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**RESEARCH ARTICLES**

**In Vivo Role of INPP4B in Tumor and Metastasis Suppression through Regulation of PI3K–AKT Signaling at Endosomes**


**Précis:** Loss of INPP4B drives localized activation of PI3K–AKT2 in early endosomes and cooperates with PTEN inactivation to promote aggressive and metastatic thyroid tumor formation.

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See article, p. 730

**ARID1A Deficiency Impairs the DNA Damage Checkpoint and Sensitizes Cells to PARP Inhibitors**


**Précis:** The identification of a role of ARID1A in the DNA damage response suggests a potential therapeutic vulnerability of ARID1A-mutant cancers.

**Targeting Translation Initiation Bypasses Signaling Crosstalk Mechanisms That Maintain High MYC Levels in Colorectal Cancer**


**Précis:** Silvestrol, an eIF4A inhibitor, circumvents feedback mechanisms that maintain MYC translation downstream of dual PI3K/mTOR inhibition to reduce MYC expression and inhibit colorectal cancer growth.

See commentary, p. 701

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**ON THE COVER**

Shen and colleagues identified ARID1A, a subunit of SWI/SNF chromatin remodeling complexes, as a binding partner of ATR, a key regulator of the DNA damage response. ARID1A is recruited to DNA double-strand breaks (DSB) in an ATR-dependent manner and promotes efficient DSB end resection, which is necessary for activation of ATR and subsequent initiation and maintenance of the G2/M checkpoint. ARID1A loss impaired homologous recombination and single-strand annealing DSB repair mechanisms and, similar to loss of BRCA1 or BRCA2, conferred sensitivity to DSB-inducing PARP inhibitors. Given that inactivating mutations in ARID1A are among the most frequent genetic events in human cancers, these findings suggest that PARP inhibitors may be effective in a broader spectrum of cancers than previously appreciated. For details, please see the article by Shen and colleagues on page 752.
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