Highlights of This Issue 1973

REVIEW

1975 Durability of Kinase-Directed Therapies—A Network Perspective on Response and Resistance
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SMALL MOLECULE THERAPEUTICS

1985 Heat Shock Protein 90 Is a Potential Therapeutic Target in Cholangiocarcinoma
Tomoki Shirota, Hidenori Ojima, Nobuyoshi Hizaoaka, Kazuaki Shimada, Hirofumi Rokutan, Yasuhito Arai, Yae Kanai, Shinichi Miyagawa, and Tatsushiro Shibata

1994 Small Molecule Inhibition of MDM2–p53 Interaction Augments Radiation Response in Human Tumors
Lauryrn 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
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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
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2081 Anti-Endosialin Antibody–Drug Conjugate: Potential in Sarcoma and Other Malignancies
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CANCER BIOLOGY AND SIGNAL TRANSDUCTION

2090 CDK1-Mediated SIRT3 Activation Enhances Mitochondrial Function and Tumor Radioresistance
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MODELS AND TECHNOLOGIES

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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 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.