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

How do leukaemia stem cells talk to the immune system in juvenile myelomonocytic leukaemia?

Project title: Characterising the cross talk between RAS mutant haematopoietic stem cells and immune effector cells in juvenile myelomonocytic leukaemia

Project stage: Complete (ended August 2025)

Funded by: CCLG and CCLG Special Named Funds including Hallie's Helping Hands, Carey's Friends, and #PearlPower

Led by: Professor Adam Mead, University of Oxford

About the project

Juvenile myelomonocytic leukaemia (JMML) is an extremely rare and aggressive form of leukaemia - only around 10 children are diagnosed in the UK per year. There are no effective current treatment options. Haematopoietic stem cell transplantation (HSCT) is the only chance of curing JMML, but there are many side effects and the cancer comes back in four in 10 children. At this point, the cancer is incurable. The unique nature of the disease and small number of cases means that there is little research into better treatment options.

In 2015, Professor Adam Mead's team at the University of Oxford found that there were specific cells which caused JMML to come back after treatment - JMML leukaemia stem cells. Based on this finding, the team found a protein, called CD96, that is only found on the surface of these cells. This work is still in progress, but could lead to the first immunotherapy for JMML. In this project, the research team hope to find a new way to target JMML cells that could be used as a treatment alongside the planned immunotherapy, which would improve survival. They will be investigating how JMML leukaemic stem cells make the cancer return after treatment.

The researchers believe that the stem cells have the ability to switch off the immune system, which should be hunting down any JMML cells that are left over after HSCT. If the immune system is switched off, it could leave JMML cells alive, leading to relapse. The team plan to study how the stem cells interact with the immune system at all times from diagnosis to relapse. Professor Adam Mead hopes that the study of these interactions will help to understand the mechanisms that make JMML resistant to treatment and suggest new ways to treat it.

Results

The researchers analysed stem cells from 30 JMML patients at diagnosis, after bone marrow transplant, and at either relapse or remission. This has created a detailed resource that will support future research

into why relapse happens. Using the data, the team developed new software that can accurately distinguish between patient cancer cells and bone marrow donor cells. This tool will be extremely useful for future research.

They also examined how JMML stem cells interact with immune cells and used this to show how these cells are arranged in the bone marrow. This work identified a specific interaction between JMML stem cells and certain immune cells that appears to help the cancer grow. Early laboratory tests suggest this interaction could be blocked with a potential new treatment, though more research is needed.

What's next?

The team will continue testing whether blocking the interaction between JMML stem cells and certain immune cells could form a safe and effective treatment. They also plan to work with clinical partners to explore whether these findings could support the development of a JMML clinical trial.

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