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 Hizaoka, Kazuaki Shimada, Hirofumi Rokutan, Yasuhiro Arai, Yae Kanai, Shinichi Miyagawa, and Tatsushiro 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

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. Fye, 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

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. Slawowski, 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)

2072 Heregulin–ErbB3-Driven Tumor Growth Persists in PI3 Kinase Mutant Cancer Cells
Define Yarar, 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. Gianollio, Robert Smale, Stephanie D. Roth, Roy Krumholz, 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 Radiosensitivity
Rui Liu, Ming Fan, Demet Candis, Lili Qin, Xiaodi Zhang, Angela Eldridge, June X. Zou, Tieqiao Zhang, Shaibi Juma, Cuilong Jiu, Robert F. Li, Julian Perks, Lun-Quan Sun, Andrew T.M. Vaughan, Chun-Xu Hai, David R. Giust, and Jian Jian Li
2103  STAT1 Activation Is Enhanced by Cisplatin and Varially 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+ Cancer Stem Cell Subclones Contribute to Breast Cancer Aggressiveness by Promoting Vasculogenic Mimicry
Tieju Liu, Baocun Sun, Xiaolan 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. Freiberger, Phil F. Cheng, Guergana Iotzova-Weiss, Johannes Neu, Qinxiu Liu, Piotr Dziunycz, John R. Zibert, Reinhard Dummer, Kresten Skak, Mitchell P. Levesque, and Günther F.L. Hofbauer

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

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-κB 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.