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

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


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


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.
ON THE COVER

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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