CHRD 2022: Abstract & Poster Submission Form

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Presenter Status
- ○ Undergraduate Students
- ○ Masters Student
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- ○ Residents
- ◉ Non-Trainee

Research Category
- ○ Basic Science
- ◉ Clinical
- ○ Community Health / Policy

Role in the project
- ☐ Design
- ☐ Perform Experiments
- ☑ Analyze Data
- ☑ Write Abstract
- ☑ Project management, genetic counselling

Title
Psychosocial benefits of whole exome sequencing for patients with suspected inherited metabolic disorders

Background

One in 12 Canadians has a rare disorder, many of which are undiagnosed. In the case of Inherited Metabolic Disorders (IMDs), this limits options for support, anticipatory guidance, and treatment. Whole exome sequencing (WES) can provide a diagnosis for patients suspected to have an IMD.

Objective

Evaluate whether offering WES early in the diagnostic evaluation of these patients will facilitate earlier diagnosis, more timely initiation of management strategies, and greater patient satisfaction than the current approach.

Methods

Patients suspected to have an IMD are referred to the Canadian Prairie Metabolic Network study. Eligible participants provide an oral sponge sample for WES. Here, we present the clinical journey of three participants.

Results

Participant 1 is a 27-year-old male with congenital cataracts and complaints of muscle weakness. WES identified a de novo (non-inherited), heterozygous likely pathogenic variant in WFS1, which is known to cause cataracts. Participant 2 is a 14-year-old female with developmental delay and prenatally detected agenesis of the corpus callosum. WES identified a de novo, heterozygous likely pathogenic variant in TCF4, establishing a diagnosis of Pitt-Hopkins syndrome. Participant 3 is a 10-year-old female with developmental delay and seizures that began in early childhood. WES identified a heterozygous likely pathogenic variant in SYNGAP1, which is associated with seizures. While these are not considered metabolic disorders and therapeutics are not currently available, we were still able to provide anticipatory guidance by reassuring the families that new manifestations are unlikely in each patient's clinical trajectory.

Conclusion

The features of IMDs can be non-specific (as in these patients) and it is therefore expected that WES will identify both metabolic (e.g., phenylketonuria, PKU) and non-metabolic disorders. These vignettes provide evidence that establishing a diagnosis using WES, even for non-metabolic disorders, will improve the patient experience and thus should be incorporated early in the diagnostic work-up.

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