An Unholy Alliance: Cooperation between BRAF and NF1 in Melanoma Development and BRAF Inhibitor Resistance ........................................... 260
G.T. Gibney and K.S.M. Smalley
See article, p. 338
See article, p. 350

Fibroblast Growth Factor Receptor Inhibitors as a Cancer Treatment: From a Biologic Rationale to Medical Perspectives ........................................... 264
M.V. Dieci, M. Arnedos, F. Andre, and J.C. Soria

Outlier Kinase Expression by RNA Sequencing as Targets for Precision Therapy ........................................... 280
Précis: Kinases in individual cancer samples with the highest absolute and differential gene expression may represent personalized therapeutic targets.
See commentary, p. 252

Mutant N-RAS Protects Colorectal Cancer Cells from Stress-Induced Apoptosis and Contributes to Cancer Development and Progression ........................................... 294
Précis: Activated NRAS triggers noncanonical MAPK signaling via RAF-1 and STAT3 to inhibit cell death and promote colorectal tumorigenesis in the context of inflammation.

In The Spotlight
Aiming for the Outliers: Cancer Precision Medicine through Targeting Kinases with Extreme Expression ........................................... 252
S. Yegnasubramanian and A. Maitra
See article, p. 280

Targeting MYCN: A Good BET for Improving Neuroblastoma Therapy? ........................................... 255
R.W. Schnepp and J.M. Maris
See article, p. 308

Bcl-2 Inhibition or FBXW7 Mutation Sensitizes Solid Tumor Cells to HDAC Inhibition In Vitro but Could Prove Difficult to Validate in Patients ........................................... 258
C.R. Pickering and J.N. Myers
See article, p. 324
Targeting MYCN in Neuroblastoma by BET Bromodomain Inhibition ........ 308

Puissant and colleagues screened a compendium of cancer cell lines to identify those most sensitive to the bromodomain and extraterminal domain (BET) protein inhibitor JQ1. Neuroblastoma cell lines were among the most JQ1-sensitive cell lines, and MYCN amplification, which is commonly observed in high-risk neuroblastoma, was the feature most predictive of JQ1 sensitivity. JQ1 displaced the BET family member BRD4 from the MYCN promoter, leading to decreased expression of MYCN and MYCN target genes, and significantly prolonged survival in several MYCN-amplified neuroblastoma models. These findings thus implicate MYCN amplification as a genetic predictor of BET inhibitor sensitivity and provide support for the development of BET inhibitors in MYCN-amplified neuroblastoma. For details, please see the article by Puissant and colleagues on page 308.

Mcl-1 and FBW7 Control a Dominant Survival Pathway Underlying HDAC and Bcl-2 Inhibitor Synergy in Squamous Cell Carcinoma. ... 324

Elucidating Distinct Roles for NF1 in Melanomagenesis ............... 338

ON THE COVER

Puissant and colleagues screened a compendium of cancer cell lines to identify those most sensitive to the bromodomain and extraterminal domain (BET) protein inhibitor JQ1. Neuroblastoma cell lines were among the most JQ1-sensitive cell lines, and MYCN amplification, which is commonly observed in high-risk neuroblastoma, was the feature most predictive of JQ1 sensitivity. JQ1 displaced the BET family member BRD4 from the MYCN promoter, leading to decreased expression of MYCN and MYCN target genes, and significantly prolonged survival in several MYCN-amplified neuroblastoma models. These findings thus implicate MYCN amplification as a genetic predictor of BET inhibitor sensitivity and provide support for the development of BET inhibitors in MYCN-amplified neuroblastoma. For details, please see the article by Puissant and colleagues on page 308.

Elucidating Distinct Roles for NF1 in Melanomagenesis ............... 338


Précis: NF1 mutations prevent BRAF-induced senescence and promote melanoma growth via activation of PI3K and ERK signaling, conferring resistance to BRAF inhibitors.

See commentary, p. 258

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• Slow Progress on Liver Cancer
• India Adds Compulsory Drug Licenses

A Genome-Scale RNA Interference Screen Implicates NF1 Loss in Resistance to RAF Inhibition ............ 350


Précis: BRAF-mutant melanoma cells lacking NF1 develop resistance to RAF and MEK blockade via sustained MAPK signaling but retain sensitivity to both ERK and irreversible RAF inhibitors.

See commentary, p. 260