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1051 Attacking a Nexus of the Oncogenic Circuitry by Reversing Aberrant eIF4F-Mediated Translation
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1062 Immunotherapy of Cancer with 4-1BB
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1071 Quantitative Proteomic Profiling Identifies Protein Correlates to EGFR Kinase Inhibition

1082 Hyperactivation of 4E-Binding Protein 1 as a Mediator of Biguanide-Induced Cytotoxicity during Glucose Deprivation
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1092 Off-Target Function of the Sonic Hedgehog Inhibitor Cyclopamine in Mediating Apoptosis via Nitric Oxide–Dependent Neutral Sphingomyelinase 2/Ceramide Induction
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1103 Evading Pgp Activity in Drug-Resistant Cancer Cells: A Structural and Functional Study of Antitubulin Furan Metotica Compounds
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1112 JAK–STAT and JAK–PI3K–mTORC1 Pathways Regulate Telomerase Transcriptionally and Posttranslationally in ATL Cells
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1122 Obatoclax Interacts Synergistically with the Irreversible Proteasome Inhibitor Carfilzomib in GC- and ABC-DLBCL Cells In Vitro and In Vivo
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1133 The Effect of Different Linkers on Target Cell Catabolism and Pharmacokinetics/Pharmacodynamics of Trastuzumab Maytansinoid Conjugates
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1143 ERK Inhibition Overcomes Acquired Resistance to MEK Inhibitors
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1155 Triggering Fbw7-Mediated Proteasomal Degradation of c-Myc by Oridonin Induces Cell Growth Inhibition and Apoptosis
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### MOLECULAR MEDICINE IN PRACTICE

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**miRNA-29b Suppresses Prostate Cancer Metastasis by Regulating Epithelial–Mesenchymal Transition Signaling**
Peng Ru, Robert Steele, Philip Newhall, Nancy J. Phillips, Karoly Toth, and Ratna B. Ray

**High TUBB3 Expression, an Independent Prognostic Marker in Patients with Early Non-Small Cell Lung Cancer Treated by Preoperative Chemotherapy, Is Regulated by K-Ras Signaling Pathway**
Guënaëlle Levallet, Emmanuel Bergot, Martine Antoine, Christian Creveuil, Adriana O. Santos, Michelle Beau-Faller, Florence de Fraipont, Elisabeth Brambilla, Jérôme Levallet, Franck Morin, Virginie Wested, Marie Wislez, Elisabeth Quoix, Didier Debieuvre, Fatemeh Dubois, Isabelle Rouquette, Jean-Louis Pujol, Denis Moro-Sibilot, Jacques Camonis, Gérard Zalcman, on behalf of the Intergroupe Francophone de Cancérologie Thoracique (IFCT)

### ABOUT THE COVER

Several allosteric MEK inhibitors are in clinical development and have been designed to treat patients with tumors harboring RAS/RAF pathway alterations. Acquired resistance to this class of inhibitors is a pressing clinical problem. To identify strategies to overcome this resistance, Hatzivassiliou and colleagues derived and characterized three independent MEK inhibitor-resistant cell lines. All of the resistant cell lines harbored mutations in the allosteric binding pocket of MEK that is targeted by arylamine MEK inhibitors. In all cases the MEK resistant cell lines retained their addiction to the MAPK pathway and remained sensitive to a selective inhibitor of the ERK1/2 kinases, suggesting a role for ERK inhibitors in combating or preventing MEK inhibitor resistance. For details, see article by Hatzivassiliou and colleagues on page 1143.