Br J Haematol 2008 Sep;142(6):986-90 Epub 2008 Jul 30

PMID: 18671703 DOI: 10.1111/j.1365-2141.2008.07180.x

Loss of the JAK2 intramolecular auto-inhibition mechanism is predicted by structural modelling of a novel exon 12 insertion mutation in a case of idiopathic erythrocytosis

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Abstract

We report a novel gain-of-function JAK2 exon 12 insertion mutation in a patient with idiopathic erythrocytosis and low serum erythropoietin level. To date, only rare cases of such mutations have been reported in the JAK2 exon 12. Using computer-based structural modelling we propose that this mutation causes the loss of the JAK2 auto-inhibition step, leading to the constitutive activation of JAK2 tyrosine kinase-dependent activity. Our model-based hypothesis provides a useful approach for the investigation of the phenotype-genotype relationship in myeloproliferative disorders involving JAK2.