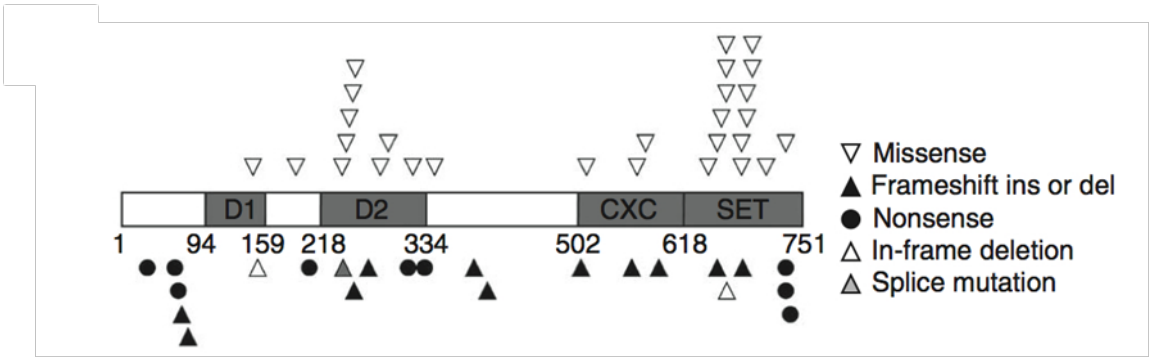
EZH2 (Enhancer of Zeste Homolog 2)

EZH2 belongs to the PRC2 complex (polycomb repressive complex 2) involved in the regulation of expression of genes taking part in the control of the self-renewal / cell differenciation balance. EZH2 constitutes the catalytic sub-unit allowing *via* its SET domain (suppressor of variegation 3–9, enhancer of zeste and trithorax) the trimethylation of lysin 27 of H3 histone. So, the PRC2 complex allows the repression of gene expression by promoting DNA methylation or PRC1 complex recruitment.[1]

In myeloid malignancies, *EZH2* mutations can affect all the exons (even the introns sometimes) and most mutations are predicted to be inactivating. They often lead to protein truncation with deletion of the SET domain, or to the loss of aminoacids essential to the protein activity.[2] Generally, they are associated to the deletion of the other copy of the *EZH2* gene, or most frequently to a loss of heterozygosity by acquired uniparental disomy, suggesting a tumor suppressor activity. These mutations are observed in 6% of myelodysplastic syndromes (MDS), 6-13% of primary and post-myeloproliferative neoplasm (MPN) myelofibrosis and in frontier MPN/MDS syndromes, 13% of atypical chronic myelogenous leukemia and chronic myelomonocytic leukemia, and 10% of unclassifiable MPN/MDS. In contrast, they only affect 3% of polycythaemia vera patients and have not been described in essential thrombocythaemia in non-fibrotic phase. *EZH2* mutations are associated with a unfavorable pronostic.[2–5] These mutations can be associated with *JAK2*, *MPL*, *TET2*, *ASXL1* and *CBL* mutations, and they can appear during the chronic phase of the disease.[3,4]



Ernst T et al. Nature Genet 2010.

D1: domain I; D2: domain II; CXC: cysteine-rich domain; SET: suppressor of variegation 3-9, enhancer of zeste and trithorax (SET) domain.

References

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