Abstract

Aging is characterized by clonal expansion of myeloid-biased hematopoietic stem cells and by increased risk of myeloid malignancies. Exome sequencing of three elderly females with clonal hematopoiesis, demonstrated by X-inactivation analysis, identified somatic TET2 mutations. Recurrence testing identified TET2 mutations in 10 out of 182 individuals with X-inactivation skewing. TET2 mutations were specific to individuals with clonal hematopoiesis without hematological malignancies and were associated with alterations in DNA methylation.