

## Highlights of This Issue 1973

## REVIEW

- 1975** Durability of Kinase-Directed Therapies—A Network Perspective on Response and Resistance  
Brion W. Murray and Nichol Miller

## SMALL MOLECULE THERAPEUTICS

- 1985** Heat Shock Protein 90 Is a Potential Therapeutic Target in Cholangiocarcinoma  
Tomoki Shirota, Hidenori Ojima, Nobuyoshi Hiraoka, Kazuaki Shimada, Hirofumi Rokutan, Yasuhito Arai, Yae Kanai, Shinichi Miyagawa, and Tatsuhiro Shibata
- 1994** Small Molecule Inhibition of MDM2–p53 Interaction Augments Radiation Response in Human Tumors  
Lauryn R. Werner, Shyhmin Huang, David M. Francis, Eric A. Armstrong, Fang Ma, Chunrong Li, Gopal Iyer, Jude Canon, and Paul M. Harari
- 2004** LY2606368 Causes Replication Catastrophe and Antitumor Effects through CHK1-Dependent Mechanisms  
Constance King, H. Bruce Diaz, Samuel McNeely, Darlene Barnard, Jack Dempsey, Wayne Blosser, Richard Beckmann, David Barda, and Mark S. Marshall
- 2014** Small Molecule Inhibition of MERTK Is Efficacious in Non–Small Cell Lung Cancer Models Independent of Driver Oncogene Status  
Christopher T. Cummings, Weihe Zhang, Kurtis D. Davies, Gregory D. Kirkpatrick, Dehui Zhang, Deborah DeRyckere, Xiaodong Wang, Stephen V. Frye, H. Shelton Earp, and Douglas K. Graham
- 2023** Altiratinib Inhibits Tumor Growth, Invasion, Angiogenesis, and Microenvironment-Mediated Drug Resistance via Balanced Inhibition of MET, TIE2, and VEGFR2  
Bryan D. Smith, Michael D. Kaufman, Cynthia B. Leary, Benjamin A. Turner, Scott C. Wise, Yu Mi Ahn, R. John Booth, Timothy M. Caldwell, Carol L. Ensinger, Molly M. Hood, Wei-Ping Lu, Tristan W. Patt, William C. Patt, Thomas J. Rutkoski, Thiwanka Samarakoon, Hanumaiah Telikepalli, Lakshminarayana Vogeti, Subha Vogeti, Karen M. Yates, Lawrence Chun, Lance J. Stewart, Michael Clare, and Daniel L. Flynn

- 2035** AKT Antagonist AZD5363 Influences Estrogen Receptor Function in Endocrine-Resistant Breast Cancer and Synergizes with Fulvestrant (ICI182780) *In Vivo*  
Ricardo Ribas, Sunil Pancholi, Stephanie K. Guest, Elisabetta Marangoni, Qiong Gao, Aurélie Thuleau, Nikiana Simigdala, Urszula M. Polanska, Hayley Campbell, Aradhana Rani, Gianmaria Liccardi, Stephen Johnston, Bary R. Davies, Mitch Dowsett, and Lesley-Ann Martin

## LARGE MOLECULE THERAPEUTICS

- 2049** Antitumor Effects of MEHD7945A, a Dual-Specific Antibody against EGFR and HER3, in Combination with Radiation in Lung and Head and Neck Cancers  
Chunrong Li, Shyhmin Huang, Eric A. Armstrong, David M. Francis, Lauryn R. Werner, Mark X. Sliwkowski, Albert van der Kogel, and Paul M. Harari
- 2060** Cyclophosphamide-Mediated Tumor Priming for Enhanced Delivery and Antitumor Activity of HER2-Targeted Liposomal Doxorubicin (MM-302)  
Elena Geretti, Shannon Curtis Leonard, Nancy Dumont, Helen Lee, Jinzi Zheng, Raquel De Souza, Daniel F. Gaddy, Christopher W. Espelin, David A. Jaffray, Victor Moyo, Ulrik B. Nielsen, Thomas J. Wickham, and Bart S. Hendriks
- 2072** Heregulin–ErbB3-Driven Tumor Growth Persists in PI3 Kinase Mutant Cancer Cells  
Defne Yazar, Johanna Lahdenranta, William Kubasek, Ulrik B. Nielsen, and Gavin MacBeath
- 2081** Anti-Endosialin Antibody–Drug Conjugate: Potential in Sarcoma and Other Malignancies  
Cecile Rouleau, Diego A. Gianolio, Robert Smale, Stephanie D. Roth, Roy Krumbholz, Jay Harper, Kenneth J. Munroe, Tessa L. Green, Bruce C. Horten, Steven M. Schmid, and Beverly A. Teicher

## CANCER BIOLOGY AND SIGNAL TRANSDUCTION

- 2090** CDK1-Mediated SIRT3 Activation Enhances Mitochondrial Function and Tumor Radioresistance  
Rui Liu, Ming Fan, Demet Candas, Lili Qin, Xiaodi Zhang, Angela Eldridge, June X. Zou, Tieqiao Zhang, Shuaib Juma, Cuihong Jin, Robert F. Li, Julian Perks, Lun-Quan Sun, Andrew T.M. Vaughan, Chun-Xu Hai, David R. Gius, and Jian Jian Li

# Table of Contents

**2103** STAT1 Activation Is Enhanced by Cisplatin and Variably Affected by EGFR Inhibition in HNSCC Cells  
Nicole C. Schmitt, Sumita Trivedi, and Robert L. Ferris


**2112** Nicotine Induces Tumor Growth and Chemoresistance through Activation of the PI3K/Akt/mTOR Pathway in Bladder Cancer  
Kazuyuki Yuge, Eiji Kikuchi, Masayuki Hagiwara, Yota Yasumizu, Nobuyuki Tanaka, Takeo Kosaka, Akira Miyajima, and Mototsugu Oya

**2121** USP44<sup>+</sup> Cancer Stem Cell Subclones Contribute to Breast Cancer Aggressiveness by Promoting Vasculogenic Mimicry  
Tiejun Liu, Baocun Sun, Xiulan Zhao, Yanlei Li, Xueming Zhao, Ying Liu, Zhi Yao, Qiang Gu, Xueyi Dong, Bing Shao, Xian Lin, Fang Liu, and Jindan An

**2132** Ingenol Mebutate Signals via PKC/MEK/ERK in Keratinocytes and Induces Interleukin Decoy Receptors IL1R2 and IL13RA2  
Sandra N. Freiburger, Phil F. Cheng, Guergana Iotzova-Weiss, Johannes Neu, Qinxu Liu, Piotr Dziunycz, John R. Zibert, Reinhard Dummer, Kristen Skak, Mitchell P. Levesque, and Günther F.L. Hofbauer

**2143** Histone Deacetylase Inhibitors Inhibit Rhabdomyosarcoma by Reactive Oxygen Species–Dependent Targeting of Specificity Protein Transcription Factors  
Erik Hedrick, Lisa Crose, Corinne M. Linardic, and Stephen Safe

## MODELS AND TECHNOLOGIES

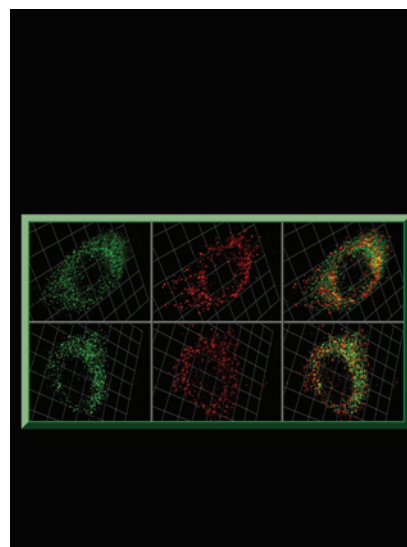
**2154** Identification of Circadian Determinants of Cancer Chronotherapy through *In Vitro* Chronopharmacology and Mathematical Modeling  
 Sandrine Dulong, Annabelle Ballesta, Alper Okyar, and Francis Lévi

 AC icon indicates Author Choice

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

## ABOUT THE COVER

SIRT3, a member of the sirtuin family of protein deacetylases, prevents cell aging by enhancing metabolic homeostasis through regulation of mitochondrial protein deacetylation. How it functions in tumor response to anticancer therapy is unknown. Liu and colleagues discovered that *SIRT3* was transcriptionally regulated by NF- $\kappa$ B upon radiation, and its enzymatic activity was further enhanced via phosphorylation also by mitochondria-localized Cyclin B1/CDK1 complex. The phosphorylation of SIRT3 by CDK1 was required for mitochondrial functions as well as for cell survival tested by *in vitro* and *in vivo* radiation. Thus, targeting CDK1-SIRT3 phosphorylation-mediated mitochondrial metabolism provides an alternative approach to enhance tumor response to radiotherapy. For details, see the article by Liu and colleagues on page 2090.



# Molecular Cancer Therapeutics

**14 (9)**

*Mol Cancer Ther* 2015;14:1973-2164.

**Updated version** Access the most recent version of this article at:  
<http://mct.aacrjournals.org/content/14/9>

**E-mail alerts** [Sign up to receive free email-alerts](#) related to this article or journal.

**Reprints and Subscriptions** To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at [pubs@aacr.org](mailto:pubs@aacr.org).

**Permissions** To request permission to re-use all or part of this article, use this link <http://mct.aacrjournals.org/content/14/9>.  
Click on "Request Permissions" which will take you to the Copyright Clearance Center's (CCC) Rightslink site.