Immune system genes linked to most common type of leukaemia

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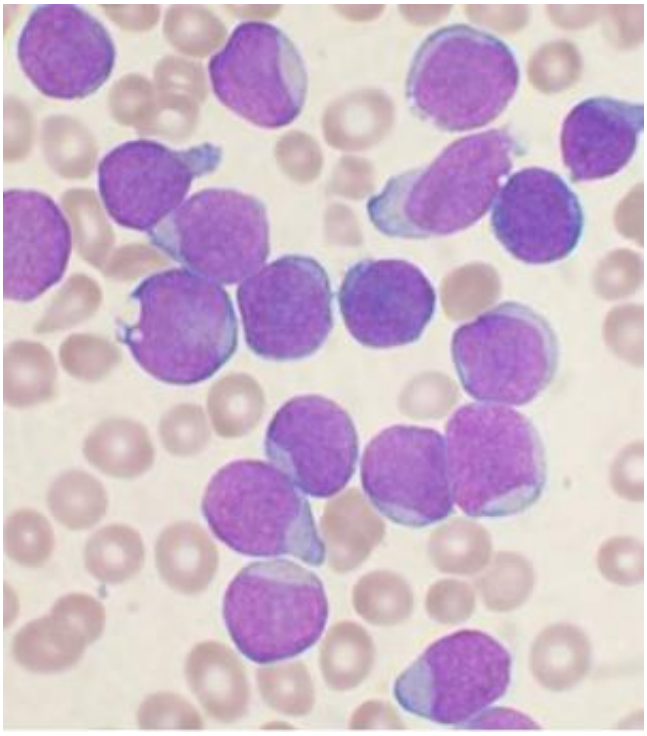

A Wright's stained bone marrow aspirate smear of patient with precursor B-cell acute lymphoblastic leukemia. Credit: VashiDonsk/Wikipedia

People who inherit genetic variants affecting the function of their immune system are at increased risk of developing the most common form of leukaemia, a major new study reveals.

Scientists have linked the risk of developing chronic lymphocytic

leukaemia (CLL) to the inheritance of nine regions of DNA, five of which help white blood cells fight disease.

The research sheds fresh light on the causes of CLL, and could lead researchers to new targeted drugs for the disease, or help in selecting existing immunotherapy treatments.

An international team, co-led by scientists at The Institute of Cancer Research, London, conducted the largest study of its kind in CLL.

These new variants affecting the immune system were each individually associated with an increased risk of up to 17 per cent of developing CLL.

Two fell within regions of DNA that have previously been linked with autoimmune disorders – multiple sclerosis and lupus.

The research was funded by the charity Bloodwise, and is published in *Nature Communications* today.

The researchers have now found 41 DNA changes– that influence the risk of developing CLL.

CLL is a slow-growing a cancer of the white blood cells that affects around 3,500 people a year.

The cancerous white blood cells aren't as good at fighting infection as their healthy counterparts, and, competing for space with other essential cells such as red blood cells and platelets.

The new study combined data from six previous studies and two new studies involving 6,200 people with CLL.

One of the new variants resides in the gene BANK1, only ever activated in a type of white blood cell called B cells, and linked to the autoimmune disease lupus.

Another was found in the gene ZBTB7A, which regulates B cells numbers – so errors in this gene could lead to too many B cells in the bloodstream and bone marrow.

A third was found in a region of chromosome 22 which has been linked with the risk of developing multiple sclerosis.

Study co-leader Professor Richard Houlston, Professor of Molecular and Population Genetics at The Institute of Cancer Research, London, said:

"We knew people were more likely to develop chronic lymphocytic leukaemia if someone in their family had suffered from the disease, but our new research takes a big step towards explaining the underlying genetics.

"CLL is essentially a disease of the immune system, and it's fascinating that so many of the new genetic variants we have uncovered seem to directly affect the behaviour of white blood cells and their ability to fight disease.

"Understanding the genetics of CLL can point us towards new treatments for the disease, and help us to use existing targeted drugs more effectively."

Dr Alasdair Rankin, Director of Research at Bloodwise said:

"At the moment, CLL is incurable and we desperately need to find new ways to tackle this blood cancer. This important research provides another valuable layer in understanding how genetic variations cause

CLL to develop. We are beginning to gain a detailed picture of what drives this disease, and we hope this eventually leads to more accurate diagnosis and more informed personalised treatment for people affected by CLL."

Professor Paul Workman, Chief Executive of The Institute of Cancer Research, London, said:

"We're increasingly appreciating that part of the key to understanding cancer and how to treat it lies in the immune system. This fascinating study makes a link between genetic variants in the immune system and the development of leukaemia, and implicates regions of DNA which are also involved in auto-immune diseases. The findings could point us towards new ways of treating leukaemia or better ways of using existing treatments – potentially including immunotherapies."

Provided by Institute of Cancer Research