CCLG RESEARCH PROJECT UPDATE

# Developing a new understanding of the genetics of a rare lymphoma subtype

**Project title:** Developing a new understanding of the genetics of a rare lymphoma subtype (Anaplastic Lymphoma Kinase negative Anaplastic Large Cell Lymphoma)

**Lead researcher:** Dr Suzanne Turner, University of Cambridge

**Project Stage:** Complete (ended March 2023)

**Funded by:** Super Ru

## ABOUT THE PROJECT

Lymphoma is caused when white blood cells (infection-fighting cells) start to grow in an out of control in the body's lymph nodes. Anaplastic large cell lymphoma (ALCL) is a type of lymphoma that affects a white blood cell called a T-cell. Within this group, there are many different subtypes, which can be identified by different genes or protein markers. Most ALCL subtypes affect children and young adults. It is important for clinicians to understand as much as possible about the different subtypes of lymphoma, as this helps them decide the best treatment option.

Children with ALCL usually have a form of lymphoma where a protein called Anaplastic Lymphoma Kinase (ALK+) is activated. Adults normally don't have the ALK+ form, but instead can have a range of other genetic errors. However, no one has looked into whether these mutations also occur in children and, if they do, whether they affect a patient's treatment, diagnosis or clinical outcome. There is no research currently into children whose ALCL doesn't have the usual Anaplastic Lymphoma Kinase (ALK-) protein marker. Little is known about whether the tumours from these children also show other genetic mutations, and how this might affect their prognosis.

Dr Suzanne Turner is the chair of biological studies for the European Intergroup for Childhood Non-Hodgkin Lymphoma (EICNHL). As part of this, her research team at the University of Cambridge have found 25 cases of childhood ALK- ALCL. The researchers will look at the DNA of tumours to try to find genetic markers for this subtype of ALCL. They will also try to find if there are any other genetic changes in ALK- ALCL that can affect how their cancer progresses. Dr Suzanne Turner hopes their help to support the development of more effective tailored treatments for children with this rarer sub-form of cancer.

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## RESULTS

So far, Dr Turner's team have identified 17 cases of systemic ALK- ALCL cancer across the globe. They have also identified a further 11 cases that are skin-associated forms of ALK- ALCL, rather than systemic ALCL which can be present anywhere in the body and is usually in lymph nodes. This is the most extensive collection of these cancers anywhere in the world.

First, they checked that the lymphoma cells definitely didn't have the ALK protein to make sure they were ALK- ALCL. The team then analysed their DNA to see if they have any of the genetic errors seen in adult ALK- ALCL. They only found one case with an error similar to the adult cancer, suggesting that this type of lymphoma in children and young adults is different than in older patients.

Dr Turner looked for other genetic errors that might be driving ALK- ALCL in children and young adults, and found that two types of genetic errors were present: one group which affects how the tumour cells interpret the DNA code, and one which allows the cells to grow without the proper signals. Both of these errors allow the cells to 'go rogue' and grow out of control, but they also could be target to make a new way to treat these children in the future. Drugs targeting these genetic errors and their effects already exist, such as ruxolitinib and bromodomain inhibitors. The next step will be to find out if these drugs can kill the tumour cells in model systems, and to collect more ALK- ALCL samples of build on this work.

## WHAT'S NEXT?

The team are still waiting to receive more childhood ALK- ALCL samples, which they will then analyse. The team have had problems getting these samples due to a number of legal and ethical issues, but they team hope to receive these samples soon to analyse, and plan to publish a scientific paper by the end of the year.

Dr Turner also wants to get follow-up clinical data on the patients to see whether certain errors could be linked to patient outcome. This is also a slow process, but she is hopeful that everything will come together soon.

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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