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**RESEARCH ARTICLES**

**A Large-Scale Analysis of Genetic Variants within Putative miRNA Binding Sites in Prostate Cancer** ............................................. 368

**Précis:** A large association study identified 22 SNPs in predicted microRNA binding sites (miRSNP) that are linked to prostate cancer risk, including miRSNPs in KLK3 and VAMP8 that are differentially regulated by specific miRNAs.

See commentary, p. 351

**The Genetics of Splicing in Neuroblastoma** ............................................. 380

**Précis:** An integrative genomic analysis of differential alternative splicing patterns across the genome identified recurrently mutated intrinsic splicing motifs and genes potentially relevant to neuroblastoma and glioblastoma development.

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Old Habits Die Hard: Addiction of BRAF-Mutant Cancer Cells to MAP Kinase Signaling ............... 348
C.B. Meador and W. Pao
See article, p. 358

**miRSNP-Based Approach Identifies a miRNA That Regulates Prostate-Specific Antigen in an Allele-Specific Manner** ............... 351
G.M. Yousef
See article, p. 368

**Targeting Autophagy in BRAF-Mutant Tumors** ............... 353
A. Thorburn and M.J. Morgan
See article, p. 410

**Paralog-Specific Kinase Inhibition of FGFR4: Adding to the Arsenal of Anti-FGFR Agents** ............... 355
L.M. Packer and P.M. Pollock
See article, p. 424

**Clinical Acquired Resistance to RAF Inhibitor Combinations in BRAF-Mutant Colorectal Cancer through MAPK Pathway Alterations** ............... 358

**Précis:** Genetic alterations that drive sustained MAPK signaling in patients with BRAF-mutant colorectal cancer confer acquired resistance to RAF/EGFR and RAF/MEK inhibition but retain sensitivity to ERK inhibitors.

See commentary, p. 348

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**views**

**In The Spotlight**

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**on July 10, 2017. © 2015 American Association for Cancer Research. cancerdiscovery.aacrjournals.org Downloaded from cancerdiscovery.aacrjournals.org on July 10, 2017. © 2015 American Association for Cancer Research.**
A Genetic Platform to Model Sarcomagenesis from Primary Adult Mesenchymal Stem Cells .......... 396


Précis: Hypoxic culture of Trp53-null bone marrow mesenchymal stem cells provides a platform to identify genetic drivers of undifferentiated sarcoma and reveals a critical role for the LRF–DLK1–SOX9 pathway in sarcomagenesis.

Atg7 Overcomes Senescence and Promotes Growth of BrafV600E-Driven Melanoma .......... 410

X. Xie, J.Y. Koh, S. Price, E. White, and J.M. Mehnert

Précis: Deletion of the essential autophagy gene Atg7 in BrafV600E, Pten-null melanoma increases oxidative stress and senescence and suppresses tumor growth, establishing that autophagy supports the growth of these tumors.

See commentary, p. 353

First Selective Small Molecule Inhibitor of FGFR4 for the Treatment of Hepatocellular Carcinomas with an Activated FGFR4 Signaling Pathway .......... 424


Précis: HCC cells with FGF19 gene amplification or overexpression and an intact FGFR4 signaling pathway are sensitive to potent and selective FGFR4 inhibition by the small molecule BLU9931 in vitro and in xenograft models.

See commentary, p. 355

FGFR-Mediated Reactivation of MAPK Signaling Attenuates Antitumor Effects of Imatinib in Gastrointestinal Stromal Tumors .......... 438

F. Li, H. Huynh, X. Li, D.A. Ruddy, Y. Wang, R. Ong, P. Chow, S. Qiu, A. Tam, D.P. Rakiec, R. Schlegel, J.E. Monahan, and A. Huang

Précis: Long-term imatinib treatment leads to downregulation of Sprouty proteins and FGFR-driven reactivation of the MAPK–ERK pathway in KIT-mutant GIST cells, which can be repressed by FGFR inhibition.

Deregulated control of alternative splicing has been implicated in many cancers. To map the genetic regulation of splicing in neuroblastoma, Chen and colleagues integrated genome and transcriptome data from a mouse model of neuroblastoma. Characterization of splicing quantitative trait loci (sQTL) highlighted genes that regulate alternative splicing and strain-specific splicing of genes that correlated with patient survival. In addition, the authors identified unique intronic splicing motifs in genes that were recurrently mutated in human neuroblastoma and glioblastoma. Mutation of these motifs resulted in functional changes in alternative splicing, and altered expression of the corresponding genes correlated with patient outcome in neuroblastoma. These results identify splicing factors and intronic splicing motifs that modulate alternative splicing across cancers and highlight candidate genes potentially involved in neuroblastoma. For details, please see the article by Chen and colleagues on page 380.

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