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Human milk oligosaccharides are associated with maternal genetics and respiratory health of human milk-fed children

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Amirthagowri Ambalavanan[1], Le Chang[1,2], Jihoon Choi[1], Yang Zhang[2], Sara A. Stickley[1], Zhi Y. Fang[1], Kozeta Miliku[3,4], Bianca Robertson[3], Chloe Yonemitsu[5], Stuart E. Turvey[6], Piushkumar J. Mandhane[7,8], Elinor Simons[9], Theo J. Moraes[10], Sonia S. Anand[11], Guillaume Paré[12], Janet E. Williams[13], Brenda M. Murdoch[13], Gloria E. Otoo[14], Samwel Mbugua[15], Elizabeth W. Kamau-Mbuthia[15], Egidioh W. Kamundia[15], Debela K. Gindola[16], Juan M. Rodriguez[17], Rossina G. Pareja[18], Daniel W. Sellen[19], Sophie E. Moore[20,21], Andrew M. Prentice[21], James A. Foster[22], Linda J. Kvist[23], Holly L. Neibergs[24], Mark A. McGuire[13], Michelle K. McGuire[25], Courtney L. Meehan[26], Malcolm R. Sears[5], Padmaja Subbarao[3,10], Meghan B. Azad[9,27,28] ✉, Lars Bode[5,28] ✉ & Qingling Duan[1,2,28] ✉

Breastfeeding provides many health benefits, but its impact on respiratory health remains unclear. This study addresses the complex and dynamic nature of the mother-milk-infant triad by investigating maternal genomic factors regulating human milk oligosaccharides (HMOs), and their associations with respiratory health among human milk-fed infants. Nineteen HMOs are quantified from 980 mothers of the CHILD Cohort Study. Genome-wide association studies identify HMO-associated loci on chromosome 19p13.3 and 19q13.33 (lowest P = 2.4e−118), spanning several fucosyltransferase (*FUT*) genes. We identify novel associations on chromosome 3q27.3 for 6′-sialyllactose (P = 2.2e−9) in the sialyltransferase (*ST6GAL1*) gene. These, plus additional associations on chromosomes 7q21.32, 7q31.32 and 13q33.3, are replicated in the independent INSPIRE Cohort. Moreover, gene-environment interaction analyses suggest that fucosylated HMOs may modulate overall risk of recurrent wheeze among preschoolers with variable genetic risk scores ($P < 0.01$). Thus, we report novel genetic factors associated with HMOs, some of which may protect the respiratory health of children.

Breastfeeding and consumption of human milk have many health benefits for infants such as a lower prevalence of infections and childhood obesity[1]. It is unclear, however, whether breastfeeding protects against respiratory health outcomes such as asthma, which affects over 339 million individuals worldwide and is the most common chronic disease among children[2]. A meta-analysis reported protective effects of breastfeeding on asthma and wheeze[3], but other studies reported conflicting results or no associations[4].

A major limitation of earlier research is that breastfeeding and human milk were typically considered as a single homogeneous exposure. This fails to acknowledge the complex and dynamic interactions of the mother-milk-infant "triad" as a coadapted system where

A full list of affiliations appears at the end of the paper. ✉e-mail: meghan.azad@umanitoba.ca; lbode@health.ucsd.edu; qingling.duan@queensu.ca