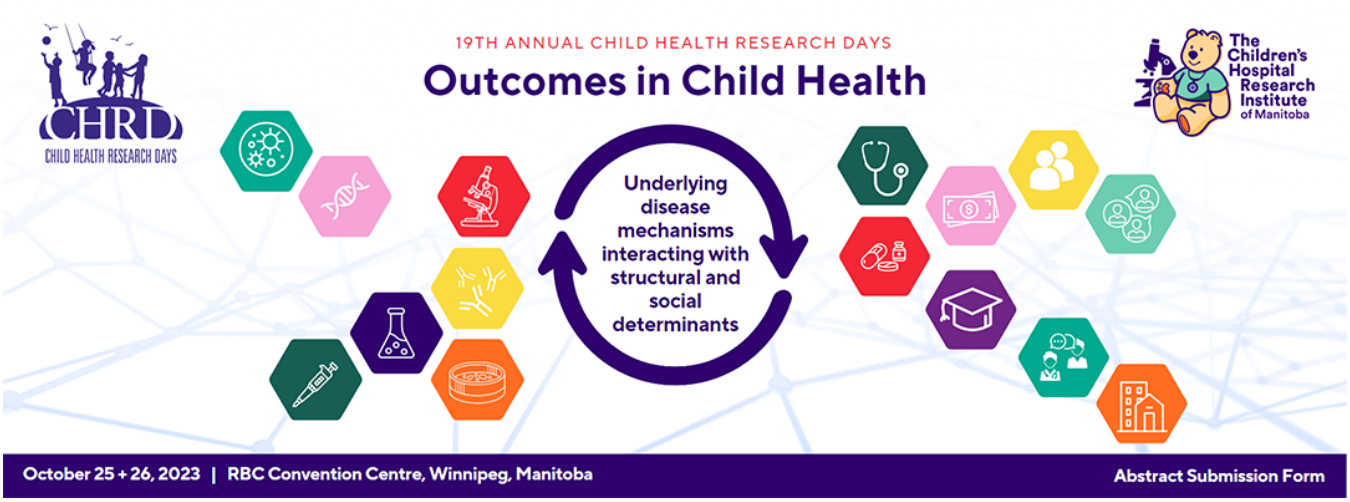

CHRD 2023: Abstract Submission Form

Submitter Name
Tamiris Souza

Presenter Name
Tamiris Souza

Presenter Status
Post-Doctoral Fellows

Research Category
Basic Science

Role in the project
Analyze Data
Write Abstract

Title
Breast milk extracellular vesicles from mothers with asthma modulate inflammatory mediators released by human airway smooth muscle cells

Background
Breastfeeding provides substantial benefits for infant growth, including protection against asthma development. Breastmilk (BM) is a rich source of bioactive molecules including extracellular vesicles (EVs), which transfer biomolecular cargo to facilitate inter-cellular communication. Depending on their cargo, BM-EVs exert immunomodulatory signalling in recipient cells, and their cargo is affected by maternal characteristics.

Objective
Here we investigated the effect of BM-EVs from mothers with or without asthma (CHILD study) on the release of cytokines from primary human hTERT-immortalized airway smooth muscle cells (hASMs) from donors with or without asthma.

Methods
Samples of BM from healthy and asthmatic donors (N=5/group) were collected 3-4 months post-partum. BM-EVs were isolated from 200µl of BM using size exclusion chromatography (Izon). BM-EVs were co-cultured (48hrs) with primary hASMs from both non-asthmatic and asthmatic donors to determine if effects of BM-EVs were dependent on recipient cell milieu. Cell viability was evaluated by MTT assay. Immunomodulatory cytokine release (GM-CSF, IFN-γ, IL-1β, IL-1ra, IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IL-12(p40), IL-12(p70), IL-13, MCP-1 and TNFα) was quantified in conditioned media collected from hASMs using Human Focused 15-Plex Discovery Assay (Eve Technologies, Alberta, Canada).

Results
BM-EV treatment did not alter cell viability of hASMs, regardless of BM-EV donor asthma status. Only BM-EVs from asthmatic donors exerted immunomodulatory effects in a recipient cell-specific manner: in non-asthmatic hASMs, BM-EVs from asthmatic donors decreased MCP-1 secretion by 45% (p=0.0286), IL-6 by 45% (p=0.0801) and IL-2 by 25% (p=0.0970) vs. control-BM-EVs. In contrast, in asthmatic hASMs, BM-EVs from asthmatic donors increased IL-10 by 33% (p=0.0660).

Conclusion
BM-EVs exerted differential effects on cytokine release in a BM-donor and recipient-cell specific manner. Treatment with asthmatic donor-derived BM-EVs reduced pro-inflammatory (MCP-1, IL-6 and IL-2) in non-asthmatic hASMs, and increased anti-inflammatory (IL-10) in asthmatic-hASMs. Ongoing work to assess proteomic composition of BM-EV cargo for mechanistic discovery is underway.

Authors

Name	Email	Role	Profession
Tamiris F. G. Souza	tsouza@chrim.ca	Presenting Author	Graduate
Taiana M. Pierdona	taianapierdona@gmail.com	Co Author	Graduate
Samira Seif	samira.seif@umanitoba.ca	Co Author	Graduate
Benjamin Bydak	umbydakr@myumanitoba.ca	Co Author	Graduate
Patience O. Obi	obip@myumanitoba.ca	Co Author	Graduate
Joseph W. Gordon	joseph.gordon@umanitoba.ca	Co Author	Associate Professor
Stuart Turvey	sturvey@bcchr.ca	Co Author	Full Professor
Elinor Simons	elinor.simons@umanitoba.ca	Co Author	Assistant Professor
Piushkumar Mandhane	mandhane@ualberta.ca	Co Author	Associate Professor
Theo Moraes	theo.moraes@sickkids.ca	Co Author	Associate Professor
Padmaja Subbarao	padmaja.subbarao@sickkids.ca	Co Author	Associate Professor
Shreya A. Raghavan	sraghavan@tamu.edu	Co Author	Assistant Professor
Andrew J. Halayko	andrew.halayko@umanitoba.ca	Co Author	Full Professor
Meghan B. Azad	meghan.azad@umanitoba.ca	Co Author	Assistant Professor

Ayesha Saleem	asaleem@chrim.ca	Co Author	Associate Professor