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Précis: Bisphosphonates bind granular microcalcifications and are internalized by tumor-associated macrophages in breast tumors.
See commentary, p. 14

The Vigorous Immune Microenvironment of Microsatellite Instable Colon Cancer Is Balanced by Multiple Counter-Inhibitory Checkpoints .......................... 43

Précis: Mismatch repair-deficient colorectal cancers counteract Th1/CTL immune responses by upregulating immune checkpoint proteins, including PD-1 and PD-L1.
See commentary, p. 16

Mutant KRAS-Induced Expression of ICAM-1 in Pancreatic Acinar Cells Causes Attraction of Macrophages to Expedite the Formation of Precancerous Lesions ............... 52

Précis: Crosstalk between pancreatic acinar cells and proinflammatory macrophages promotes initiation of acinar-to-ductal metaplasia via KRASG12D-induced expression of the macrophage chemoattractant ICAM1.
**Prospective Blinded Study of BRAF<sup>V600E</sup> Mutation Detection in Cell-Free DNA of Patients with Systemic Histiocytic Disorders**


**Précis:** Cell-free DNA testing using plasma and urine samples may be a reliable, noninvasive method to identify mutations and monitor treatment response in histiocytic disorders.

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**Measuring Residual Estrogen Receptor Availability during Fulvestrant Therapy in Patients with Metastatic Breast Cancer**

M. van Kruchten, E.G. de Vries, A.W. Glaudemans, M.C. van Lanschot, M. van Faassen, I.P. Kema, M. Brown, C.P. Schröder, E.F. de Vries, and G.A. Hospers

**Précis:** Decreased [18F]fluorooestradiol uptake visualized by PET/CT provides a measure of tumor ER availability and correlates with fulvestrant treatment outcome in patients with metastatic breast cancer.

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**Induction of Telomere Dysfunction Mediated by the Telomerase Substrate Precursor 6-Thio-2'-Deoxyguanosine**

I. Mender, S. Gryaznov, Z.G. Dikmen, W.E. Wright, and J.W. Shay

**Précis:** 6-thio-2'-deoxyguanosine is a precursor of a telomerase substrate that is incorporated into newly synthesized telomeres, leading to telomere dysfunction and death in telomerase-expressing cells.

See commentary, p. 19

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Hyman, Diamond, and colleagues carried out a prospective, blinded study to quantitatively detect the BRAF<sup>V600E</sup> mutation in circulating tumor cell-free DNA (cfDNA) from the urine and plasma of patients with Langerhans cell histiocytosis or Erdheim-Chester disease. Urinary cfDNA analysis defined the BRAF genotype of all 30 patients and was 100% concordant with tissue genotypes among treatment-naïve patients. Furthermore, serial urinary cfDNA analyses in patients treated with a BRAF inhibitor or immunomodulatory therapy showed a progressive decrease in BRAF<sup>V600E</sup> allele burden, consistent with radiographic evidence of disease improvement. Tissue and cfDNA genotyping also identified a previously unreported somatic KRAS<sup>G12S</sup> mutation in a BRAF wild-type patient. These data suggest cfDNA testing as a reliable, noninvasive method to detect BRAF<sup>V600E</sup> mutations and monitor response to therapy in histiocytic disorders. For details, please see the article by Hyman, Diamond, and colleagues on page 64.