# Molecular Cancer Therapeutics

## Highlights of This Issue 553

### REVIEW

**New Paradigms in Microtubule-Mediated Endocrine Signaling in Prostate Cancer**

Sucharita J. Mistry and William K. Oh

### CHEMICAL THERAPEUTICS

**A Novel Antiandrogen, Compound 30, Suppresses Castration-Resistant and MDV3100-Resistant Prostate Cancer Growth In Vitro and In Vivo**

Hidetoshi Kuruma, Hiroaki Matsumoto, Masaki Shiota, Jennifer Bishop, Francois Lamoureux, Christian Thomas, David Briere, Gerrit Los, Martin Gleave, Andrea Fanjul, and Amina Zoubeidi

**Dual PI3K/AKT/mTOR Inhibitor BEZ235 Synergistically Enhances the Activity of JAK2 Inhibitor against Cultured and Primary Human Myeloproliferative Neoplasm Cells**

Warren Fiskus, Srdan Verstovsek, Taghi Manshouri, Jacqueline E. Smith, Karissa Peth, Sunil Abhyankar, Joseph McGuirk, and Kapil N. Bhalla

**Afatinib Prolongs Survival Compared with Gefitinib in an Epidermal Growth Factor Receptor-Driven Lung Cancer Model**

Takashi Ninomiya, Nagio Takigawa, Eiki Ichihara, Nobuaki Ochi, Toshi Murakami, Yoshihiro Honda, Tosio Kubo, Daisuke Minami, Kenichiro Kudo, Mitsune Tanimoto, and Katsuyuki Kiura

**Tandutinib Inhibits the Akt/mTOR Signaling Pathway to Inhibit Colon Cancer Growth**

Sivapriya Ponnurangam, David Standing, Parthasarathy Rangarajan, and Dharmalingam Subramaniam

**Small-Molecule Inhibitors of Acetyltransferase p300 Identified by High-Throughput Screening Are Potent Anticancer Agents**

Heng Yang, Christie E. Pinello, Jian Luo, Dawei Li, Yunfei Wang, Lisa Y. Zhao, Stephan C. Jahn, Sanjay Adrian Saldanha, Jamie Planck, Kyla R. Geary, Haiching Ma, Brian K. Law, William R. Roush, Peter Hodder, and Daqing Liao

## SMALL MOLECULE THERAPEUTICS

**Spongian Diterpenoids Inhibit Androgen Receptor Activity**

Yu Chi Yang, Labros G. Meimetis, Amy H. Tien, Nasrin R. Maji, Gavin Carr, Jun Wang, Raymond J. Andersen, and Marianne D. Sadar

**Activity of the Fibroblast Growth Factor Receptor Inhibitors Dovitinib (TKI258) and NVP-BGJ398 in Human Endometrial Cancer Cells**


**Regression of Lung Cancer by Hypoxia-Sensitizing Ruthenium Polypyridyl Complexes**

Abhishek Yadav, Thamarara Janaratne, Arthi Krishnan, Sharad S. Singhal, Sushma Yadav, Adam S. Dayoub, Doyle L. Hawkins, Sanjay Awasthi, and Frederick M. MacDonnell

**Designing and Developing S100P Inhibitor 5-Methyl Cromolyn for Pancreatic Cancer Therapy**


**A Novel Sulindac Derivative Inhibits Lung Adenocarcinoma Cell Growth through Suppression of Akt/mTOR Signaling and Induction of Autophagy**

Evrim Gurpinar, William E. Grizzle, John J. Shacka, Burton J. Mader, Nan Li, Nicholas A. Piazza, Suzanne Russo, Adam B. Keeton, and Gary A. Piazza

**Activity of a Py–Im Polyamide Targeted to the Estrogen Response Element**

Nicholas G. Nickols, Jerzy O. Szabolowski, Amanda E. Hargrove, Benjamin C. Li, Jevgenij A. Raskatov, and Peter B. Dervan
LARGE MOLECULE THERAPEUTICS

685 A Novel Monoclonal Antibody to Secreted Frizzled-Related Protein 2 Inhibits Tumor Growth
Emily Fontenot, Emma Rossi, Russell Mumper, Stephanie Snyder, Sharareh Siamakpour-Reihani, Ping Ma, Eleanor Hilliard, Bradley Bone, David Ketelsen, Charlene Santos, Cam Patterson, and Nancy Klauber-DeMore

696 ALK Inhibitor PF02341066 (Crizotinib) Increases Sensitivity to Radiation in Non–Small Cell Lung Cancer Expressing EML4-ALK
Yunguang Sun, Kamila A. Nowak, Nicholas C. Zaorsky, Chia-Lin Winchester, Kunal Dalal, Nicholas J. Giacalone, Ningbo Liu, Maria Werner-Wasik, Mariusz A. Wasik, Adam P. Dicker, and Bo Lu

705 The Efficacy of CHK1 Inhibitors Is Not Altered by Hypoxia, but Is Enhanced after Reoxygenation
Grete Hasvold, Viola Nåhse-Kumpf, Kinga Tkacz-Stachowska, Einar K. Rofstad, and Randi G. Syljåsen

717 Colorectal Cancer Cells Refractory to Anti-VEGF Treatment Are Vulnerable to Glycolytic Blockade due to Persistent Impairment of Mitochondria
Jie Xu, Jilin Wang, Bin Xu, Haiyan Ge, Xiaodin Zhou, and Jing-Yuan Fang

725 Small-Molecule Inhibitor BMS-777607 Induces Breast Cancer Cell Polyploidy with Increased Resistance to Cytotoxic Chemotherapy Agents
Sharad Sharma, Jun-Ying Zeng, Chun-Mei Zhuang, Yong-Qing Zhou, Hang-Ping Yao, Xing Hu, Ruiwen Zhang, and Ming-Hai Wang

737 Y-box Binding Protein-1 Contributes to Both HER2/ErbB2 Expression and Lapatinib Sensitivity in Human Gastric Cancer Cells
Tomohiro Shibata, Hitoshi Kan, Yuichi Murakami, Hiroki Ureshino, Kisuake Watarai, Akihiko Kawahara, Masayoshi Kage, Satoshi Hattori, Mayumi Ono, and Michihiko Kuwano

747 Bortezomib and SAHA Synergistically Induce ROS-Driven Caspase-Dependent Apoptosis of Nasopharyngeal Carcinoma and Block Replication of Epstein–Barr Virus
Kwai Fung Hui, Benjamin H.W. Lam, Dona N. Ho, Sai Wah Tsao, and Alan K.S. Chiang

759 Targeting FoxM1 Effectively Retards p53-Null Lymphoma and Sarcoma
Zebin Wang, Yu Zheng, Hyun Jung Park, Jing Li, Janai R. Carr, Yi-ju Chen, Megan M. Kiefer, Dragana Kopanja, Srilata Bagchi, Angela L. Tyner, and Pradip Raychaudhuri

768 Inhibition of Mutant GNAQ Signaling in Uveal Melanoma Induces AMPK-Dependent Autophagic Cell Death
Grazia Ambrosini, Elgildá Musí, Alan L. Ho, Elisa de Stanchina, and Gary K. Schwartz

777 Crizotinib Induces PUMA-Dependent Apoptosis in Colon Cancer Cells
Xingnan Zheng, Kan He, Lin Zhang, and Jian Yu

787 Impact of Tumor Vascularity on Responsiveness to Antiangiogenesis in a Prostate Cancer Stem Cell-Derived Tumor Model
Kexiong Zhang and David J. Waxman

799 Targeting CXCR2 Enhances Chemotherapeutic Response, Inhibits Mammary Tumor Growth, Angiogenesis, and Lung Metastasis
Bhawna Sharma, Dhananjay M. Nawandar, Kalyan C. Nannuru, Michelle L. Varney, and Rakesh K. Singh

809 A Phase II Study of Temozolomide in Patients with Advanced Aerodigestive Tract and Colorectal Cancers and Methylation of the O\(^6\)-Methylguanine-DNA Methyltransferase Promoter
Daniel Hochhauser, Rob Glynn-Jones, Vanessa Potter, Cristina Grávalos, Thomas J. Doyle, Kumudu Pathiraja, Qing Zhang, Ling Zhang, and Edward A. Sausville

TOOLS & TECHNOLOGIES

819 \(^{18}\text{F}\)-FLT Positron Emission Tomography Can Be Used to Image the Response of Sensitive Tumors to PI3-Kinase Inhibition with the Novel Agent GDC-0941
Christopher Cawthorne, Natalie Burrows, Roben G. Gieling, Christopher J. Morrow, Duncan Forster, Jamil Gregory, Marc Radigois, Alison Smigova, Muhammad Babur, Kathryn Simpson, Cassandra Hodkinson, Gavin Brown, Adam McMahon, Caroline Dive, Duncan Hiscock, Ian Wilson, and Kaye J. Williams
ABOUT THE COVER

Mitochondria is the powerhouse of cells (structure, green), supplying the majority of ATP that is essential for cell survival. However, cancer cells present a distinct glycolytic metabolism profile (Warburg effect), which is linked to the malignant transformation process. The emerging anti-VEGF therapy fights cancers by starving the energy supplement, but it was found to enhance the Warburg effect and induce even more aggressive phenotypes. Cancer cells with acquired resistance to anti-VEGF therapy display impaired mitochondria structure and hyperactive glycolytic metabolism, which render them vulnerable to glycolysis blockade therapy. For details, see article by Xu and colleagues on page 717.