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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