Clinical Response to a Lapatinib-Based Therapy for a Li-Fraumeni Syndrome Patient with a Novel HER2\(^{V659E}\) Mutation 1238


Précis: Tumors of a patient with a germline TP53 mutation were found to harbor alterations in either EGFR or HER2 and were responsive to targeted therapy with lapatinib.

Androgen Receptor Signaling Regulates DNA Repair in Prostate Cancers 1245


Précis: Antiandrogen therapy suppresses androgen receptor–mediated induction of DNA repair genes, resulting in increased DNA damage and enhanced radiosensitivity of prostate cancer cells.

In The Spotlight

Small RNAs Deliver a Blow to Ovarian Cancer 1220
A. Kasinski and F.J. Slack
See article, p. 1302

Androgen Receptor Signaling Fuels DNA Repair and Radioresistance in Prostate Cancer 1222
J. Bartek, M. Mistrik, and J. Bartkova
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Tumor-Promoting and -Suppressive Roles of Autophagy in the Same Mouse Model of Braf\(^{V600E}\)-Driven Lung Cancer 1225
S. Chen and J.-L. Guan
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Misregulation of Pre-mRNA Alternative Splicing in Cancer 1228
J. Zhang and J.L. Manley

A Hormone–DNA Repair Circuit Governs the Response to Genotoxic Insult 1254
J.F. Goodwin, M.J. Schiewer, J.L. Dean, R.S. Schrecengost, R. de Leeuw, S. Han, T. Ma, R.B. Den, A.P. Dicker, F.Y. Feng, and K.E. Knudsen

Précis: Androgen receptor activation in response to DNA damage promotes double-strand break repair via DNAPKcs and confers resistance to genotoxic insult in advanced prostate cancer.

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See commentary, p. 1222
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Autophagy Sustains Mitochondrial Glutamine Metabolism and Growth of BrafV600E-Driven Lung Tumors


Précis: Autophagy ablation suppresses the growth of BrafV600E-driven lung tumors by limiting glutamine availability and impairing mitochondrial function.

See commentary, p. 1225

Targeting the Wnt Pathway in Synovial Sarcoma Models


Précis: Constitutive activation of WNT/β-catenin signaling by the SYT-SSX oncogene is required for the initiation and progression of synovial sarcoma.

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Therapeutic Synergy between microRNA and siRNA in Ovarian Cancer Treatment


Précis: Combined inhibition of EPHA2 using siRNA and miR-520d-3p synergistically suppresses ovarian cancer tumorigenesis.

See commentary, p. 1220

Strohecker and colleagues found that deletion of the essential autophagy gene Atg7 initially induced oxidative stress and accelerated the formation of BrafV600E-driven lung tumors but eventually slowed tumor growth and prolonged survival. Atg7 deficiency led to an accumulation of morphologically and functionally defective mitochondria in BrafV600E-driven lung tumors and rendered tumor cells dependent on exogenously supplied glutamine for survival. BrafV600E-driven tumors may therefore become addicted to autophagy to sustain cell survival and proper mitochondrial function through the clearance of damaged organelles and recycling of metabolites for biosynthesis, and may thus be sensitive to autophagy inhibitors. For details, please see the article by Strohecker and colleagues on page 1272.