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660 MET Activation Mediates Resistance to Lapatinib Inhibition of HER2-Amplified Gastric Cancer Cells
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670 CEP-28122, a Highly Potent and Selective Orally Active Inhibitor of Anaplastic Lymphoma Kinase with Antitumor Activity in Experimental Models of Human Cancers
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680 Low-Dose Metronomic Oral Dosing of a Prodrug of Gemcitabine (LY2334737) Causes Antitumor Effects in the Absence of Inhibition of Systemic Vasculogenesis
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690 Ponatinib (AP24534), a Multitargeted Pan-FGFR Inhibitor with Activity in Multiple FGFR-Amplified or Mutated Cancer Models

700 TAK-960, a Novel, Orally Available, Selective Inhibitor of Polo-Like Kinase 1, Shows Broad-spectrum Preclinical Antitumor Activity in Multiple Dosing Regimens
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660 An Integrated Genomic Approach to Identify Predictive Biomarkers of Response to the Aurora Kinase Inhibitor PF-03814735
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720 Comprehensive Predictive Biomarker Analysis for MEK Inhibitor GSK1120212
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730 The Novel Oral Hsp90 Inhibitor NVP-HSP990 Exhibits Potent and Broad-spectrum Antitumor Activities In Vitro and In Vivo

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Molecular Cancer Therapeutics
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Molecular Cancer Therapeutics
The Aurora Kinase A Inhibitor MLN8237 Enhances Cisplatin-Induced Cell Death in Esophageal Adenocarcinoma Cells
Vikas Sehdev, DunFa Peng, Mohammed Soutto, M. Kay Washington, Frank Revetta, Jeffrey Ecsedy, Alexander Zaika, Tilman T. Rau, Regine Schneider-Stock, Abbes Belkhiri, and Wael El-Rifai

MOLECULAR MEDICINE IN PRACTICE

Next Generation Sequencing of Prostate Cancer from a Patient Identifies a Deficiency of Methylthioadenosine Phosphorylase, an Exploitable Tumor Target

ABOUT THE COVER

The uracil-metabolizing enzyme dUTPase is a key component of de novo thymidine nucleotide biosynthesis and its expression is tightly regulated in replicating tissues such as the follicular germinal centers of human palatine tonsil (pictured). However, dUTPase is frequently overexpressed in human cancers and this has been firmly linked to drug resistance to chemotherapeutic agents that target thymidylate synthase (TS). Using immunohistochemistry and quantitative RT-PCR, evidence of dUTPase overexpression in a cohort of non-small cell lung cancers (NSCLC) was observed. Small interfering RNA-mediated gene silencing of dUTPase induced a strong synthetic lethal effect in NSCLC cell lines to two class-specific TS-targeted therapies including pemetrexed and fluorodeoxyuridine. Inhibition of dUTPase represents a promising, mechanism-based therapeutic approach to significantly enhance the efficacy of TS-targeted chemotherapeutic agents by overcoming a critical drug resistance pathway. For details, see article by Wilson and colleagues on page 616.