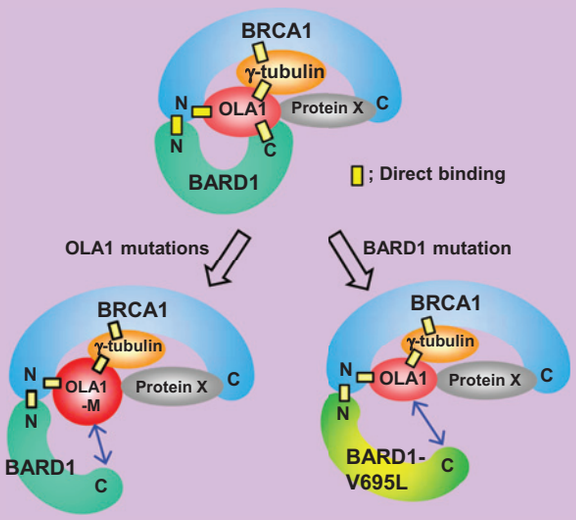
Molecular Cancer Research

Highlights

October 2018 • Volume 16 • Number 10

Selected Articles from This Issue



OLA1 Requires BARD1 to Regulate Centrosome Number

Yoshino *et al.* **Page 1499**

Obg-like ATPase 1 (OLA1) was identified as a protein that functions in centrosome regulation together with BRCA1. Yoshino and colleagues identified five missense mutants of OLA1 that are deficient in the regulation of centrosome number. Three of them did not bind to BARD1, a heterodimer partner of BRCA1. Two phosphomimetic mutations restored the binding to BARD1. A BARD1 mutant, reported in cancer, failed to bind to OLA1 and rescue the BARD1 knockdown-induced centrosome amplification. These findings demonstrate that the OLA1-BARD1 interaction is critical for the regulation of centrosome number. Thus, OLA1 is important for the genome integrity to prevent tumor development.

GBM Sensitivity to ER Stress Requires PERK

Dadey *et al.* **Page 1447**

Resistance to radiation therapy is a hallmark of glioblastoma multiforme (GBM). Radiation can induce ER stress and downstream signaling associated with the endoplasmic reticulum stress response (ERSR). Protein kinase R-like endoplasmic reticulum kinase (PERK) is one of the regulators of ERSR. The current Rapid Impact, investigates the significance of PERK in GBM after ionizing radiation (IR). It was determined that radiation enhanced PERK-eIF2α-ATF4 pathway in GBM, thereby influencing survival and death processes. The dual function of PERK as a mediator of survival and death provides multiple approaches to enhance the efficacy of radiation therapy.

Hypoxia Promotes EGFR Inhibitor Resistance

Lu *et al.* **Page 1458**

Development of resistance to small molecule EGFR inhibitors in non-small cell lung cancer (NSCLC) patients with activating EGFR mutations has limited the efficacy of such treatment. Though recent studies have deepened the understanding of the molecular mechanisms, fully understanding and overcoming the resistance is still a challenge. This study, by Lu and colleagues, demonstrates that hypoxia promotes resistance to gefitinib in NSCLC cells in a pathway linked to features of epithelial-to-mesenchymal transition (EMT) and dependent on the function of the histone lysine demethylases, LSD1 and PLU-1. The results provide the rationale for combining EGFR inhibitors with LSD1 inhibitors as a therapeutic strategy for NSCLC.

LCK-Mediated YAP Tyrosine Phosphorylation in CCA

Sugihara *et al.* **Page 1556**

Cholangiocarcinoma (CCA) is a rare tumor type with very limited treatment options. To identify new molecular susceptibilities, this study interrogated the Hippo signaling pathway and its effector protein YAP. In the models tested, YAP regulation was independent of the Hippo pathway and was driven by SRC family kinase-mediated tyrosine phosphorylation. Tyrosine phosphorylation lead to nuclear retention of YAP, a so-called nuclear retention signal. Subsequently, LCK was identified as the most potent mediator of YAP phosphorylation, a previously undescribed function for LCK. Finally, LCK-mediated YAP phosphorylation was found to be targetable *in vivo*, utilizing the pan-SFK inhibitor dasatinib.

Molecular Cancer Research

Highlights of This Issue

Mol Cancer Res 2018;16:1445.