DNA-Damage Response during Mitosis Induces Whole-Chromosome Missegregation

S.F. Bakhoum, L. Kabeche, J.P. Murnane, B.I. Zaki, and D.A. Compton

Précis: Activation of the DNA damage response during mitosis leads to whole chromosome segregation defects via PLK1/Aurora A–mediated stabilization of kinetochore–microtubule attachments.

See commentary, p. 1256

L-2-Hydroxyglutarate: An Epigenetic Modifier and Putative Oncometabolite in Renal Cancer


Précis: Accumulation of l-2-hydroxyglutarate in renal cell carcinoma as a result of somatic L2HGDH deficiency is associated with alterations in DNA and histone methylation.

Brain Tumor Cells in Circulation Are Enriched for Mesenchymal Gene Expression


Précis: Circulating tumor cells with invasive mesenchymal characteristics can be detected in patients with glioblastoma and may prove useful in disease monitoring.

See commentary, p. 1259

Collateral Genome Instability by DNA Damage in Mitosis

N. Jelluma and G.J.P.L. Kops

See article, p. 1281

Escaping Out of the Brain

J. Seoane and L. De Mattos-Arruda

See article, p. 1299

Insights into the Mechanism of Organ-Specific Cancer Metastasis

M.A. Rubin

See article, p. 1310

Social Interactomes for Enabling Research Communities

J. Guinney, R. Dienstmann, C. Ferté, S. Friend, and F. McCormick

Resistance to Anti-EGFR Therapy in Colorectal Cancer: From Heterogeneity to Convergent Evolution

S. Misale, F. Di Nicolantonio, A. Sartore-Bianchi, S. Siena, and A. Bardelli

See article, p. 1299

In Focus

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See article, p. 1299
The Androgen-Regulated Protease TMPRSS2 Activates a Proteolytic Cascade Involving Components of the Tumor Microenvironment and Promotes Prostate Cancer Metastasis 1310


Précis: The serine protease TMPRSS2 enhances androgen-driven prostate cancer metastasis by inducing HGF cleavage and activation of c-MET signaling, and may represent a potential therapeutic target.

See commentary, p. 1262

The Genomic Landscape of Pediatric Ewing Sarcoma 1326


Précis: Ewing sarcoma tumors exhibit a low mutation rate but frequently harbor somatic mutations in STAG2, which are mutually exclusive with CDKN2A loss and correlate with TP53 mutations and poor prognosis.

Genomic Landscape of Ewing Sarcoma Defines an Aggressive Subtype with Co-Association of STAG2 and TP53 Mutations 1342


Précis: Using next-generation sequencing, Crompton, Stewart, and colleagues found that Ewing sarcoma tumors were relatively genetically stable, but exhibited recurrent loss of stromal antigen 2 (STAG2) expression, which was associated with metastatic progression. In addition, relapsed tumors displayed an increased mutation rate compared with tumors at diagnosis. Using whole-genome sequencing, Tirole, Surdez, and colleagues also detected few somatic alterations in Ewing sarcoma and identified STAG2 as the most frequently mutated gene. STAG2 mutations were mutually exclusive with CDKN2A deletion, but often coexisted with TP53 mutations, were associated with poor outcome, and expanded at tumor relapse. Together, these findings provide insight into the genomic landscape of Ewing sarcoma and suggest potential therapeutic targets. For details, please see the article by Crompton, Stewart, and colleagues on page 1326 and the article by Tirole, Surdez, and colleagues on page 1342.