Early-life cytomegalovirus infection is associated with gut microbiota perturbations and increased risk of atopy

Hind Sbihi¹, Karen Simmons¹, Malcolm Sears², Theo Moraes³, Allan Becker⁴, PJ Mandhane⁵, Padmaja Subbarao³, Darlene Dai¹, B. Brett Finlay¹, Stuart Turvey⁶, and Soren Gantt⁷

¹The University of British Columbia ²McMaster University ³University of Toronto ⁴University of Manitoba ⁵University of Alberta ⁶University of British Columbia ⁷University of Montreal

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Abstract

Background: The 'old friends' hypothesis posits that reduced exposure to previously ubiquitous microorganisms is one factor involved in the increased rates of allergic diseases. Cytomegalovirus (CMV) may be one of the "old friends" hypothesized to help prevent allergic diseases. We sought to elucidate whether early-life CMV infection is associated with childhood atopy via perturbations of the gut microbiota. Methods: Participants were recruited from a population-based birth cohort (CHILD study) and followed prospectively until age five years in four Canadian cities. A total of 928 participants provided stool microbiome data, urine for CMV testing, skin-prick tests, and questionnaires-based detailed environmental exposures. CMV infection was assessed in the first year of life while the main outcome was defined by persistent sensitization to any allergen at ages 1, 3, and 5 years. Results: Early CMV infection was associated with increased beta and decreased alpha diversity of the gut microbiota. Both changes in diversity measures and early CMV infection were associated with persistent allergic sensitization at age 5 years (aOR= 2.08; 95%CI: 1, 4.33). Mediation analysis demonstrated that perturbation of gut microbial composition explains 30% of the association. Conclusions: Early-life CMV infection is associated with an alteration in the intestinal microbiota, which mediates the effect of the infection on childhood atopy. This work indicates that preventing CMV infection would not put children at increased risk of developing atopy. Rather, a CMV vaccine, in addition to preventing CMV-associated morbidity and mortality, might reduce the risk of childhood allergic diseases.

Full title: Early-life cytomegalovirus infection is associated with gut microbiota perturbations and increased risk of atopy

Authors: Hind Sbihi, PhD^{1,7}, Karen E. Simmons, MSc¹, Malcolm R. Sears, MBChB², Theo J. Moraes, MD PhD³, Allan B. Becker, MD⁴, Piush J. Mandhane, MD PhD⁵, Padmaja Subbarao, MD³, Darlene L.Y. Dai¹, B. Brett Finlay, PhD¹, Stuart E. Turvey, MBBS DPhil¹, Soren Gantt⁶, MD PhD MPH

¹ University of British Columbia, Vancouver, British Columbia, Canada

- ² McMaster University, Hamilton, Ontario, Canada
- ³ Hospital for Sick Children, Toronto, Ontario Canada

- ⁴ University of Manitoba, Winnipeg, Manitoba, Canada
- ⁵ University of Alberta, Edmonton, Alberta, Canada
- ⁶ Université de Montréal, Montréal, Québec, Canada
- ⁷ BC Centre for Disease Control, Vancouver, British Columbia, Canada
- These authors contributed equally

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Corresponding authors :

Stuart E. Turvey, MBBS, DPhil, FRCPC

BC Children's Hospital 950 West 28th Avenue Vancouver, BC, V5Z 4H4, Canada Phone: 604 875 2345 ext. 3130 Email: stu

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	No Sensitization	Persistent Sensitization		Adjusted Odds Ratio	P-Value
Participants	873	55			
CMV status					
No CMV	707 (81%)	35 (63.6%)		Ref	
Early CMV	109 (12.5%)	13 (23.6%)	⊢ −−−−1	2.08 (1, 4.33)	0.05
Late CMV	57 (6.5%)	7 (12.7%)	⊢ − − − 1	1.85 (0.67, 5.08)	0.23
Child Ethnicity (Caucasian white)	291 (33.7%)	36 (65.5%)	⊢	2.62 (1.39, 4.94)	0.0029
Parental Atopy	688 (80.5%)	51 (92.7%)	⊢ −−−−−	2.43 (0.84, 7.01)	0.1
Home Occupancy (adults)	83 (10.5%)	12 (25%)	⊢ − − − −	1.89 (0.91, 3.93)	0.088
		0.5	10 20 40		

No Sensitization	Persistent Sensitization		Adjusted Odds Ratio	P-value
873	55			
1.2 (0.2, 4.2)	0.9 (0.5, 3.1)	⊢ •−1	0.37 (0.17, 0.80)	0.011
291 (33.7%)	36 (65.5%)	⊢ •−1	4.14 (1.77, 9.70)	0.0011
688 (80.5%)	51 (92.7%)	• • • •	5.66 (0.72, 44.8)	0.1
83 (10.5%)	12 (25%)	⊢ •–-1	2.22 (0.91, 5.43)	0.08
No Sensitization	Persistent Sensitization	0.25 0.5 1 2 4 8 16 32	Adjusted Odds Ratio	P-Value
873	55		-	
0.1 (-1.7, 1.8)	0.4 (-1.4, 1.8)		3.10 (1.60, 6.03)	<0.001
0.1 (-1.7, 1.8) 291 (33.7%)	0.4 (-1.4, 1.8) 36 (65.5%)		3.10 (1.60, 6.03) 4.03 (1.71, 9.50)	<0.001 0.0014
	1.2 (0.2, 4.2) 291 (33.7%) 688 (80.5%) 83 (10.5%) No Sensitization	1.2 (0.2, 4.2) 0.9 (0.5, 3.1) 291 (33.7%) 36 (65.5%) 688 (80.5%) 51 (92.7%) 83 (10.5%) 12 (25%) No Sensitization	1.2 (0.2, 4.2) 0.9 (0.5, 3.1) 291 (33.7%) 36 (65.5%) 688 (80.5%) 51 (92.7%) 83 (10.5%) 12 (25%) 0.25 0.5 1 2 Ao Sensitization Persistent Sensitization	1.2 (0.2, 4.2) 0.9 (0.5, 3.1) 0.37 (0.17, 0.80) 291 (33.7%) 36 (65.5%) 4.14 (1.77, 9.70) 688 (80.5%) 51 (92.7%) 5.66 (0.72, 44.8) 83 (10.5%) 12 (25%) 2.22 (0.91, 5.43) 0.25 0.5 1 2.4 8 16 32 Adjusted Odds Ratio

