LNK

Also called SH2B3, LNK is a member of the SH2B family, a group of adaptor proteins characterized 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 thrombopoietin receptor signalling, even in the presence of JAK2V617F or MPLW515 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 JAK2V617F mutation.⁴,⁶,⁸

References