Highlights from Recent Cancer Literature

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

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

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

ATOH1 Promotes Leptomeningeal Dissemination and Metastasis of Sonic Hedgehog Subgroup Medulloblastomas

Précis: These findings illuminate a metastasis pathway in the common pediatric brain tumor medulloblastoma, which offers possible theranostic opportunities.

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, Srephag Haghghat, Isidore Rigoutsos, Greg Gomye, and Bruce M. Boman

Précis: By defining miRNAs that sustain stem cells in the crypts of normal colon tissue, this study illuminates a pivotal mechanism through which cancer stem-like cells may be created to seed colorectal cancers.

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

Précis: This important paper describes the discovery of a positive feedback mechanism that sustains PI3K/Akt signaling in tumor cells that lack PI3K/Akt mutations, illuminating the nearly universal role this pathway has in tumor cell survival.

NEMO, a Transcriptional Target of Estrogen and Progesterone, Is Linked to Tumor Suppressor PML in Breast Cancer
Hanan S. Elsarraj, Kelli E. Valdez, Yan Hong, Sandra L. Grimm, Lawrence R. Ricci, Fang Fan, Osasama 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

Précis: These findings challenge the notion of the detrimental role of estrogen plus progesterone in breast cancer, revealing a signaling cascade that upregulates the tumor suppressor protein PML in response to both hormones.
**A Systematic Analysis of Oncogenic Gene Fusions in Primary Colon Cancer**
Wigard P. Kloosterman, Robert R.I. Coebergh van den Braak, Mark Pieterse, Markus J. van Roosmalen, Anieta M. Sieruwerts, Christiaan Stangl, Ronne Brunekeveer, Zarina S. Lalmahomed, Salo Ooof, Anne van Galen, Marcel Smid, Armel Lefebvre, Fried Zwartkruis, John W.M. Martens, John A. Foekens, Katharina Biermann, Marco J. Koudijs, Jan N.M. Ijzermans, and Emile E. Voest

**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.

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**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.

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

**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.

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**Exosome-Derived miR-25-3p and miR-92a-3p Stimulate Liposarcoma Progression**
Lucia Casadei, Federica Calore, Chad J. Creighton, Michele Guercini, Karla Batte, O. Hans Iwenofu, Abeba Zewdu, Danielle A. Braggio, Kate Lynn Bill, Paolo Fadda, Francesca Lovat, Gonzalo Lopez, Pierluigi Gasparini, James L. Chen, Raleigh D. Kladney, Gustavo Leone, Dina Lev, Carlo M. Croce, and Raphael E. Pollock

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

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**Nicotinic Acid Phosphoribosyltransferase Regulates Cancer Cell Metabolism, Susceptibility to NAMPT Inhibitors, and DNA Repair**
Francesco Placenta, Irene Caffa, Silvia Ravera, Giovanna Sociali, Mario Passalacqua, Valerio G. Vellone, Pamela Becherini, Daniela Reverberi, Fiambretta Monacelli, Alberto Ballesteros, Patrizio Odetti, Antonia Cagnetta, Michele Cea, Aimable Nahimana, Michel Duchosal, Santina Brauzzone, 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.

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**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 Averett 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.

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**Venetoclax Synergizes with Radiotherapy for Treatment of B-cell Lymphomas**

**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. Coroller, Giselle Cruz, Olya Stringfield, Zhaoxiang Ye, Mike Makrigiorgos, Fiona Fennousy, 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.

PREVENTION AND EPIDEMIOLOGY

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.

CORRECTIONS

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

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.
Cancer Res 2017;77:3723-3962.

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