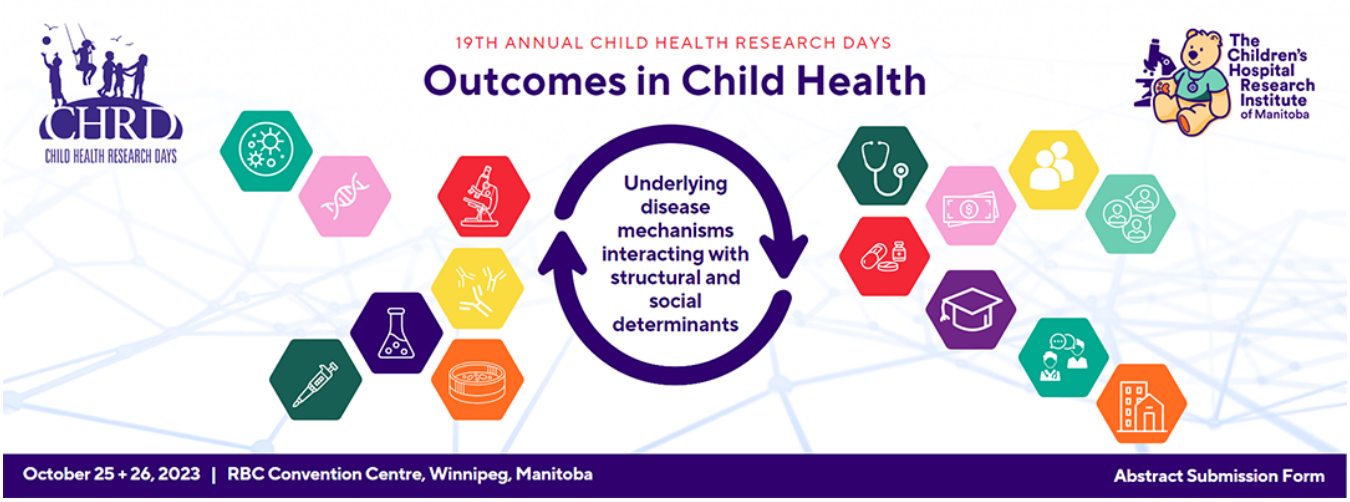

CHRD 2023: Abstract Submission Form

Submitter Name
Jose Peralta-Huertas

Presenter Name
Jose Peralta-Huertas

Presenter Status
Non-Trainee

Research Category
Basic Science

Role in the project
Design
Analyze Data
Write Abstract

Title
Multi-OMICS for Variants of Uncertain Significance identified on Genome Wide Sequencing in Patients with Suspected Inherited Metabolic Disorders

Background
The Canadian Prairie Metabolic Network (CPMN) offers genome-wide sequencing (GWS) to patients suspected of having inherited metabolic disorders. A DNA variant identified by GWS is classified as Pathogenic (P), Likely Pathogenic (LP), Benign (B), Likely Benign (LB) or as a Variant of Uncertain Significance (VUS). P and LP, and B and LB mean that there is >90% certainty of the variant being disease-causing or harmless, respectively. A VUS means that the significance of the variant is inconclusive and may be of limited clinical utility. VUSs present challenges for genetic health care providers (HCP) when disclosing GWS results to patients and their families. In our experience, 33% of CPMN patients receiving GWS have VUS variants detected. In the attempt to reclassify a VUS into a P, LP, B, or LB variant, further analyses may be helpful.

Objective
Integrating Multi-OMICS approaches into the diagnostic pipeline has been shown to increase the diagnostic utility of GWS.

Methods
A team of University of Manitoba scientists will lead the Multi-OMICS pipeline by providing bioinformatics, functional studies using fruit flies (Drosophila), transcriptomics, induced pluripotent stem cell (iPSC) studies, proteomics, and/or metabolomic studies. The terms of reference for the Multi-OMICS pipeline are

being finalized.

Results
To date, several VUS and LP variants identified through CPMN have been investigated, and reclassified or confirmed using clinically available technologies such as flow cytometry, histochemical assays, and immunoassays.

Conclusion
We anticipate the Multi-OMICS platform will lead to reclassification of VUSs and increase the diagnostic yield of GWS by 10 to 20%. Integration of Multi-OMICS into clinical genetic practice will help realize the full potential of GWS. Multi-OMICs will enhance our interpretation of genomic variants, promote collaboration between clinicians and research scientists, provide Manitoban patients with access to state-of-the-art science and positively impact clinical care and quality of life.

Authors

Name	Email	Role	Profession
Jose Peralta-Huertas	jose.peraltahuertas@umanitoba.ca	Presenting Author	Other
Katherine Chimney	katherine.chimney@umanitoba.ca	Co Author	Other
James Elmore	james.elmore@umanitoba.ca	Co Author	Other
Angela Krutish	angela.krutish@umanitoba.ca	Co Author	Other
Paul Marcogliese	paul.marcogliese@umanitoba.ca	Co Author	Assistant Professor
Athanasios Zovoilis	athanasios.zovoilis@umanitoba.ca	Co Author	Associate Professor
Richard LeDuc	richard.leduc@umanitoba.ca	Co Author	Associate Professor
Rene Zahedi	rene.zahedi@umanitoba.ca	Co Author	Professor
Michel Aliani	michel.aliani@umanitoba.ca	Co Author	Professor
Sanjiv Dhingra	sanjiv.dhingra@umanitoba.ca	Co Author	Professor
Aizeddin Mhanni	amhanni@hsc.mb.ca	Co Author	Associate Professor
Cheryl Rockman-Greenberg	cgreenberg@hsc.mb.ca	Co Author	Distinguished Professor