REVIEWS

AXL-Driven EMT State as a Targetable Conduit in Cancer
Jane Antony and Ruby Yun-Ju Huang

RNA Editing in Pathogenesis of Cancer
Bora E. Baysal, Shraddha Sharma, Seyedsasan Hashemikhabir, and Sarath Chandra Janga

PERSPECTIVE

Cancer Cell–Autonomous Parainflammation Mimics Immune Cell Infiltration
Audrey Lasry, Dvir Aran, Atul J. Butte, and Yinson Ben-Neriah

MOLECULAR AND CELLULAR PATHOBIOLOGY

Oncogenic RAS Regulates Long Noncoding RNA Orilnc1 in Human Cancer
Dongmei Zhang, Gao Zhang, Xiaowen Hu, Lawrence Wu, Yi Feng, Sidan He, Youyou Zhang, Zhongyi Hu, Lu Yang, Tian Tian, Weiting Xu, Zhi Wei, Yiling Lu, Keith T. Flaherty, Xiaomin Zhong, Gordon B. Mills, Phyllis A. Gimotty, Xiaowei Xu, Meenhard Herlyn, and Lin Zhang

ETV1-Positive Cells Give Rise to BRAFV600E-Mutant Gastrointestinal Stromal Tumors
Leili Ran, Devan Murphy, Jessica Sher, Zhen Cao, Shangjian Wang, Edward Walczak, Youxin Guan, Yuanyuan Xie, Shipta Shukla, Yu Zhan, Cristina R. Antonescu, Yu Chen, and Ping Chi

NEMO, a Transcriptional Target of Estrogen and Progesterone, Is Linked to Tumor Suppressor PML in Breast Cancer
Hanah S. Elsarraj, Kelli E. Valdez, Yan Hong, Sandra L. Grimm, Lawrence R. Ricci, Fang Fan, Ossama Tawfik, Lisa May, Therese Cusick, Marc Inciardi, Mark Redick, Jason Gatewood, Onalisa Winblad, Susan Hilsenbeck, Dean P. Edwards, Christy R. Hagan, Andrew K. Godwin, Carol Fabian, and Fariba Behbod

TUMOR AND STEM CELL BIOLOGY

ATOH1 Promotes Leptomeningeal Dissemination and Metastasis of Sonic Hedgehog Subgroup Medulloblastomas

An miRNA Expression Signature for the Human Colonic Stem Cell Niche Distinguishes Malignant from Normal Epithelia
Vignesh Viswanathan, Shirish Damle, Tao Zhang, Lynn Opdenaker, Shirin Modarai, Monica Accerbi, Skye Schmidt, Pamela Green, Deni Galileo, Juan Palazzo, Jeremy Fields, Sepehr Haghighat, Isidore Rigoutsos, Greg Gonye, and Bruce M. Boman

Akt Signaling Is Sustained by a CD44 Splice Isoform–Mediated Positive Feedback Loop
Sali Liu and Chonghui Cheng

Précis: This study offers a useful in vivo model of human sporadic forms of BRCA1-mutant GIST to help unravel its pathogenesis and therapeutic response to novel experimental agents.
A Systematic Analysis of Oncogenic Gene Fusions in Primary Colon Cancer


Précis: This deep sequencing study of stage I-III colon cancer specimens identifies novel oncogenic gene fusions in colorectal cancer that may drive malignant progression and offer new targets for personalized therapy.

Mdm2 Is Required for Survival and Growth of p53-Deficient Cancer Cells

Kyle P. Feeley, Clare M. Adams, Ramkrishna Mitra, and Christine M. Eischen

Précis: By refuting the prevailing view that cells lacking Mdm2 can survive if p53 is also absent, this important study provides a therapeutic rationale for targeting Mdm2 to eliminate p53-null lymphomas and sarcomas.

Therapeutic Rationale to Target Highly Expressed CDK7 Conferring Poor Outcomes in Triple-Negative Breast Cancer

Bo Li, Triona Ni Chonghaile, Yue Fan, Stephen F. Madden, Rut Klinger, Aislind O’Connor, Louise Walsh, Gillian O’Hurley, Girish Mallya Udupi, Jesuchristopher Joseph, Finbar Tarrant, Emer Conroy, Alexander Gaber, Suet-Feung Chin, Helen A. Bardwell, Elena Provenzano, John Crown, Thierry Dubois, Sabine Linn, Karin Jirstrom, Carlos Caldas, Darran P. O’Connor, and William M. Gallagher

Précis: This potentially seminal study offers preclinical proof of concept for combining CDK7 and BCL-2/BCL-XL inhibitors as a mechanism-based therapeutic strategy to improve the management of aggressive triple-negative breast cancers, which still lack effective biomarkers and precision treatment approaches.

Exosome-Derived miR-25-3p and miR-92a-3p Stimulate Liposarcoma Progression

Lucia Casadei, Federica Calore, Chad J. Creighton, Michele Guiscini, Sara Barre, O. Hans Iwenofu, Abeba Zewdu, Danielle A. Braggio, Kate Lynn Hill, Paolo Fadda, Francesca Lovat, Gonzalo Lopez, Pierluigi Gasparini, James L. Chen, Raghil D. Kladney, Gustavo Leone, Dina Lev, Carlo M. Croce, and Raphael E. Pollock

Précis: Two extracellular vesicle-derived microRNAs are found to drive liposarcoma progression by stimulating the secretion of proinflammatory IL6 from tumor-associated macrophages, offering new therapeutic opportunities in this cancer setting.

Nicotinic Acid Phosphoribosyltransferase Regulates Cancer Cell Metabolism, Susceptibility to NAMPT Inhibitors, and DNA Repair

Francesco Piacenti, Irene Caffa, Silvia Raver, Giovanna Sociali, Mario Passalaqua, Valerio G. Vellone, Pamela Becherini, Daniele Reverberi, Fiorello Monaccelli, Alberto Ballesteros, Patrizio Odetti, Antonia Cagnetta, Michele Cea, Aimable Nahirama, Michel Duchosal, Santina Buzzzone, and Alessio Nencioni

Précis: Targeting a second enzyme involved in NAD^+ biosynthesis overcomes the resistance to NAMPT inhibitors observed in clinical trials, offering a path toward new therapies.

CHK1 Inhibition in Small-Cell Lung Cancer Produces Single-Agent Activity in Biomarker-Defined Disease Subsets and Combination Activity with Cisplatin or Olaparib

Triparna Sen, Pan Tong, C. Allison Stewart, Sandra Cristea, Aly Valliani, David S. Shames, Abena B. Redwood, You Hong Fan, Lerong Li, Bonnie S. Glisson, John D. Minna, Julien Sage, Don L. Gibbons, Helen Piwnica-Worms, John V. Heymach, Jing Wang, and Lauren Avrett Byers

Précis: These findings demonstrate potent antitumor activity of targeting CHK1 in chemosensitive and chemoresistant models of small cell lung cancer, especially those with MYC amplification or overexpression.

Venetoclax Synergizes with Radiotherapy for Treatment of B-cell Lymphoma


Précis: Combining the BCL-2 inhibitor venetoclax with radioimmunotherapy yields a synergistic therapeutic response in preclinical models of three lymphoma subtypes, with optimal dosing curing all mice with no detectable toxicity.
Oncolytic Adenovirus and Tumor-Targeting Immune Modulatory Therapy Improve Autologous Cancer Vaccination

Hong Jiang, Yisel Rivera-Molina, Candelaria Gomez-Manzano, Karen Clise-Dwyer, Laura Bover, Luis M. Vence, Ying Yuan, Frederick F. Lang, Carlo Toniatti, Mohammad B. Hossain, and Juan Fueyo

Précis: Combining an oncolytic virus with an immune checkpoint drug creates an in situ autologous vaccine effect, establishing a tumor-specific treatment that is both efficacious and durable.

INTEGRATED SYSTEMS AND TECHNOLOGIES

Pharmacokinetics and Drug Interactions Determine Optimum Combination Strategies in Computational Models of Cancer Evolution

Shaon Chakrabarti and Franziska Michor

Précis: In seeking to improve responses to combination therapy, a model that incorporates parameters for cancer evolution suggests variations in dosing regimens that can safely increase therapeutic efficacy, with immediate clinical implications.

Somatic Mutations Drive Distinct Imaging Phenotypes in Lung Cancer

Emmanuel Rios Velazquez, Chintan Parmar, Ying Liu, Thibaud P. Cortier, Giselle Cruz, Olya Stringfield, Zhaoxiang Ye, Mike Makrigiorgos, Fiona Fennessy, Raymond H. Mak, Robert Gillies, John Quackenbush, and Hugo J.W.L. Aerts

Précis: The findings of this important study add to the understanding of the biological basis for tumor phenotypes, which can be quantified by medical imaging.

Noninvasive Interrogation of DLL3 Expression in Metastatic Small Cell Lung Cancer


Précis: A companion diagnostic PET imaging agent can enable clinicians to rapidly identify small cell lung cancer patients most likely to benefit from treatment with a Notch ligand-targeting therapy, despite low levels of ligand expression on the surface of the cancer cells.

Highly Accurate Detection of Cancer In Situ with Intraoperative, Label-Free, Multimodal Optical Spectroscopy

Michael Jermy, Jeanne Mercier, Kelly Aubertin, Joannie Desroches, Kirk Urmey, Jason Karananchandani, Eric Marple, Marie-Christine Gaiot, Frederic Leblond, and Kevin Petecca

Précis: These findings present the design, development, and clinical testing of a cancer detection system of nearly perfect accuracy that can improve surgical resections while in the operating room.

Androgens Are Differentially Associated with Ovarian Cancer Subtypes in the Ovarian Cancer Cohort Consortium


Précis: These findings show significant differences in the associations between circulating androgen concentrations and invasive ovarian cancer risk by subtype, underscoring the importance of examining etiologic differences by subtype.

Correction: MYC Mediates Large Oncosome-Induced Fibroblast Reprogramming in Prostate Cancer

3961

Correction: Wnt5a Drives an Invasive Phenotype in Human Glioblastoma Stem-like Cells

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ABOUT THE COVER

The image shows a single breast tumor tissue core derived from a tissue microarray of patients with triple-negative breast cancer that was immunohistochemically stained with an anti-CDK7 antibody. Brown staining in cell nuclei represents positive expression of CDK7 protein, allowing for further analysis of CDK7 positivity using a nuclear algorithm. The stained tumor tissue was recorded using a digital slide scanning device. For details, see article by Li and colleagues on page 3834.