A molecular approach to predict recurrence or spread of cancer that will lead to improving outcomes for children with rhabdomyosarcoma

Project title: MG-fnRMS and CINSARC Gene Expression Signatures to Predict Relapse in Fusion Gene Negative Rhabdomyosarcomas: Assessing an Approach to Improve Patient Outcomes

Lead researcher: Professor Janet Shipley, The Institute of Cancer Research

Project Stage: Complete (ended February 2022)

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ABOUT THE PROJECT

Rhabdomyosarcoma is a major cause of death from cancer in childhood. Whilst around two-thirds of young people with rhabdomyosarcoma survive, the treatments often have long-lasting toxic effects on quality of life. If doctors knew that a child's rhabdomyosarcoma was unlikely to spread or return after treatment, the child could potentially avoid more toxic treatments.

Two molecular tests could help predict whether rhabdomyosarcoma will spread or come back:

1. MG-fnRMS test: The research team previously identified a set of 5 genes, called MG-fnRMS, that are different in patients who relapse. Analysis of a small number of rhabdomyosarcoma patient samples with the MG-fnRMS test was promising but needs further work.
2. CINSARC test: A set of 67 genes, called CINSARC, are found in adult sarcomas and can help predict outcome in adult sarcomas and other types of adult cancers. Due to similarities between adult sarcomas and childhood rhabdomyosarcomas, the researchers will test this for childhood rhabdomyosarcoma.

The research team at The Institute of Cancer Research, led by Dr Janet Shipley, will use these tests on samples from rhabdomyosarcoma patients who were treated in previous clinical trials to see how well they can help predict relapse and poor outcome. The best test will start to be used to test patients in the FaR-RMS international clinical trial.

Better prediction of disease recurrence will help stop low-risk rhabdomyosarcoma patients from having unnecessary treatments, with their related toxicities. High-risk rhabdomyosarcoma patients may need closer monitoring, more intense or new and more targeted cancer treatments

to prevent or treat recurrence or disease spread. An exciting future prospect is to use these genes (MG-fnRMS or CINSARC) to create new targeted treatments, based on the roles of these genes. The researchers hope this will improve outcomes for children with rhabdomyosarcoma.

RESULTS

There are two main groups of rhabdomyosarcoma, one with 'gene fusions' that often spread and have poor outcomes, and another more common gene fusion negative group. Whilst children without gene fusions the often have good outcomes, doctors need to be able to recognise those that are at high-risk of relapse so that their treatment plan can be adjusted. Currently, patient's risk is only calculated using clinical details.

This project wanted to find a better way to identify fusion gene negative rhabdomyosarcoma patients who are likely to relapse and have a poor prognosis by using new molecular tests. The MG-fnRMS test successfully showed a difference in survival between patients with high and low gene activity. This means that the MG-fnRMS test could be useful in the current clinical trial for rhabdomyosarcoma patients. Ultimately, in addition to using clinical information from the patient, this new test may be better at estimating their risk of relapse, and enable patients to be given the most appropriate treatment.

WHAT'S NEXT?

Some final analyses are pending, but the researchers expect that the final results will lead to the MG-fnRMS test being used in the FaR-RMS clinical trial. The team also have plans to present and discuss their research with parents of RMS patients who are also involved in patient advocacy as part of the European paediatric Soft Tissue Sarcoma Study Group (EpSSG).

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