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Q1 What led you to specialise in the field of infant nutrition and the microbiome?

I had done my PhD in cancer cell biology and was looking for a change. My original motivation to pursue a career in science was to influence human health, and I realised through my PhD work that very basic science, while important, was quite far removed from clinical impact. I audited a course in epidemiology and realised this was more aligned with my goals, so I looked for a postdoc position in this area and was fortunate to connect with Anita Kozkyrskyj, an epidemiologist who had just received a grant to study the microbiome in babies from the CHILD Cohort Study. One of our major discoveries was how breastfeeding was crucial to microbiome development. So, when I started my own lab, I decided to dive deeper into this topic and find out how breast milk shapes microbiomes. The CHILD study had collected breast milk, so I had a fantastic opportunity to expand my postdoc research and explore this question.

Q2 You are Director of the THRiVE Discovery Lab, which studies how early life nutrition shapes the infant microbiome and child health, and lead the CHILD Cohort Study, which follows 3,500 children from mid-pregnancy into adolescence. Can you tell us more about these two initiatives? What have your key discoveries been to date?

CHILD is a birth cohort study that started around 2010 and is following 3,500 pregnant women from four centres across Canada. It was established to investigate the recent epidemic of childhood allergies and asthma and understand how genes and the environment (very broadly speaking) influence the development of these conditions. It's a massive initiative led by a fantastic multidisciplinary team of researchers and staff across the country. As a postdoc, I was lucky to join the CHILD team to help with some of the first microbiome analyses in this cohort, and when I started my own lab a few years later, I took the lead on breast milk research within CHILD. It has been a wonderful place to 'grow up' as a scientist! There have been tons of discoveries from CHILD, including many related to the microbiome and breastfeeding and how they relate to various child health outcomes, ranging from allergies and asthma to obesity and behaviour. The CHILD babies are now entering their teenage years and we are still following them!

THRiVE is my research program, focused on understanding how early nutrition shapes the microbiome and lifelong health. Building on my research with the CHILD study, we now have additional projects focused on breast milk and child development in other global contexts, donor human milk for premature infants, colostrum (the very first milk produced, which has unique immunological properties), and education about breastfeeding for professional and public audiences. Our team is very multidisciplinary, with members specialising not only in nutrition and microbiology, but also neonatology,

anthropology, midwifery, data science, knowledge translation, and more.

Our key discoveries range from epidemiologic evidence on breastfeeding and chronic disease prevention to mechanistic research on breast milk compounds and the infant microbiome. Our clinical research shows that breastfeeding shapes the early immune system, and is linked to lower rates of childhood asthma and obesity.

> **Our clinical research shows that breastfeeding shapes the early immune system**

We dive deeper into these questions than many other studies, paying attention to nuances in the duration, exclusivity, and method of feeding. We've shown that pumped milk, while still beneficial, is not equivalent to feeding at the breast, and we are doing more research to understand why. Our breast milk research shows that milk composition is highly variable and personalised, with some components (like omega-3 fats) affected by maternal diet, others (like prebiotic sugars) controlled by genetics, and still others (like microbes) more influenced by the physical environment. We have linked specific milk components to infant gut and nasal microbiome development and shown that these relationships are important for supporting respiratory health and preventing asthma.

Q3 Focusing on your work with the International Milk Composition (IMiC) Consortium, what insights have emerged about the variability in human milk composition and its impact on the microbiome?

IMiC is still underway, but our results so far demonstrate enormous variability in milk composition among women, across time from early to later lactation, and between settings (Canada, Pakistan, Tanzania, and Burkina Faso). Some milk components (like microbes) are highly variable, while others (like macronutrients) are less variable. Some are affected by maternal diet while others are not. Some compounds are yet-to-be identified; we have analysed over 50,000 metabolites and many of these chemical structures are still unknown. Our initial focus is to understand how milk composition relates to infant growth, but we are excited to explore relationships with infant microbiomes as a next step. The four studies participating in IMiC all have microbiome data, so this is a feasible and exciting prospect!

Q4 How can donor human milk be optimised to better support preterm neonates' microbiome development and overall health?

Donor human milk is very important for preterm neonates and their fragile microbiomes. Unfortunately, some bioactive compounds in human milk are lost or diminished through the pasteurisation process. Researchers are working on improving this process to maintain safety and preserve as much bioactivity as possible. It might also be possible to 'match' milk donors to infant recipients in ways that optimise their microbiomes.

Q5 What role does the microbiome play in resilience against chronic conditions, such as asthma, allergies, and diabetes? How could clinical interventions be designed to harness this potential?

Microbes help train the immune system during early life. When this process is disrupted, conditions like allergies and asthma can result. By understanding how microbes support immune development during the critical

first months of life, we can develop microbiome-targeted preventive approaches to avoid these conditions. For example, we are finding that some microbes are missing from babies who go on to develop asthma later in childhood. Some of these particular microbes are found in breast milk and/or rely on breast milk sugars to survive, so it might be possible to design asthma prevention strategies that replenish these microbes through probiotic supplements given during breastfeeding, or alongside breast milk compounds.

Q6 What are the most significant challenges in translating microbiome research into public health policies or clinical guidelines for early nutrition?

Microbiomes are dynamic (always changing) and personalised (unique to each individual). We are still learning what a 'healthy' microbiome actually is, and how this might differ among individuals of different ages, geographies and circumstances.

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The ideal microbiome is probably different for a baby or child in Canada versus Tanzania or Pakistan. So, it's a challenge to identify the specific microbes or microbial products necessary for optimal health, and to translate this knowledge into effective products. However, is abundantly clear that human milk, which is also dynamic and personalised, supports human microbiome development in early life, so we should do everything possible to support breastfeeding through public policies and clinical guidelines. For scenarios where exclusive breastfeeding isn't possible, we can draw inspiration from breast milk and its impact on the microbiome to inform alternative feeding strategies.

Q7 Looking ahead, what do you envision as the next major breakthrough in infant microbiome research, and what role do you see your work playing in that evolution?

Our new research shows that timing is critical in early microbiome development: it is not only about having the 'right microbes' (or microbial functions), they need to arrive in the right sequence, at the right time. This is true not only in the gut, but also in the nose, and likely other body sites, too. Breastmilk is key to this progression because it gradually changes over time and guides this delicate maturation of the microbiome. I think the next major breakthroughs in infant microbiome research will centre on understanding this progression at a deeper resolution, enabling us to pinpoint specific milk components and microbes that temporally orchestrate microbiome development during infancy. Understanding these processes will facilitate the development of microbiome-targeted 'tools' for optimising health during infancy and across the lifespan.