Coamplification of \textit{EGFR} and \textit{ERBB2} is associated with afatinib response in patients with trastuzumab-refractory esophagogastric cancer, whereas selection for \textit{MET} amplification or loss of \textit{EGFR} amplification is associated with resistance. See commentary, p. 166

Brca Reversion Mutations in Circulating Tumor DNA Predict Primary and Acquired Resistance to the PARP Inhibitor Rucaparib in High-Grade Ovarian Carcinoma

PPT1 Promotes Tumor Growth and Is the Molecular Target of Chloroquine Derivatives in Cancer

Cells Lacking the RB1 Tumor Suppressor Gene Are Hyperdependent on Aurora B Kinase for Survival
Aurora A Kinase Inhibition Is Synthetic Lethal with Loss of the RB1 Tumor Suppressor Gene 248

Précis: A screen of cell-cycle inhibitors reveals that RB1-mutant cancer cells are selectively dependent on Aurora kinase A.

See commentary, p. 169

EIF1AX and RAS Mutations Cooperate to Drive Thyroid Tumorigenesis through ATF4 and c-MYC 264

Précis: The EIF1AX-A113sp1 mutation results in an alternatively spliced transcript that cooperates with RAS mutations to stabilize MYC, activate mTOR, and promote tumorigenesis.

TGFβ Antagonizes IL1-driven JAK/STAT activation, which induces an inflammatory pancreatic ductal adenocarcinoma cancer-associated fibroblast (CAF) phenotype, to promote CAF heterogeneity.

See commentary, p. 173

IL1-Induced JAK/STAT Signaling Is Antagonized by TGFβ to Shape CAF Heterogeneity in Pancreatic Ductal Adenocarcinoma 282

Correction: An Acquired HER2T798I Gatekeeper Mutation Induces Resistance to Neratinib in a Patient with HER2 Mutant-Driven Breast Cancer 303

Correction: Neoadjuvant Trials in ER+ Breast Cancer: A Tool for Acceleration of Drug Development and Discovery 304

ON THE COVER

Aurora kinase A (AURKA) and Aurora kinase B (AURKB) were found to be synthetic lethal with RB1 loss using a “gene–gene” interaction CRISPR/Cas9-based screening approach initiated by Oser and colleagues and a “gene–drug” interaction approach involving a screen of cell-cycle inhibitors performed by Gong, Du, Parsons, and colleagues. Both an AURKB-specific inhibitor, AZD2811, and the developed AURKA-specific inhibitor, LY3295668, specifically eliminated RB1-mutant but not RB1–wild-type cells and had in vivo efficacy against RB1-mutant tumors. Mechanistic studies suggested that RB1 and AURKA or AURKB have partially redundant roles in mitosis, explaining their synthetic lethal interaction. These findings suggest a potential therapeutic vulnerability caused by RB1 loss and a possible way forward for treatment of RB1-mutant tumors. For details, please see the article by Oser and colleagues on page 230 and the article by Gong, Du, Parsons, and colleagues on page 248.