LNK

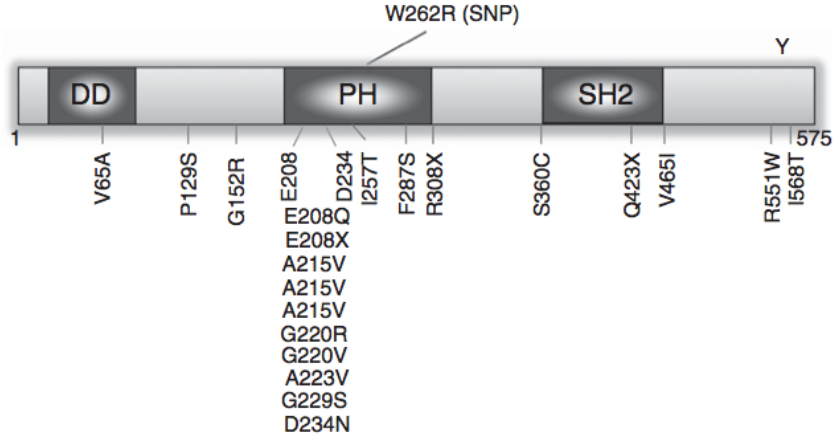
Also called SH2B3, LNK is a member of the SH2B family, a group of adaptator proteins caracterized by a structure in 3 domains:

- A proline-rich N-terminal domain,
- A central PH domain (Plekstrin Homology) allowing the localisation to the cell membrane,
- A SH2 domain (Src Homology) involved in the interaction with LNK targets.[1]

Due to its SH2 domain, LNK can inhibit erythropoietin and throbopoietin receptor signalling, even in the presence of *JAK2*V617F or *MPL*W515 mutations.[2,3]

LNK mutations affecting exon 2 (which encode part of the PH domain) have been discovered in myeloproliferative neoplasms (MPNs). More rarely, *LNK* mutations may occur in exons 4, 5, 7 and 8.[4–8] They consist in false-sense mutations or deletions, and are most often heterozygous.[6] They are associated with complete or partial loss-of-function, and thus led to an excessive activation of the JAK-STAT pathways.[4]

LNK mutations are rare in MPNs during the chronic phase (about 5%)[4,6–9] but their frequency is higher during the blastic phase (9.8%).[6] *LNK* mutations have been described in idiopathic erythrocytosis (with a frequency of 5%), suggesting that the phenotype depends of other factors, probably the existence of other mutations.[5,10,11] *LNK* mutations may coexist with the *JAK2*V617F mutation.[4,6,8]



Gery et Koeffler. Oncogene 2013

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