A Tale of Metabolites: The Cross-Talk between Chromatin and Energy Metabolism
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Molecular Dissection of Microsatellite Instable Colorectal Cancer
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Relief of Feedback Inhibition of HER3 Transcription by RAF and MEK Inhibitors Attenuates Their Antitumor Effects in BRAF-Mutant Thyroid Carcinomas

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De-Repression of PDGFRβ Transcription Promotes Acquired Resistance to EGFR Tyrosine Kinase Inhibitors in Glioblastoma Patients. .......... 534
Précis: Transcriptional derepression of PDGFRβ in response to EGFR inhibition renders EGFR-mutant glioblastomas dependent on PDGFRβ for survival.

Coordinate Direct Input of Both KRAS and IGF1 Receptor to Activation of PI3 Kinase in KRAS-Mutant Lung Cancer .......... 548
M. Molina-Arcas, D.C. Hancock, C. Sheridan, M.S. Kumar, and J. Downward
Précis: KRAS-mutant NSCLC cells are selectively sensitive to inhibition of IGF1R, which is required for KRAS-mediated activation of PI3K signaling.
See commentary, p. 491

Bone Marrow–Derived Gr1+ Cells Can Generate a Metastasis-Resistant Microenvironment Via Induced Secretion of Thrombospondin-1 .......... 578
Précis: Metastasis-incompetent tumors systemically reprogram bone marrow–derived myeloid cells in the premetastatic niche to produce TSP-1 to suppress metastatic outgrowth.

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ON THE COVER
Montero-Conde and colleagues show that BRAF-mutant thyroid cancer cells are resistant to RAF and MAP/ERK (MEK) inhibitors. Reactivation of RAS signaling in these cells was associated with de-repression of HER3 transcription due to decreased binding of C-terminal binding protein 1 and 2 (CTBP1/CTBP2) to the HER3 promoter. RAF/MEK inhibition also triggered increased HER3 phosphorylation and activation of HER2/HER3 heterodimers specifically in BRAF-mutant thyroid cancer cells. This effect was dependent on autocrine production of the HER3 ligand neuregulin 1 in thyroid cancer cells, identifying a lineage-specific mechanism of MAPK inhibitor resistance. Treatment with lapatinib sensitized thyroid cancer cells to RAF/MEK blockade and inhibited the growth of murine thyroid tumors, suggesting that this combination may overcome resistance in patients with thyroid cancer. For details, please see the article by Montero-Conde and colleagues on page 520.