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

Understanding why some childhood blood cancers are incurable

Project title: Understanding molecular mechanisms that drive high-risk childhood acute lymphoblastic leukaemia

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

Funded by: CCLG and CCLG Special Named Funds including Ruby's 'Live Kindly, Live Loudly' Fund, Fred Bennett's 'Don't Look Down' Fund, Toti Worboys Fund, Harley James Reynolds Fund, Josh's Gold Star Fund, Seren's ALL Stars, Thomas Fight Tall, and Ariana's Rainbow Friends.

Led by: Professor Anindita Roy, University of Oxford

About the project

Although we can now cure nine out of 10 children with leukaemia, there are still some children who can't be treated successfully. These children have 'high-risk' types of leukaemia that are usually caused by errors in specific genes. These patients often don't respond to treatment and their cancer can return after treatment. We urgently need a better understanding of these treatment resistant subtypes, so that we can cure every child with leukaemia.

Professor Anindita Roy and her team at the University of Oxford have developed a way to create models which behave like cancer, by giving leukaemia genes to normal cells. They will use these models to understand how high-risk leukaemias develop, the pathways that drive this aggressive disease and to test new drugs for treatment. Previous research by their lab has shown that leukaemia cells can need certain genes to be mistakenly turned on or off in order to survive.

In this project, Professor Anindita Roy will use leukaemia cells from these models, and from patients, to understand how these leukaemia survival genes cause the cancer cells to develop and resist treatment. To do this, her team will analyse how different types of healthy cells change when given leukaemia genes, and see whether preventing these changes can make the leukaemia less aggressive. The results of these experiments will show suggest new targets for treatment - especially if the researchers can find a preventable change that is only found in treatment-resistant leukaemia cells.

Progress

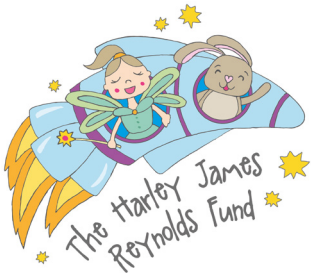
So far, the team have been working on creating a model with a genetic error called MLL::AF4 translocation. This error can be formed in a few different ways, which causes distinct differences in the leukaemia. The researchers have successfully introduced three versions of the translocation into healthy cells in the lab. They are also gathering data to enable the creation of further models with different leukaemia mutations.

Prof Roy's team are also working on understanding how giving these genetic errors to normal cells leads to leukaemia. They have found that there are differences in leukaemia subtype caused by the different translocation versions. These experiments are ongoing, and the team plan to analyse this further.

What's next?

Over the next year, the team plan to create more models with another genetic errors, called a BCR::ABL1 translocation. They will also design a new lab test that will help them identify and evaluate DNA containing this error.

To understand more about how cells can be transformed from healthy cells into leukaemia cells, the team will then investigate transformed cells' genetic material at multiple timepoints. They hope that this will provide a foundation that will allow further research into the alteration of leukaemia cells. In particular, this knowledge will enable the identification of new pathways and targets that influence cancer development and can be harnessed to find new treatments.



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