Highlights from Recent Cancer Literature

From Integrative Genomics to Therapeutic Targets
Rachael Natrajan and Paul Wilkerson

HER2 and Breast Cancer Stem Cells: More than Meets the Eye
Hasan Korkaya and Max S. Wicha

APOBEC3 Cytidine Deaminases in Double-Strand DNA Break Repair and Cancer Promotion
Roni Nowarski and Moshe Kotler

Immune Infiltrates Are Prognostic Factors in Localized Gastrointestinal Stromal Tumors
Sylvie Rusakiewicz, Michaela Semeraro, Matthieu Sarabi, Melanie Desbois, Clara Locher, Rosa Mendez, Nadege Vimon, Angel Concha, Federico Garrido, Nicolas Isambert, Loic Chaigneau, Valerie Le Brun-Ly, Patrice Duhreuil, Isabelle Cremer, Anne Caignard, Vichnou Poirier-Colame, Axel Le Cesne, Jean-Yves Blay, and Laurence Zitvogel

Kinetic Modeling-Based Detection of Genetic Signatures That Provide Chemoresistance via the E2F1-p73/DNp73-miR-205 Network
Julio Vera, Ulf Schnitz, Xin Lai, David Engelmann, Faiz M. Khan, Olaf Wolkenhauer, and Brigitte M. Pitzler

Mathematical Modeling of Tumor Cell Proliferation Kinetics and Label Retention in a Mouse Model of Lung Cancer
Yanyan Zheng, Helen Moore, Alexandra Piryatinska, Trinidad Solis, and E. Alejandro Sweet-Cordero

Tumor–Immune Dynamics Regulated in the Microenvironment Inform the Transient Nature of Immune-Induced Tumor Dormancy
Kathleen P. Wilkie and Philip Hahnfeldt

Booster Vaccinations against Cancer Are Critical in Prophylactic but Detrimental in Therapeutic Settings
Alessia Ricupito, Matteo Grioni, Arianna Calciniotto, Rodrigo Hess Michelini, Renato Longhi, Anna Mondino, and Matteo Bellone

These findings encourage the prospective validation of immune biomarkers for optimal risk stratification of GIST, and they prompt clinical use of immunomodulators in conjunction with imatinib used to treat this disease.
### A Novel Model for Evaluating Therapies Targeting Human Tumor Vasculature and Human Cancer Stem–like Cells

Daniela Burgos-Ojeda, Karen McLean, Shoumei Bai, Heather Pulaski, Yusong Gong, Ines Silva, Karl Skorecki, Maty Tzukerman, and Ronald J. Buckanovich

**Précis:** There remains a great need for preclinical models that can more accurately predict clinical responses to novel experimental therapeutic agents in development.

### Enhanced Effector Responses in Activated CD8+ T Cells Deficient in Diacylglycerol Kinases


**Précis:** Targeting of diacylglycerol kinases offers a general approach to enhance the function of chimeric antigen receptor T cells (CART cells), a promising new strategy for cancer immunotherapy.

### SOCS3 Transactivation by PPARγ Prevents IL-17–Driven Cancer Growth

Hélène Berger, Frédérique Végran, Madjid Chikh, Federica Gilardi, Sylvain Ladoire, Hélène Bugaut, Grégoire Mignot, Fanny Chalnin, Mélanie Bruchard, Valentin Derangère, Angélique Chevriaux, Cédric Rêbé, Bernhard Ryffel, Caroline Pot, Aziz Ichhami, Béatrice Desvergne, François Ghiringhelli, and Lionel Apetoh

**Précis:** This study reveals new mechanistic insights into how inflammation supports cancer, and how blocking certain inflammatory pathways can restrict cancer.

### Dual Blockade of PD-1 and CTLA-4 Combined with Tumor Vaccine Effectively Restores T-Cell Rejection Function in Tumors

Jaikumar Duraiswamy, Karen M. Kaluza, Gordon J. Freeman, and George Coukos

**Précis:** Combined checkpoint blockade is synergistic and strongly augments the efficacy of vaccination to restore T-cell exhaustion and promote tumor rejection.

### BMP-6 in Renal Cell Carcinoma Promotes Tumor Proliferation through IL-10–Dependent M2 Polarization of Tumor-Associated Macrophages

Jae-Ho Lee, Geum Taek Lee, Seung Hye Woo, Yun-Sok Ha, Seok Joo Kwon, Wun-Jae Kim, and Isaac Yi Kim

**Précis:** Elevated IL-10 levels have been broadly associated with tumor tolerance and immune escape, but the basis for IL-10 upregulation and its critical cellular targets in tumors have not been fully clear.
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<td>3661</td>
<td>DOG1 Regulates Growth and IGFBP5 in Gastrointestinal Stromal Tumors</td>
<td>Susanne Simon, Florian Gradellaus, Loretta Ferrera, Luis Galietta, Benjamin Schwindenhammer, Thomas Mühlenberg, Georg Taeger, Grant Eilers, Juergen Treckmann, Frank Breitenbuecher, Martin Schuler, Takahiro Taguchi, Jonathan A. Fletcher, and Sebastian Bauer</td>
<td><em>Précis:</em> These findings reveal a novel oncogenic mechanism in GIST that highlights the importance of the tumor microenvironment as a therapeutic target in this disease.</td>
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<td>3665</td>
<td>Pak1 Kinase Links ErbB2 to β-Catenin in Transformation of Breast Epithelial Cells</td>
<td>Luis E. Arias-Romero, Olga Villamar-Cruz, Min Huang, Klaus P. Hoeflich, and Jonathan Chernoff</td>
<td><em>Précis:</em> Important mechanistic insights suggest new therapeutic strategies to treat breast cancers that involve HER2 overexpression.</td>
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<td>3681</td>
<td>ATR Inhibition Broadly Sensitizes Ovarian Cancer Cells to Chemotherapy Independent of BRCA Status</td>
<td>Catherine J. Huntoon, Karen S. Flatten, Andrea E. Wahner Hendrickson, Amelia M. Huehls, Shari L. Sutor, Scott H. Kaufmann, and Larry M. Karnitz</td>
<td><em>Précis:</em> Findings that directly affect clinical treatment of BRCA1/2-deficient cancer cells are provided in this study, which addresses long-standing questions of how to leverage these conditions to improve effective therapeutic targeting.</td>
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<td>3701</td>
<td>Inhibition of c-Met Reduces Lymphatic Metastasis in RIP-Tag2 Transgenic Mice</td>
<td>Barbara Sennino, Toshina Ishiguro-Oonuma, Brian J. Schriver, James G. Christensen, and Donald M. McDonald</td>
<td><em>Précis:</em> VEGF inhibition increases expression of c-Met, which can promote lymph node metastases, with consequences for understanding how resistance arises to antiangiogenic therapies.</td>
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<td>3721</td>
<td>Antioxidant Enzymes Mediate Survival of Breast Cancer Cells Deprived of Extracellular Matrix</td>
<td>Calli A. Davison, Sienna M. Durbin, Matthew R. Thau, Victoria R. Zellmer, Sarah E. Chapman, Justin Diener, Connor Watlien, Matthew Levey, and Zachary T. Schaler</td>
<td><em>Précis:</em> This study offers evidence that blocking antioxidant enzymes may help kill cancer cells that are poised to metastasize, a finding that is counterintuitive in light of a large body of literature encouraging antioxidant treatments to prevent cancer.</td>
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<td>3751</td>
<td>FGFR1 Is Essential for Prostate Cancer Progression and Metastasis</td>
<td>Feng Yang, Yongyou Zhang, Steven J. Bessler, Michael M. Ittmann, Gustavo E. Ayala, Truong D. Dang, Fen Wang, and David R. Rowley</td>
<td><em>Précis:</em> Fibroblast growth factor signaling in prostate cancer is emerging as an important area of therapeutic potential, as shown in this study of FGFR1, which suggests a rationale to attack metastatic tumors.</td>
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<td>3771</td>
<td>Androgen Receptor-Independent Function of FoxA1 in Prostate Cancer Metastasis</td>
<td>Hong-Jian Jin, Jonathan C. Zhao, Irene Ogden, Raymond C. Bergan, and Jindan Yu</td>
<td><em>Précis:</em> This study may explain why recurrent FoxA1 mutations that have been found to occur in prostate cancer contribute to malignant progression in this disease.</td>
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<td>3788</td>
<td>NF-κB Regulates Radioresistance Mediated By β1 Integrin in Three-Dimensional Culture of Breast Cancer Cells</td>
<td>Kazi Mokim Ahmed, Hui Zhang, and Catherine C. Park</td>
<td><em>Précis:</em> The results of this study suggest a novel approach to radiosensitize malignant breast cancers by targeting a forward feedback cell adhesion pathway.</td>
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<td>3812</td>
<td>ING5 Is a Tip60 Cofactor That Acetylates p53 in Response to DNA Damage</td>
<td>Nansong Liu, Jiadong Wang, Jifeng Wang, Rukai Wang, Zhongle Liu, Yao Yu, and Hong Lu</td>
<td><em>Précis:</em> This study illuminates one of the mechanisms through which cells determine whether to undergo cell-cycle arrest or apoptosis after p53 activation.</td>
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<td>3840</td>
<td>MTA1 Promotes STAT3 Transcription and Pulmonary Metastasis in Breast Cancer</td>
<td>Suresh B. Pakala, Suresh K. Rayala, Rui-An Wang, Kazutomi Ohshiro, Prakriti Mudvari, Sirigiri Divijendra Natha Reddy, Yi Zheng, Ricardo Pires, Sandra Casimiro, M. Radhakrishna Pillai, Luis Costa, and Rakesh Kumar</td>
<td><em>Précis:</em> Endogenous levels of a prometastatic transcriptional coregulator are sufficient to support its function in metastasis, whether or not it is overexpressed in cancer.</td>
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DDB2 Suppresses Epithelial-to-Mesenchymal Transition in Colon Cancer
Nilotpal Roy, Prashant V. Bommi, Uppoor G. Bhat, Shaumick Bhattacharjee, Indira Elangovan, Jing Li, Krushna C. Patra, Dragana Kopanja, Adam Blunier, Richard Benya, Srilata Bagchi, and Pradip Raychaudhuri

Précis: A nucleotide excision repair protein is found to function as an inhibitor of EMT, a phenotypic change in transformed epithelial cells that facilitates invasion and metastasis, suggesting a direct link between these processes during tumorigenesis.

GDNF–RET Signaling in ER-Positive Breast Cancers Is a Key Determinant of Response and Resistance to Aromatase Inhibitors
Andrea Morandi, Lesley-Ann Martin, Qiong Gao, Sunil Pancholi, Alan Mackay, David Robertson, Marketa Zvelebil, Mitch Dowsett, Ivan Plaza-Menacho, and Clare M. Isacke

Précis: This study addresses the clinical challenge of therapeutic resistance in oncology, in this case by defining an important tractable pathway of resistance to aromatase inhibitors used to fight ER-positive breast cancer.

Sox2 Requirement in Sonic Hedgehog-Associated Medulloblastoma
Julia Ahlfeld, Rebecca Favaro, Pierfrancesco Pagella, Hans A. Kretzschmar, Silvia Nicolis, and Ulrich Schüller

Précis: This study links a core pathogenic driver of an aggressive pediatric tumor to a central regulator of cancer stem-like function, with potential therapeutic implications.