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See commentary, p. 16

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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 .................64


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.

Induction of Telomere Dysfunction Mediated by the Telomerase Substrate Precursor 6-Thio-2'-Deoxyguanosine .... 82

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

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 urine 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.

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