

# Table of Contents

February 2019 • Volume 17 • Number 2

**Highlights of This Issue 335****REVIEW**

- 337** Internalization of Exosomes through Receptor-Mediated Endocytosis  
Amber Gonda, Janviere Kabagwira, Girish N. Senthil, and Nathan R. Wall

*MCR RapidIMPACT*

- 348** Cyclooxygenase-2 Inhibition Potentiates the Efficacy of Vascular Endothelial Growth Factor Blockade and Promotes an Immune Stimulatory Microenvironment in Preclinical Models of Pancreatic Cancer  
 Yuqing Zhang, Amanda Kirane, Huocong Huang, Noah B. Sorrelle, Francis J. Burrows, Michael T. Dellinger, and Rolf A. Brekken

**CELL CYCLE AND SENESCENCE**

- 356** AXL Is a Putative Tumor Suppressor and Dormancy Regulator in Prostate Cancer  
 Haley D. Axelrod, Kenneth C. Valkenburg, Sarah R. Amend, Jessica L. Hicks, Princy Parsana, Gonzalo Torga, Angelo M. DeMarzo, and Kenneth J. Pienta

- 370** UNC-45A Is a Novel Microtubule-Associated Protein and Regulator of Paclitaxel Sensitivity in Ovarian Cancer Cells  
Ashley Mooneyham, Yoshie Iizuka, Qing Yang, Courtney Coombes, Mark McClellan, Vijayalakshmi Shridhar, Edith Emmings, Mihir Shetty, Liqiang Chen, Teng Ai, Joyce Meints, Michael K. Lee, Melissa Gardner, and Martina Bazzaro

**CELL DEATH AND SURVIVAL**

- 384** Inhibiting Integrin  $\beta 8$  to Differentiate and Radiosensitize Glioblastoma-Initiating Cells  
Laure Malric, Sylvie Monferran, Caroline Delmas, Florent Arnauduc, Perrine Dahan, Sabrina Boyrie, Pauline Deshors, Vincent Lubrano, Dina Ferreira Da Mota, Julia Gilhodes, Thomas Filleron, Aurore Siegfried, Solène Evrard, Aline Kowalski-Chauvel, Elizabeth Cohen-Jonathan Moyal, Christine Toulas, and Anthony Lemarié

- 398**  $\alpha_v\beta_3$  Integrin Mediates Radioresistance of Prostate Cancer Cells through Regulation of Survivin  
 Tao Wang, Jiayi Huang, Mai Vue, Michael R. Alavian, Hira Lal Goel, Dario C. Altieri, Lucia R. Languino, and Thomas J. FitzGerald

- 409** PARP1 Trapping by PARP Inhibitors Drives Cytotoxicity in Both Cancer Cells and Healthy Bone Marrow  
 Todd A. Hopkins, William B. Ainsworth, Paul A. Ellis, Cherrie K. Donawho, Enrico L. DiGiammarino, Sanjay C. Panchal, Vivek C. Abraham, Mikkel A. Algire, Yan Shi, Amanda M. Olson, Eric F. Johnson, Julie L. Wilsbacher, and David Maag

- 420** Loss of Fas Expression and Function Is Coupled with Colon Cancer Resistance to Immune Checkpoint Inhibitor Immunotherapy  
Wei Xiao, Mohammed L. Ibrahim, Priscilla S. Redd, John D. Klement, Chunwan Lu, Dafeng Yang, Natasha M. Savage, and Kebin Liu

**DNA DAMAGE AND REPAIR**

- 431** PARP Inhibition Induces Enrichment of DNA Repair-Proficient CD133 and CD117 Positive Ovarian Cancer Stem Cells  
 Chiara Bellio, Celeste DiGloria, Rosemary Foster, Kaitlyn James, Panagiotis A. Konstantinopoulos, Whitfield B. Growdon, and Bo R. Rueda

**GENOMICS**

- 446** Genetic and Epigenetic Determinants of Aggressiveness in Cribiform Carcinoma of the Prostate  
 Habiba Elfandy, Joshua Armenia, Filippo Pederzoli, Eli Pullman, Nelma Pertega-Gomes, Nikolaus Schultz, Kartik Viswanathan, Aram Vosoughi, Mirjam Blattner, Konrad H. Stöpsack, Giorgia Zadra, Kathryn L. Penney, Juan Miguel Mosquera, Svitlana Tyekucheva, Lorelei A. Mucci, Christopher Barbieri, and Massimo Loda

- 457** Frequent ESR1 and CDK Pathway Copy-Number Alterations in Metastatic Breast Cancer  
Ahmed Basudan, Nolan Priedigkeit, Ryan J. Hartmaier, Ethan S. Sokol, Amir Bahreini, Rebecca J. Watters, Michelle M. Boisen, Rohit Bhargava, Kurt R. Weiss, Maria M. Karsten, Carsten Denkert, Jens-Uwe Blohmer, Jose P. Leone, Ronald L. Hamilton, Adam M. Brufsky, Esther Elishaev, Peter C. Lucas, Adrian V. Lee, and Steffi Oesterreich

# Table of Contents

- 469 High Prevalence of a Hotspot of Noncoding Somatic Mutations in Intron 6 of *GPR126* in Bladder Cancer**  
Simon Garinet, Géraldine Pignot, Sophie Vacher, Constance Le Goux, Anne Schnitzler, Walid Chemlali, Nanor Sirab, Nicolas Barry Delongchamps, Marc Zerbib, Mathilde Sibony, Yves Allory, Diane Damotte, and Ivan Bieche
- 476 Molecular Correlates of Metastasis by Systematic Pan-Cancer Analysis Across The Cancer Genome Atlas**  
Fengju Chen, Yiqun Zhang, Sooryanarayana Varambally, and Chad J. Creighton
- 488 Mitochondrial DNA Mutations are Associated with Ulcerative Colitis Preneoplasia but Tend to be Negatively Selected in Cancer**  
Kathryn T. Baker, Daniela Nachmanson, Shilpa Kumar, Mary J. Emond, Cigdem Ussaklı, Teresa A. Brentnall, Scott R. Kennedy, and Rosa Ana Risques
- 499 Activation of AXL as a Preclinical Acquired Resistance Mechanism Against Osimertinib Treatment in EGFR-Mutant Non-Small Cell Lung Cancer Cells**  
Kei Namba, Kazuhiko Shien, Yuta Takahashi, Hidejiro Torigoe, Hiroki Sato, Takahiro Yoshioka, Tatsuaki Takeda, Eisuke Kurihara, Yusuke Ogoshi, Hiromasa Yamamoto, Junichi Soh, Shuta Tomida, and Shinichi Toyooka
- 544 c-MYC Drives Breast Cancer Metastasis to the Brain, but Promotes Synthetic Lethality with TRAIL**  
Ho Yeon Lee, Junghwa Cha, Seon Kyu Kim, Jun Hyung Park, Ki Hoon Song, Pilnam Kim, and Mi-Young Kim
- 555 DNA Damage, Liver Injury, and Tumorigenesis: Consequences of *DDX3X* Loss**  
Chieh-Hsiang Chan, Chun-Ming Chen, Yan-Hwa Wu Lee, and Li-Ru You
- 567 *Sleeping Beauty* Screen Identifies *RREB1* and Other Genetic Drivers in Human B-cell Lymphoma**  
Eric P. Rahrmann, Natalie K. Wolf, George M. Otto, Lynn Heltemes-Harris, Laura B. Ramsey, Jingmin Shu, Rebecca S. LaRue, Michael A. Linden, Susan K. Rathe, Timothy K. Starr, Michael A. Farrar, Branden S. Moriarity, and David A. Largaespada
- 583 *PTPN11* Plays Oncogenic Roles and Is a Therapeutic Target for *BRAF* Wild-Type Melanomas**  
Kristen S. Hill, Evan R. Roberts, Xue Wang, Ellen Marin, Taeun D. Park, Sorany Son, Yuan Ren, Bin Fang, Sean Yoder, Sungjune Kim, Lixin Wan, Amod A. Sarnaik, John M. Koomen, Jane L. Messina, Jamie K. Teer, Youngchul Kim, Jie Wu, Charles E. Chalfant, and Minjung Kim
- 594 Modulation of Mutant *Kras*<sup>G12D</sup>-Driven Lung Tumorigenesis *In Vivo* by Gain or Loss of *PCDH7* Function**  
 Xiaorong Zhou, Mahesh S. Padanad, Bret M. Evers, Bethany Smith, Nicole Novaresi, Shruthy Suresh, James A. Richardson, Emily Stein, Jingfei Zhu, Robert E. Hammer, and Kathryn A. O'Donnell
- 604 CCR2 Chemokine Receptors Enhance Growth and Cell-Cycle Progression of Breast Cancer Cells through SRC and PKC Activation**  
Min Yao, Wei Fang, Curtis Smart, Qingting Hu, Shixia Huang, Nehemiah Alvarez, Patrick Fields, and Nikki Cheng
- 618 PDCD4 Is an Androgen-Repressed Tumor Suppressor that Regulates Prostate Cancer Growth and Castration Resistance**  
Kenji Zennami, Su Mi Choi, Ross Liao, Ying Li, Wikum Dinalankara, Luigi Marchionni, Fatema H. Rafiqi, Akira Kurozumi, Koji Hatano, and Shawn E. Lupold
- ONCOGENES AND TUMOR SUPPRESSORS**
- 508 RNA-Binding Protein HuR Regulates Both Mutant and Wild-Type IDH1 in IDH1-Mutated Cancer**  
Mahsa Zarei, Shruti Lal, Ali Vaziri-Gohar, Kevin O'Hayer, Venugopal Gunda, Pankaj K. Singh, Jonathan R. Brody, and Jordan M. Winter
- 521 Oncogenic STRAP Supports Hepatocellular Carcinoma Growth by Enhancing Wnt/β-Catenin Signaling**  
Wenhui Wang, Shan Li, Pengyu Liu, Kostandinos Sideras, Harmen J.G. van de Werken, Marieke van der Heide, Wanlu Cao, Marla Lavrijsen, Maikel P. Peppelenbosch, Marco Bruno, Qiuwei Pan, and Ron Smits
- 532 The FGFR1 V561M Gatekeeper Mutation Drives AZD4547 Resistance Through STAT3 Activation and EMT**  
Molly R. Ryan, Christal D. Sohl, BeiBei Luo, and Karen S. Anderson



# Table of Contents

## SIGNAL TRANSDUCTION

- 628** Epigenetic Silencing of *THY1* Tracks the Acquisition of the Notch1–EGFR Signaling in a Xenograft Model of CD44<sup>+</sup>/CD24<sup>low</sup>/CD90<sup>+</sup> Myoepithelial Cells

Micaela Montanari, Maria Rita Carbone, Luigi Coppola, Mario Giuliano, Grazia Arpino, Rossella Lauria, Agostina Nardone, Felicia Leccia, Meghana V. Trivedi, Corrado Garbi, Roberto Bianco, Enrico V. Avvedimento, Sabino De Placido, and Bianca Maria Veneziani

- 642** Efficacy of a Covalent ERK1/2 Inhibitor, CC-90003, in KRAS-Mutant Cancer Models Reveals Novel Mechanisms of Response and Resistance

Ida Aronchik, Yumin Dai, Matt Labenski, Carmen Barnes, Terri Jones, Lixin Qiao, Lisa Beebe, Mehnaz Malek, Winfried Elis, Tao Shi, Konstantinos Mavrommatis, Gordon L. Bray, and Ellen H. Filvaroff

- 655** Nuclear E-Cadherin Acetylation Promotes Colorectal Tumorigenesis via Enhancing  $\beta$ -Catenin Activity

Yongxu Zhao, Tao Yu, Nan Zhang, Jianxia Chen, Peng Zhang, Shuang Li, Lijun Luo, Zhenling Cui, Yue Qin, and Feng Liu

 AC icon indicates AuthorChoice

For more information please visit [www.aacrjournals.org](http://www.aacrjournals.org)

## ABOUT THE COVER

In this issue (beginning on page 370), Mooneyham and colleagues demonstrate that UNC-45A is a novel microtubule-associated protein that antagonizes the effect of paclitaxel in ovarian cancer cells, leading to chemoresistance. The immunofluorescent cover image shows strong co-localization between UNC-45A (red) and alpha tubulin (green) in synchronized metaphase HeLa cells. This finding was key in the later identification of UNC-45A as a novel microtubule-associated protein that functions to destabilize microtubules and confer paclitaxel resistance. Together, this study reveals UNC-45A as a promising biomarker and molecular target for paclitaxel-resistant human cancers.

Cover image by Mooneyham not featured in article.

