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

Investigating the role of a PRMT5 in Ewing sarcoma and its potential as a target for treatment

Project title: Treating Ewing sarcoma with PRMT5 inhibitors – a novel opportunity with real translational potential

Project stage: Starting soon (October 2025)

Funded by: Funded by Bone Cancer Research Trust, the Ewing's Sarcoma Research Trust, Great Ormond Street Hospital Charity, CCLG and CCLG Special Named Funds; #PearlPower, the Kieran Maxwell Legacy, Rosie Rocks the World, and the David Vernon Fund

Led by: Professor Clare Davies and Dr Susanne Gatz, University of Birmingham

About the project

Ewing sarcoma is driven by a genetic error called EWSR1-FLI1, which helps the cancer cells replicate quickly and grow out of control. However, it is notoriously difficult to target for treatment. Instead, the researchers want to target EWS-FLI1 indirectly, by focusing on the 'replication stress response' process.

When the cancer cells are forced to grow faster by EWSR1-FLI1, it can cause a lot of damage to the new cancer cells - this is called 'replication stress'. Therefore, the fast growth has to be kept in check by molecules, such as the PRMT5 protein, that manage the replication stress response. This ensures that the cancer cells survive their fast growth. Replication stress, therefore, represents a key vulnerability and potential target for treatment as, if it remains unchecked, the Ewing sarcoma cells will not survive.

Led by Professor Clare Davies and Dr Susanne Gatz at the University of Birmingham, this project will investigate the role of PRMT5, which is a known drug target for several other cancers, in the replication stress response. They aim to investigate the link between PRMT5 and EWSR1-FLI1, exploring how they might work together to help Ewing sarcoma cells survive, and how this effect could be blocked by drugs known as 'inhibitors' of PRMT5.

The researchers will look for possible markers which could show which Ewing sarcoma patients these drugs could work for, and will compare the levels and activity of PRMT5 in Ewing sarcoma and other (healthy and breast cancer) tissues. Furthermore, this research will also explore whether combining PRMT5 inhibitors with other drugs also known to target aspects of the replication stress response could lead to a more effective treatment response.

Since EWSR1-FLI1 is very difficult to target, PRMT5 could represent an exciting potential avenue for treatment. Several pharmaceutical companies are already testing PRMT5 inhibitors in clinical trials for adult cancers, which would mean this treatment could be given to patients much sooner than an entirely new drug would be. If successful, this research could represent a significant step towards translation in Ewing sarcoma, leading to a much deeper understanding of the cancer's underlying biology and addressing the crucial need for more targeted, more effective treatment options with fewer toxic side effects.

ROSIE ROCKS THE WORLD

Kieran Maxwell Legacy

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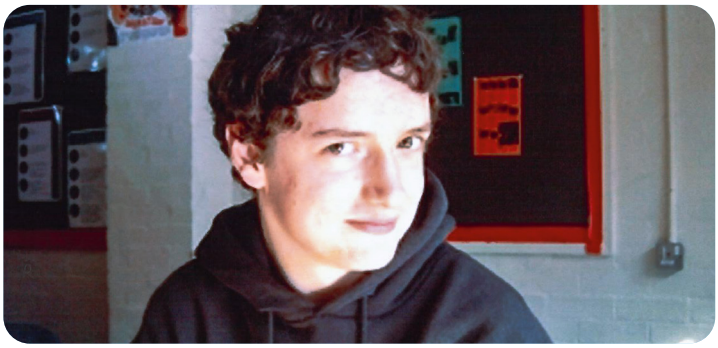

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