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

Exploring surrounding epigenetic influences in Ewing sarcoma

Project title: Epigenetic disruption of EWSR1-FLI1 condensates

Project stage: In progress (Started May 2025, planned end May 2028)

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: Dr Sara Sánchez Molina, Institut de Recerca Sant Joan de Déu

About the project

Ewing sarcoma has a characteristic genetic mutation involving the fusion of two genes, EWSR1 and FLI1. This results in a cancer-driving 'fusion protein' (EWSR1-FLI1) which binds to DNA. However, whilst known to play a key role in the development of Ewing sarcoma, this protein is known to be difficult to target for treatment.

Instead, a project led by Dr Sara Sánchez Molina, a sarcoma researcher based at the Institut de Recerca Sant Joan de Déu in Barcelona, will use advanced techniques to indirectly target this genetic error. They will do so by investigating partners of the fusion protein that collaborate at the place in the DNA where it is binding and exerting its cancer-causing effects.

This approach harnesses 'epigenetics', which refers to the different ways in which our genetic code is influenced, without altering the code itself. For example, the way proteins may bind to the genetic code (DNA), causing the switching on or off of genes that lead to cancerous changes.

Dr Sánchez Molina and team are aiming to develop a targeted approach to treating Ewing sarcoma by understanding what is happening at an epigenetic level.

Specifically, they will use state of the art technology to investigate how the EWSR1-FLI1 fusion protein and other proteins cluster together and support the reprogramming of cells from 'normal' to cancerous. The team will explore whether it is possible to bypass EWSR1-FLI1 and instead reverse this reprogramming by 'untangling' or disrupting these networks.

In doing so, they are hoping to identify a way of indirectly targeting EWSR1-FLI1 and preventing the processes leading to tumour development and progression, uncovering new approaches for treatment.

Treatment options for patients with Ewing sarcoma remain outdated, limited and extremely toxic. Whilst EWSR1-FLI1 is known to be the key genetic mutation driving tumour formation, treatment approaches directly targeting this crucial fusion protein remain challenging and have not yet reached clinic.

Building on developing evidence relating to the epigenetics of Ewing sarcoma, this research will explore the potential to harness a much needed alternative target and pave the way towards a kinder, more effective treatment.

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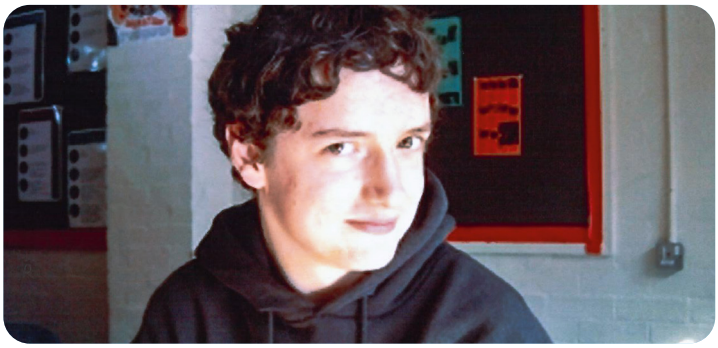

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