CANCER DISCOVERY CONTENTS

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Précis: Frequent *AURKA* and *MYCN* amplification is identified in an aggressive prostate cancer subtype.

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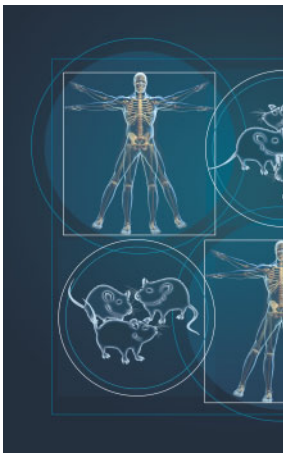
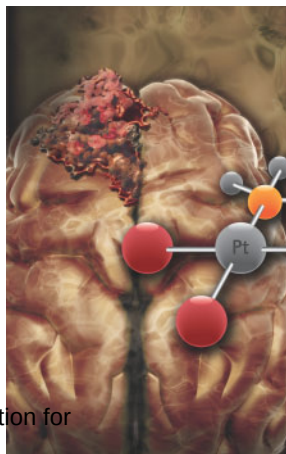
T. Enzler, Y. Sano, M-K. Choo, H.B. Cottam, M. Karin, H. Tsao, and J.M. Park
Précis: Host- and tumor-specific cellular responses, respectively, underlie the adverse and therapeutic effects of NF-κB blocking agents.





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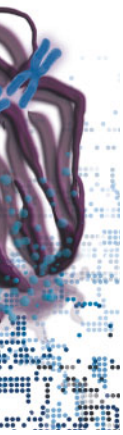

A Molecularly Annotated Platform of Patient- Derived Xenografts ("Xenopatients") Identifies HER2 as an Effective Therapeutic Target in Cetuximab-Resistant Colorectal Cancer 508

A. Bertotti, G. Migliardi, F. Galimi, F. Sassi, D. Torti, C. Isella, D. Corà, F. Di Nicolantonio, M. Buscarino, C. Petti, D. Ribero, N. Russolillo, A. Muratore, P. Massucco, A. Pisacane, L. Molinaro, E. Valtorta, A. Sartore-Bianchi, M. Risio, L. Capussotti, M. Gambacorta, S. Siena, E. Medico, A. Sapino, S. Marsoni, P.M. Comoglio, A. Bardelli, and L. Trusolino

Précis: Population-based preclinical testing identifies HER2 amplification as a novel biomarker of cetuximab resistance in metastatic colon cancer and indicates dual targeting of HER2 and EGFR may be a more effective therapeutic approach.

Oncogenic EGFR Signaling Activates an mTORC2–NF-κB Pathway That Promotes Chemotherapy Resistance 524

K. Tanaka, I. Babic, D. Nathanson, D. Akhavan, D. Guo, B. Gini, J. Dang, S. Zhu, H. Yang, J. De Jesus, A.N. Amzajerdi, Y. Zhang, C.C. Dibble, H. Dan, A. Rinkenbaugh, W.H. Yong, H.V. Vinters, J.F. Gera, W.K. Cavenee, T.F. Cloughesy, B.D. Manning, A.S. Baldwin, and P.S. Mischel

Précis: mTORC2 is identified as a novel mediator of drug resistance and regulator of NF-κB signaling in glioblastoma.

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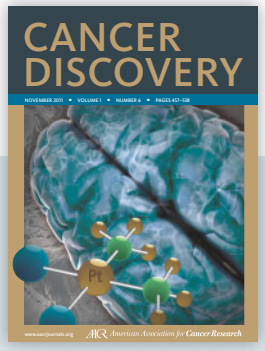
- Making Molecular Diagnostics Ready for Prime Time
- Optical Tomography May Aid 3D Diagnostics
- What's Cost-Effective in Cancer Care?
- Chemotherapy May Target Mitochondria on the Edge



ON THE COVER Tanaka and colleagues demonstrate that mTORC2 is activated in the majority of glioblastomas and mediates chemoresistance in an AKT-independent manner via NF-κB pathway activation. Surprisingly, they show increased activity of this mTORC2–NF-κB signaling pathway in GBM cells in response to rapamycin, which may provide an explanation for the failure of rapamycin to demonstrate efficacy in GBM clinical trials. Instead, dual mTOR kinase inhibitors that block the activity of both mTORC1 and mTORC2 may improve clinical outcome, particularly when combined with other chemotherapeutic agents. For details, please see the article by Tanaka and colleagues on page 524.

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Cancer Discovery 2011;1:457-538.

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