

Docket #: S10-001

LNK mutations in myeloproliferative neoplasms

A team of Stanford researchers has identified mutations in the LNK gene in a subset of patients with chronic myeloproliferative neoplasms (MPNs). LNK (also known as SH2B3) is an adaptor protein that inhibits JAK-STAT signaling. The LNK mutations are the first linked to human disease and were discovered in patients with JAK2 V617F and MPL 515-negative MPNs. This finding can be used to characterize the molecular basis of the disease in the ~40-50% of MPN patients in which no recurrent genetic abnormality has been identified and may also exist as a concurrent mutation in patients with other genetic abnormalities. This discovery could serve as 1) the basis for developing molecular diagnostic tests; 2) as a clonal genetic marker for measuring allele burden and minimal residual disease in treated patients; and 3) LNK could be a novel target for therapeutics.

Ongoing Research

The inventors continue to characterize new mutations in the LNK gene in patients with MPNs and other hematolymphoid malignancies.

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Applications

- **Diagnostic** - DNA or RNA screening of the LNK gene in patients with MPNs, such as essential thrombocythemia , primary myelofibrosis, polycythemia vera, or other hematolymphoid malignancies
- **Disease monitoring** - a molecular marker to assess the allele burden of disease during the course of the illness or in response to treatment
- **Therapeutic target** - for screens of novel agents to treat patients with MPNs or other hematolymphoid malignancies

Advantages

- Currently there is no diagnostic test for evaluating LNK mutations in hematolymphoid malignancies. This would serve as the first foray into diagnostic evaluation of LNK mutations in blood disorders.

Publications

- Stephen T. Oh, Erin F. Simonds, Carol Jones, Matthew B. Hale, Yury Goltsev, Kenneth D. Gibbs, Jr., Jason D. Merker, James L. Zehnder, Garry P. Nolan, and Jason Gotlib, "[Novel mutations in the inhibitory adaptor protein LNK drive JAK-STAT signaling in patients with myeloproliferative neoplasms](#)" *Blood*, published online April 19, 2010.

Patents

- Published Application: [20120046233](#)
- Published Application: [WO2011088125](#)
- Issued: [8,945,846 \(USA\)](#)

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