CCLG: The Children & Young People's Cancer Association research:

Identifying a new blood cancer to improve the outlook for patients with acute lymphoblastic leukaemia

Project title: Expanding our understanding of CML-like Ph+ALL – are all patients at increased risk of relapse?

Project stage: Ongoing (started June 2023, planned end June 2026)

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Led by: Dr Gillian Horne, University of Glasgow

About the project

Acute lymphoblastic leukaemia (ALL) is a type of blood cancer that affects children and adults. It is an aggressive disease that needs intensive treatment with chemotherapy. One reason people may get leukaemia is because errors have developed in their genes. One example is the Philadelphia chromosome (Ph+), which happens when two of the chromosomes that store DNA get stitched together incorrectly. When a patient has the Philadelphia chromosome, their ALL is normally more likely to not respond to treatment or to come back after treatment.

This chromosome error is also seen in another type of leukaemia, called chronic myeloid leukaemia (CML). This type of leukaemia behaves very differently to Ph+ALL because the broken chromosome happens in a different cell – a type of early stem cell. Stem cells are the manufacturing system in the bone marrow and can grow into any of the three main types of blood cells. This means that the genetic error affects a lot more cells than in Ph+ALL, where the error happens in a mature white blood cell. It has always been assumed that CML and Ph+ALL are different diseases.

However, recent scientific research has suggested that there could be similarities in some children. These cases have been called 'CML-like Ph+ALL'. This is a new type of leukaemia and research is needed to understand the disease better. We already know that these patients may have poorer outcomes to routine treatment and that they may need to be treated more like CML patients.

In this project, Dr Gillian Horne from the University of Glasgow will investigate CML-like Ph+ALL in children. Her team has 3 main aims:

- To discover how CML-like Ph+ALL develops, they will look at individual cells from multiple children with this disease to help find out if there is a 'genetic fingerprint' that doctors could use in the clinic to identify these patients at diagnosis.
- To discover whether the new cancer is behaving more like CML than Ph+ALL, the team will find out if it looks like a stem cell. They will use new types of experiments to identify the 'genetic fingerprint' of cells that have Ph+ and cells that do not.
- To find out if these cells are also behaving like a stem cell, like CML cells do. They will do this by using experiments in the laboratory to assess stem cell function.

Dr Horne hopes that this will have an enormous impact on patients and their families because, if her team can characterise CML-like Ph+ALL better, it will help patients to get the right treatment from diagnosis.

Progress

The researchers have analysed individual cancer cells from several patients and found a group of genes that could help doctors spot which type of Ph+ALL a child has. This is important bacause, if we can identify CML-like Ph+ALL early, doctors can give the right treatment from the start.

The team is also trying to find out whether these cancer cells act like stem cells, as they do in CML. So far, they've looked at three samples in detail and are continuing to test more to see if the cells grow and behave in the same way as stem cells do.

What's next?

The team is now waiting on final results from a test called clonoSEQ, which will help confirm earlier findings about different groups of cancer cells and where the disease may have started. These early results are very promising and show patterns that haven't been seen before in Ph+ALL.

Looking ahead, the researchers plan to study the environment around the cancer cells - both in the bone marrow and the central nervous system - to find new markers of disease and ways to target the more resistant stem-like cells.

Over the coming year, the team will bring together all of the data they've collected so far, finish their remaining lab experiments, and start thinking about future studies, which could include testing treatments in 3D lab models or living systems.

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CCLG The Children & Young People's Cancer Association

Century House, 24 De Montfort Street, Leicester, LE1 7GB
0333 050 7654 | **info@cclg.org.uk** | **www.cclg.org.uk**
@cclgUK