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 Hizaka, Kazuki Shimada, Hirofumi Rokutan, Yasuhiro Arai, Yae Kanai, Shinichi Miyagawa, and Tatsuo Hirota

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 Mark S. Marshall

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 S. Slivkovski, 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
Defne Yarar, Johanna Lahdenranta, William Kubasek, Ulrik R. Nielsen, and Gavin MacBeath

2081 Anti-Endosialin Antibody–Drug Conjugate: Potential in Sarcoma and Other Malignancies
Cecilia Rouleau, Diego A. Gianolli, 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 Radiosensitivity
Rui Liu, Ming Fan, Demet Candas, Lili Qin, Xiaodi Zhang, Angela Eldridge, June X. Zou, Tieqiao Zhang, Shuaib Juma, Cuilong Jia, Robert F. Li, Julian Perks, Lun-Quan Sun, Andrew T. Vaughan, Chun-Xu Hai, David R. Giuss, and Jian Jian Li
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<td>STAT1 Activation Is Enhanced by Cisplatin and Variably Affected by EGFR Inhibition in HNSCC Cells</td>
<td>Nicole C. Schmitt, Sumita Trivedi, and Robert L. Ferris</td>
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<td>Nicotine Induces Tumor Growth and Chemoresistance through Activation of the PI3K/Akt/mTOR Pathway in Bladder Cancer</td>
<td>Kazuyuki Yuge, Eiji Kikuchi, Masayuki Hagiwara, Yota Yasumizumi, Nobuyuki Tanaka, Takeo Kosaka, Akira Miyajima, and Mototsugu Oya</td>
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<td>USP44+ Cancer Stem Cell Subclones Contribute to Breast Cancer Aggressiveness by Promoting Vasculogenic Mimicry</td>
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<td>Ingenol Mebutate Signals via PKC/MEK/ERK in Keratinocytes and Induces Interleukin Decoy Receptors IL1R2 and IL13RA2</td>
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**MODELS AND TECHNOLOGIES**

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