Cracking the mechanisms of a devastating disorder

Researchers around the world are desperately looking for a treatment for Rett syndrome, a severe genetic disease that causes babies to lose movement and communication.

A multidisciplinary team across SCHN and CMRI is making progress in breaking down the molecular mechanisms of the disease, following the discovery of biomarkers in an innovative study funded by the Luminesce Alliance.

The absence of a biomarker – a measurable indicator of a disease or condition detectable in blood or other body fluids – has resulted in difficulties and often delays in diagnosis of Rett syndrome. It also makes it challenging to develop treatments or establish clinical trials, because it's impossible to measure the efficacy of an intervention.

"There have been around 60 clinical trials for treatments for Rett syndrome, but none have made it to the clinic as it's not possible to demonstrate if they are effective. That's because there's not an easy biomarker that can measure the change in the disease," says A/Prof Wendy Gold, Head of the Molecular Neurobiology Research Laboratory at Kids Research, SCHN.

A/Prof Gold and her team set out on a "fishing expedition" to search for a biomarker for Rett syndrome. Using state-of-the-art technologies, they sifted through more than 700 chemicals in urine samples from patients with Rett syndrome and compared them to controls.

They were able to identify biomarkers in the first phase of the research, and the next phase will see the combined use of 'omics' to better understand the disease drivers and potential targets for treatments.

Multi-omic approach

The use of high-input approaches, known as omics, has developed rapidly and revolutionised both the diagnosis and the understanding of the pathophysiology of many neurological disorders.

The multidisciplinary team will analyse blood samples from Rett syndrome patients, compared to controls – this phase of the research will look at genes, proteins, metabolites and cellular pathways.

A/Prof Gold is also collaborating with the bioinformatics team at CMRI, where scientists specialise in using computational biology expertise to study biological systems, developing software and novel mathematical methods for the analysis of biological data.

"Nobody else is doing this kind of research in the Rett syndrome space – integrating all of these technologies with a common goal," says A/Prof Gold.

"The ultimate aim is for clinicians to be able to test for these biomarkers to aid in diagnosis, and for scientists and pharmaceutical companies to have a reliable measure of disease improvement in clinical trials."

Being part of CMRI and the Luminesce Alliance has opened doors for making connections with other researchers, A/Prof Gold says.

She has also established a Scientific Medical Advisory Committee with Rett Syndrome Association. The group will enable closer communication and collaboration between clinicians, scientists, and families impacted by Rett syndrome.

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