Fishing for biomarkers for Rett syndrome

Rett syndrome is a rare genetic neurological and developmental disorder that gradually causes children to lose the ability to crawl, walk and communicate from the age of about 6 to 18 months. It affects 350,000 children worldwide, mainly girls, including 430 in Australia.

Girls with Rett syndrome are commonly misdiagnosed as having autism or mitochondrial disease, and it often takes around four years to receive an accurate diagnosis. There is no effective treatment for the condition, despite numerous national and international clinical trials.

One of the reasons clinical trials have failed is that no clinically useful biomarkers have been identified for Rett syndrome. Although mutations in the MECP2 gene are the main cause of Rett syndrome, these mutations are not found in all girls and therefore diagnosis is made on clinical investigations.

Luminesce Alliance funding is being used to analyse blood and urine samples from girls with Rett syndrome to find biomarkers – molecular indicators of the disease's severity and progression.

The study is searching for biomarkers among more than 700 metabolites (chemicals) in the samples, using state-of-the-art technologies that can identify any disruptions in these chemicals in one test.

Dr Wendy Gold, Head of the Molecular Neurobiology Research Laboratory at Kids Research, says the ultimate aim is for clinicians to be able to test for these biomarkers to aid in the diagnosis, and for scientists and pharmaceutical companies to have a reliable measure of disease improvement in clinical trials.

The advantage of this study is that it is using easy-to-collect samples, rather than samples that require invasive procedures.

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"We would like to find a biomarker that is expressed at a different level between Rett patients and non-Rett patients. Then we can measure whether it changes with disease progression and treatment."

As well as this 'fishing expedition' to look for biomarkers among the metabolites, the seed funding is enabling Dr Gold and her team to study two specific biomarkers known to indicate mitochondrial stress, which they believe from laboratory tests could also indicate disease progression in Rett syndrome.

The project will determine whether these biomarkers can help diagnose the stage and severity of Rett's in girls, and whether they can predict the course of the disease.

"Traditionally, research funders don't like fishing expeditions – they want to see preliminary data first. Now we have shown there are fish out there, and hopefully this funding will enable us to catch them."