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Précis: Crosstalk between pancreatic acinar cells and proinflammatory macrophages promotes initiation of acinar-to-ductal metaplasia via KRAS(12)-induced expression of the macrophage chemotactant ICAM1.
**Prospective Blinded Study of \( \text{BRAF}^{V600E} \) 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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**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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**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 [\(^{18}\)F]fluoroestradiol 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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**ON THE COVER**

Hyman, Diamond, and colleagues carried out a prospective, blinded study to quantitatively detect the \( \text{BRAF}^{V600E} \) 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 \( \text{BRAF} \) 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 \( \text{BRAF}^{V600E} \) allele burden, consistent with radiographic evidence of disease improvement. Tissue and cfDNA genotyping also identified a previously unreported somatic \( \text{KRAS}^{G12S} \) mutation in a \( \text{BRAF} \) wild-type patient. These data suggest cfDNA testing as a reliable, noninvasive method to detect \( \text{BRAF}^{V600E} \) mutations and monitor response to therapy in histiocytic disorders. For details, please see the article by Hyman, Diamond, and colleagues on page 64.