



## 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

**Lead researcher:** Professor Adam Mead, University of Oxford

**Project Stage:** Ongoing (started September 2023, planned end August 2025)

**Funded by:** Hallie's Helping Hands, Carey's Friends, and #PearlPower

### 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. It could also form part of a test that could tell doctors whether a child is relapsing, before any symptoms are present. This could allow earlier treatment and give the best chance of survival.

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.

## PROGRESS

In the first year of the project, the team have collected detailed genetic data about JMML cells from 15 patients at diagnosis, after a bone marrow transplant, and at either relapse or remission. They have developed new software that can accurately distinguish between patient cancer cells and bone marrow donor cells. This will be extremely useful for future research. They have also looked at how cells with different genetics are located within the bone marrow, which will help them understand how JMML interacts with the immune system.

The researchers are now analysing all of this genetic and spatial data in order to select the best ways to attack JMML. The goal of any new potential treatment would be to prevent abnormal communication between the leukaemia cells and the rest of the bone marrow. Ultimately, the team hope to find a way to stop the JMML cells from surviving after a bone marrow transplant.

## WHAT'S NEXT?

Over the next year, the researchers will confirm their findings so far, and begin development of a new JMML treatment. They are already preparing a scientific paper for publication, which will share their work so researchers across the globe can learn from it. The team are also planning to apply for further funding from other charities to continue work into a new treatment, which they hope will be available for clinical trials in the next five to 10 years.



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This project was funded by Special Named Funds at Children's Cancer and Leukaemia Group raising funds for research into leukaemia and childhood cancers.



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