Finnish researchers identify the cause for LGL leukemia

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Researchers of the University of Helsinki, Helsinki University Central Hospital and Institute for Molecular Medicine Finland, have discovered that a mutation in the STAT3 gene is an underlying cause for LGL leukemia. Since the STAT3 gene is also abnormally expressed in many other cancers and autoimmune diseases, this finding has roused extensive interest. The research will be published in the *New England Journal of Medicine* on Thursday, May 17, 2012.

LGL leukemia is a relatively rare, malignant blood disease of the mature T-cells and, in many cases, it is related to autoimmune diseases such as rheumatoid arthritis. The pathogenetic mechanism of the disease has been unknown and it has previously been unclear if the disease is an overreaction of the normal defense system or a malignant hematological disease.

One of the key symptoms of LGL disease is a low count of white blood cells (neutrophils), which may predispose the patients to life-threatening infections.

It was discovered that patients suffering from LGL leukemia have a mutation in the STAT3 gene in a very restricted SH2 area, which has a key effect on the function of the gene. This is not an inherited gene mutation but a so-called acquired mutation. The cause for the mutation is not known, but probably chronic viral infection or some other long-term antigen exposure can be predisposing factors. The STAT3 gene plays a key role in many cell signaling pathways.

After the finding, the prevalence of the mutation in LGL patients was verified using a larger patient group (77 patients) in cooperation with research groups at the Ohio (Prof. Maciejewski) and Pennsylvania (Prof. Loughran) Universities. It was discovered that 40% of all LGL patients present with the STAT3 mutation.

In the future, this result can be utilized in diagnosing the disease and possibly also in treatment, since the first STAT3 inhibitors are already undergoing early clinical trials. In addition, the research discovered that those LGL patients who had a mutation in the STAT3 gene were also more likely to suffer from rheumatoid arthritis. Hence, the research group intends to clarify next if patients suffering from rheumatoid arthritis can be found with similar gene mutations. If such mutations were to be found this would introduce new opportunities to the pathogenetic mechanisms of rheumatoid arthritis and other autoimmune diseases.

Provided by University of Helsinki