bhaskar, Mariya Nestor, Jing-Jing Yang, and Lyndi M. Rice</td>
<td>Précis: These findings identify a methyltransferase for the protein phosphatase PP2A as a modifier of cancer development and a theranostic target in endometrial tumors.</td>
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<td>Juanjuan Yin, Yen-Nien Liu, Heather Tillman, Ben Barrett, Stephen Hewitt, Kris Yaya, Lei Fang, Ross Lake, Eva Corey, Colm Morrissey, Robert Vessella, and Kathleen Kelly</td>
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<td>B-cell Expansion and Lymphomagenesis Induced by Chronic CD40 Signaling Is Strictly Dependent on CD19</td>
<td>Caroline Hojer, Samantha Frankenberger, Lothar J. Strobl, Samantha Feicht, Kristina Djermanovic, Franziska Jagdhuber, Cornelia Homig-Holzel, Uta Fench, Jürgen Ruland, Klaus Rajewsky, and Ursula Zimber-Strobl</td>
<td>Précis: CD19 acts as a coreceptor not only for the B-cell receptor but also for CD40, mediating critical survival and proliferation signals in B-cell tumors.</td>
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<td>IL6 Receptor ILR4α Regulates Metastatic Colonization by Mammary Tumors through Multiple Signaling Pathways</td>
<td>Katherine T. Venmar, Kathy J. Carter, Daniel G. Hwang, E. Ashley Dozier, and Barbara Fingleton</td>
<td>Précis: Although the IL6 receptor is usually associated with immune cells, it has a significant role in controlling the metastatic capabilities of breast tumor cells, with immediate implications for targeting this receptor as a strategy to treat advanced breast cancer.</td>
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<td>miR-21 Induces Myofibroblast Differentiation and Promotes the Malignant Progression of Breast Phyllodes Tumors</td>
<td>Chang Gong, Yan Nie, Shaohua Qu, Jian-You Liao, Xiuying Cui, Herui Yao, Yunjie Zeng, Fengxi Su, Erwei Song, and Qiang Liu</td>
<td>Précis: The perspective afforded by this study confirms the suspicion that prospects for effective immunotherapy are far more likely to emerge from targeting multiple tumor antigens than single tumor antigens.</td>
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<td>Snail Recruits Ring1B to Mediate Transcriptional Repression and Cell Migration in Pancreatic Cancer Cells</td>
<td>Jiangzhi Chen, Hong Xu, Xiouan Zou, Jiamin Wang, Yi Zhuo, Hao Chen, Baiyong Shen, Xiangpeng Deng, Aiwu Zhou, Y. Eugene Chin, Frank J. Rauscher, III, Chenghong Peng, and Zhaoyuan Hou</td>
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<td>In Vivo Regulation of Human Glutathione Transferase GSTP by Chemopreventive Agents</td>
<td>Colin J. Henderson, Aileen W. McLaren, and C. Roland Wolf</td>
<td>Précis: These findings suggest how dietary components modulate an enzyme that is critical for determining cancer susceptibility and the outcome of chemotherapy treatments.</td>
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4388  Germline Mutation of Bap1 Accelerates Development of Asbestos-Induced Malignant Mesothelioma
Jinfei Xu, Yuwaraj Kadariya, Mitchell Cheung, Jianming Pei, Jacqueline Talarchek, Eleonora Sementino, Yinfei Tan, Craig W. Menges, Kathy Q. Cai, Samuel Litvin, Hongzhuang Peng, Jayashree Karar, Frank J. Rauscher, and Joseph R. Testa
Précis: Unbiased genetic findings demonstrate that BAP1 mutation carriers are predisposed to asbestos-induced mesothelioma, a hazard of certain domiciles and workplaces, where asbestos exposure would greatly synergize with inherited mutations of BAP1 in elevating risk.

PREVENTION AND EPIDEMIOLOGY
4398  Increased Dietary Vitamin D Suppresses MAPK Signaling, Colitis, and Colon Cancer
Stacey Meeker, Audrey Seamons, Jisun Paik, Piper M. Treuting, Thea Brabb, William M. Grady, and Lillian Maggio-Price
Précis: In a mouse model of colitis and colon cancer, increasing dietary vitamin D prevented inflammatory responses involved in early stages of carcinogenesis, with potential clinical implications for chemoprevention by vitamin D.

THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY
4409  Inhibition of miR17 and miR20a by Oridonin Triggers Apoptosis and Reverses Chemoresistance by Derepressing BIM-S
Hengyou Weng, Huilin Huang, Bowen Dong, Panpan Zhao, Hui Zhou, and Lianghu Qu
Précis: These results suggest the combined use of chemotherapy drugs with a natural microRNA-targeting agent to reverse cancer chemoresistance.

4420  ASC-J9 Suppresses Renal Cell Carcinoma Progression by Targeting an Androgen Receptor–Dependent HIF2α/VEGF Signaling Pathway
Dalin He, Lei Li, Guodong Zhu, Liang Liang, Zhenfeng Guan, Luke Chang, Yuan Chen, Shuyuan Yeh, and Chawnhang Chang
Précis: These findings may explain why men have a higher incidence of kidney cancer than women, by revealing contributions of the androgen receptor that offers a new candidate target in this disease.

4431  Afatinib Enhances the Efficacy of Conventional Chemotherapeutic Agents by Eradicating Cancer Stem–like Cells
Xiao-kun Wang, Jie-hua He, Jing-hong Xu, Sheng Ye, Fang Wang, Hui Zhang, Zhen-cong Huang, Kenneth Kin Wah To, and Li-wu Fu
Précis: These findings suggest use of an approved tyrosine kinase inhibitor to improve the efficacy of conventional chemotherapeutic drugs by improving eradication of cancer stem-like cells, with immediate clinical implications.

4446  NSAID Use Reduces Breast Cancer Recurrence in Overweight and Obese Women: Role of Prostaglandin–Aromatase Interactions
Précis: This study deepens the potential connections between obesity-associated inflammation and breast cancer, with implications for a straightforward treatment and prevention strategy in estrogen-positive cancers, which are the most common clinically.

4458  Selective and Potent Akt Inhibition Triggers Anti-Myeloma Activities and Enhances Fatal Endoplasmic Reticulum Stress Induced by Proteasome Inhibition
Précis: These results offer a preclinical proof of concept for the use of a novel Akt inhibitor in treating multiple myeloma, alone or in combination with proteasome inhibitors that are currently approved for this use.
### TUMOR AND STEM CELL BIOLOGY

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**Précis:** Detailed summaries of the articles are provided for each entry. These summaries highlight the key findings and implications of each study.
ABOUT THE COVER

Expression of the multidrug resistance protein ABCG2 confers chemoresistance to CSC where it serves as a potential biomarker and therapeutic target. Afatinib, a small molecule inhibitor of the tyrosine kinases EGFR, HER2, and HER4, can enhance the antitumor effect of the DNA damaging drug topotecan in vitro and in vivo. Immunofluorescence microscopic analysis showed that afatinib significantly decreased the cell surface expression of ABCG2 in a concentration-dependent manner. For details, see article by X.-K. Wang and colleagues on page 4431.