

The role of mutations in epigenetic regulators in myeloid malignancies.

Abstract

Recent genomic studies have identified novel recurrent somatic mutations in patients with myeloid malignancies, including myeloproliferative neoplasms (MPNs), myelodysplastic syndrome (MDS) and acute myeloid leukaemia (AML). In some cases these mutations occur in genes with known roles in regulating chromatin and/or methylation states in haematopoietic progenitors, and in other cases genetic and functional studies have elucidated a role for specific mutations in altering epigenetic patterning in myeloid malignancies. In this Review we discuss recent genetic and functional data implicating mutations in epigenetic modifiers, including tet methylcytosine dioxygenase 2 (TET2), isocitrate dehydrogenase 1 (IDH1), IDH2, additional sex combs-like 1 (ASXL1), enhancer of zeste homologue 2 (EZH2) and DNA methyltransferase 3A (DNMT3A), in the pathogenesis of MPN, MDS and AML, and discuss how this knowledge is leading to novel clinical, biological and therapeutic insights.