IN THIS ISSUE: Highlighted research articles

NEWS IN BRIEF: Important news stories affecting the community

NEWS IN DEPTH: Q&A: John Carpten on Cancer Disparities

RESEARCH WATCH: Selected highlights of recent articles of exceptional significance from the cancer literature

ONLINE: For more News and Research Watch, visit Cancer Discovery online at http://cancerdiscovery.aacrjournals.org/CDNews.

VIEWS: In The Spotlight

An Expanded Tool Kit for Modeling the Oncogenic Functions of KRAS
K. Kostyrko and E.A. Sweet-Cordero
See article, p. 1654

Hitting Gliomas When They Are Down: Exploiting IDH-Mutant Metabolic Vulnerabilities
C.J. Pirozzi and H. Yan
See article, p. 1672

Free Asparagine or Die: Cancer Cells Require Proteasomal Protein Breakdown to Survive Asparagine Depletion
K. Davidsen and L.B. Sullivan
See article, p. 1690

MINI REVIEW: Precision Prevention and Cancer Interception: The New Challenges of Liquid Biopsy

RESEARCH BRIEF: Epigenetic Suppression of Transgenic T-cell Receptor Expression via Gamma-Retroviral Vector Methylation in Adoptive Cell Transfer Therapy
Précis: In patients treated with T-cell receptor adoptive cell therapy, engineered T cells retained the transgenic DNA, but the DNA was subject to DNA methylation-based epigenetic silencing, which may be a cause of treatment resistance or relapse.

RESEARCH ARTICLES: An In Vivo Kras Allelic Series Reveals Distinct Phenotypes of Common Oncogenic Variants
Précis: In vivo, organ-specific expression of oncogenic mutant Kras produced different phenotypes depending on the specific mutation; for example, unlike other Kras variants studied, KrasG12D expression in the pancreas was not highly oncogenic.

Poly(ADP-ribose) Glycohydrolase Inhibition Sequesters NAD+ to Potentiate the Metabolic Lethality of Alkylating Chemotherapy in IDH-Mutant Tumor Cells
Précis: IDH mutations seen in some cancers lead to low basal NAD+ levels that are further decreased by alkylating drugs, and adding a poly(ADP-ribose) glycohydrolase inhibitor to block NAD+ pool restoration synergized with alkylators in these tumors.

See commentary, p. 1626

See commentary, p. 1629
Exploiting the Therapeutic Interaction of WNT Pathway Activation and Asparaginase for Colorectal Cancer Therapy ........ 1690

Précis: Mutations that activate the WNT pathway upstream of GSK3, which occur in 10% to 15% of colorectal cancers, caused colorectal cancer cell lines, organoids, and tumors grown in vivo to be sensitive to asparaginase.

See commentary, p. 1632

Identification of BBOX1 as a Therapeutic Target in Triple-Negative Breast Cancer ............ 1706

Précis: BBOX1 stabilized the endoplasmic reticulum (ER) calcium channel IP3R3, and loss or inhibition of BBOX1 in triple-negative breast cancer cells caused growth defects in vitro and in vivo due to faulty transport of calcium from the ER.

Disabled Homolog 2 Controls Prometastatic Activity of Tumor-Associated Macrophages ............ 1758

Précis: DAB2-expressing tumor-associated macrophages at the perilesional region promoted extracellular matrix remodeling to enhance tumor-cell invasiveness and metastasis, and DAB2 expression correlated with poor prognosis.

Many mutations that activate KRAS by raising the abundance of GTP-bound (active) protein are recognized to be oncogenic. However, Zafra and colleagues found that the effects of individual KRAS-activating mutations depended strongly on the specific amino acid–residue change and where the mutant allele was expressed. For example, Kras\(^{G12C}\) or Kras\(^{G12D}\) expression in the pancreas caused rapid tumorigenesis, whereas Kras\(^{G13D}\) expression caused slower pancreatic tumorigenesis, and Kras\(^{G12R}\) expression caused almost no pancreatic tumorigenesis even after one year. Mutation type also affected drug sensitivity, with Kras\(^{G13D}\)-expressing pancreatic organoids exhibiting sensitivity to EGFR inhibition and Kras\(^{G12C}\)-expressing pancreatic organoids being sensitive to KRAS\(^{G12C}\)-specific inhibitors only in the context of EGFR suppression. For more information, see the article by Zafra and colleagues on page 1654.