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Review
An Evolutionary Approach to Clonally Complex Hematologic Disorders
E. Schwenger and U. Steidl

Briefs
Dissecting Clonal Hematopoiesis in Tissues of Patients with Classic Hodgkin Lymphoma
Précis: In situ genetic composition of classical Hodgkin lymphoma tumors, normal lymph node tissue, and blood dissects contributions of clonal hematopoiesis to malignant lymphoma.
The presence of somatic mutations in a fraction of blood cells, termed clonal hematopoiesis (CH), is associated with increased risk of blood cancers. With a few exceptions, the exact relationships between CH and hematologic malignancies remain uncharted. A broad conceptual framework encompassing clonal relationships in cancer evolution is laid out in a review article by Schwenger and Steidl on page 201. The article on page 216 by Venanzi and colleagues dissects CH contributions to Hodgkin lymphoma in the blood lineage, tumor cells, and their microenvironment. Certain mutations with known oncogenic properties are especially common in CH. Conversely, studies of CH are often limited to a panel of these predetermined hotspots. Genomic analysis by Feusier and colleagues (page 226) expands the catalog of mutations recurrent in blood cancer and in CH. Cover images by Katie Vicari and Doug Smock.

SIRT5 Is a Druggable Metabolic Vulnerability in Acute Myeloid Leukemia


Précis: CRISPR screen identifies SIRT5 as a metabolic vulnerability in AML but not in healthy hematopoietic cells. SIRT5 controls mitochondrial and glutamine metabolic pathways in AML. SIRT5 genetic or pharmacologic inhibition triggers apoptosis and delays leukemia progression, pointing to its potential as a therapeutic target for AML.

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