Studying the genetics of leukaemia to find new treatments

Project title: Investigations into EVI1 mediated epigenetic modulation in childhood leukaemia

Lead researcher: Dr Stefan Meyer, Manchester University

Project Stage: Complete (March 2020)

Funded by: Toti Worboys Fund

ABOUT THE PROJECT

EVI1 is a gene which helps control which other genes are present in a cell, and how many of them there are. This is known as gene expression. High expression of the cancer gene EVI1 can lead to high risk and poor outcomes in childhood leukaemia. While this cancer gene has been known to be important in myeloid leukaemia for a while, it has recently been linked to lymphoblastic leukaemia too. How EVI1 causes resistance to treatment, leading to poor outcomes, is not very well understood.

Dr Stefan Meyer wants to build on his team's previous work in myeloid leukaemia with a PhD student based at Manchester University, who will study the effect of EVI1 on mouse blood cells and human leukaemia cells. The research team will be using new and advanced technology to find how the gene interacts with other proteins and identify the genes that EVI1 controls. Dr Stefan Meyers hopes that this will find new ways to treat high risk and poor prognosis leukaemia.

RESULTS

The researchers took EVI1 proteins from patients with EVI1 driven childhood leukaemia. They then changed whether the protein was phosphorylated or not and looked at how this affected EVI1's function. Phosphorylation is one of the ways that proteins are 'switched' on or off.

The team found that these phosphorylation changes to the EVI1 protein change how it works, and that the changes maintain leukaemia growth by making EVI1 interact with other proteins. The changes to EVI1 can occur when the EVI1 protein is exposed to chemotherapy or when the cells divide and move through the cell cycle.

Understanding how these changes affect EVI1's function might make it possible to specifically target the phosphorylation changes and therefore prevent the leukaemia-maintaining function

of EVI1. The researchers will now develop their work using mouse experiments and plan to generate enough data in the mouse model that they can consider preventing the phosphorylation to treat patients with EVI1-driven leukaemia.

WHAT'S NEXT?

Dr Stefan Meyers will continue to apply for funding to carry on EVI1-related research, focusing on the DNA damage response and how to prevent EVI1 phosphorylation with treatment. He hopes that this could develop targeted treatment for EVI1 overexpressing leukaemia and other cancers. They are in the process of grant applications in which they are building on the success of this grant and further preliminary results.

The PhD student, Dr James Kelly, has taken up a position in drug development for the oncology sector. The research team consider this a successful PhD project and they are pleased with the published output and career progress for the candidate.

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