

## 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?

**Lead researcher:** Dr Gillian Horne, University of Glasgow

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

**Funded by:** Kayla's Rainbow Appeal, Ayla's Fundraising Adventure, Ethan's Journey of Smiles, Ruby's 'Live Kindly, Live Loudly' Fund, Fred Bennett's 'Don't Look Down' Fund, and Toti Worboys Fund

### 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:

1. 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.
2. 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.
3. 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 Gillian 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

So far, the team have been working on aim one, discovering how CML-like Ph+ALL develops. They now have in depth genetic data from five patient samples, which is undergoing analysis, and will continue to process the remaining samples. Progress has been delayed because the team were struggling to get hold of the cancer samples, but this is now arranged. Dr Horne has also started preparing for work on aim three, finding out how CML-like PH+ALL cells behave.

## WHAT'S NEXT?

The researchers will soon start work on aims two and three. They are also in the process of using the findings from this project, and from previous work, to explore the variations within Ph+ALL in more detail. The data from this project is being used to help design next UK Ph+ALL trial. Dr Horne also expects to use it as the basis for a further research application.

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