CCLG RESEARCH PROJECT UPDATE

Improving the outlook for children with Philadelphia positive ALL

Project title: Unravelling clinical heterogeneity in Philadelphia positive ALL

Lead researcher: Professor Christina Halsey, University of Glasgow

Project Stage: Complete (ended February 2023)

Funded by: CCLG and Toti Worboys Fund, Elliott's Warrior Fund, Captain Ciara Killing Cancer and #GoTeamHuey

ABOUT THE PROJECT

Problems in the genes that control blood cell development are common causes of blood cancers, such as acute lymphoblastic leukaemia. One example involves genes moving from one chromosome to another, producing an abnormal chromosome called the Philadelphia chromosome. This genetic change can produce at least two types of leukaemia - chronic myeloid leukaemia (CML) and Philadelphia positive acute lymphoblastic leukaemia (Ph+ALL).

These types of leukaemia are usually thought of as very separate diseases and have different treatments. However, new research suggests that some cases of Ph+ALL have a lot in common with CML. These are called CML-like Ph+ALL and could be a new sub-type of leukaemia that might need different treatment approaches.

The research team at the University of Glasgow, led by Professor Christina Halsey, will investigate this newly discovered leukaemia sub-type. They have three aims:

1. To discover whether CML and CML-like Ph+ALL come from the same type of early blood cells in the bone marrow. This will help them understand how CML-like Ph+ALL develops.
2. To measure the levels of gene expression in the different leukaemia subtypes to see if they can identify a genetic "signature" that could diagnose CML-like Ph+ALL. This will help create new tests to identify patients with CML-like Ph+ALL at diagnosis.
3. To test CML-like Ph+ALL cells in the laboratory to see if they will respond to new and less toxic therapies that the research team have recently developed to treat patients with CML.

In this way, Professor Halsey aims to improve the outlook for patients diagnosed with Ph+ALL, by making sure they get the right diagnosis and treatment.

RESULTS

Using expert techniques, Professor Halsey found a group of Ph+ALL patients whose cancer behaved differently, presented differently clinically, and had different genetic signatures to other Ph+ALL patients.

A number of these patients had higher levels in some genes than would be expected in Ph+ALL, making the cancer more similar to some patients with CML. Professor Halsey also found that these patients sometimes have higher white blood cell counts at diagnosis, and that it is more likely their cancer will be hard to treat.

At the moment, CML-like Ph+ALL is identified by the presence of a gene, called BCR-ABL1. This project showed that the genetic error that creates this gene is not enough on its own to cause CML-like Ph+ALL, suggesting that there are also changes in the way DNA is read and used in this type of cancer. The team also found that the gene was first seen in a different type of cell to Ph+ALL, which could mean that CML-like Ph+ALL has the same origin as CML.

Because of the difficulties establishing a big enough group of CML-like Ph+ALL samples, and because more understanding of this cancer is needed, the research team weren't able to test possible treatments. However, further work on CML-like Ph+ALL has been funded which aims to address this.

WHAT'S NEXT?

Part of Professor Halsey's project has shown that CML-like Ph+ALL may be a group of cancers rather than just one type. This work is continuing in Dr Gillian Horne's project: https://tinyurl.com/CML-PhALL.

Dr Horne is looking at patient samples to see whether genetic tests can identify subgroups that may need altered treatment. This will give us more information about which cells are involved, how they interact, and whether there are different genes or proteins present in these cancer cells that cause the disease. She will also be investigating whether the BCR-ABL1 protein is part of causing treatment failure and relapse in Ph+ALL patients.

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Children's Cancer and Leukaemia Group
Century House, 24 De Montfort Street, Leicester LE1 7GB
Registered charity in England and Wales (1182637) and Scotland (SC049948).

0333 050 7654
info@cclg.org.uk
www.cclg.org.uk

ChildrensCLG
CCLG_UK
CCLG_UK