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 Hizakura, Kazzaki Shimada, Hirofumi Rokutan, Yasuhiro 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

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)

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. Gianolio, 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, Shuaib Juma, Cuilong Jin, Robert F. Li, Julian Perks, Lun-Quan Sun, Andrew T.M. Vaughan, Chun-Xu Hai, David R. Gius, and Jian Jian Li
STAT1 Activation Is Enhanced by Cisplatin and Variably Affected by EGFR Inhibition in HNSCC Cells
Nicole C. Schmitt, Sumita Trivedi, and Robert L. Ferris

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

USP44+ Cancer Stem Cell Subclones Contribute to Breast Cancer Aggressiveness by Promoting Vasculogenic Mimicry
Tieju 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

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

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

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

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.