Title

Tiny But Mighty: How the development of the microbiome shapes immune response in infancy and beyond

Synopsis

There was once an assumption that babies were born sterile, and didn't come into contact with microbes until the moment of birth. It is now understood that not only is there a foetal microbiome but that microbial interactions influence the development of the immune system.

Join Rebecca Edwards to learn how the smallest of forms of life have a large **impact on growing and shaping a healthy immune response in infancy, childhood, and later life.**

Rebecca will discuss the **importance of nurturing the perinatal microbiome**; detail **factors which influence the maturation of the neonatal microbiome**; and discuss how the **paediatric gastrointestinal and oral microbiota** play a role in the development of **allergies, daycare illnesses, and more.**

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Rener Expo 2026

Building the foundations of a healthy human with the microbiome

How the development of the microbiome shapes immune response in infancy and beyond

Presented by Rebecca Edwards



ACTIVATED PROBIOTICS®

A range of condition specific probiotics

Activated Probiotics is a range of targeted probiotic supplements, with each product formulated to address specific needs of patients under the guidance of a healthcare practitioner.



Biome Lift™	Biome Osteo Plus™	Biome Perinatal™	Biome Daily™	Biome Recovery™
Biome Baby™	Biome Lax™	Biome Eczema™	Biome IBS™	Biome Dental™
Biome Daily Kids™	Biome Cholesterol™	Biome Iron+™	Biome Advanced™	
Biome Breathe™	Biome Her™	Biome Acne™		

Acknowledgement

We respectfully acknowledge the traditional owners of the land on which we meet, and pay our respects to their elders past and present, and all Aboriginal and Torres Strait Islander Peoples here today.

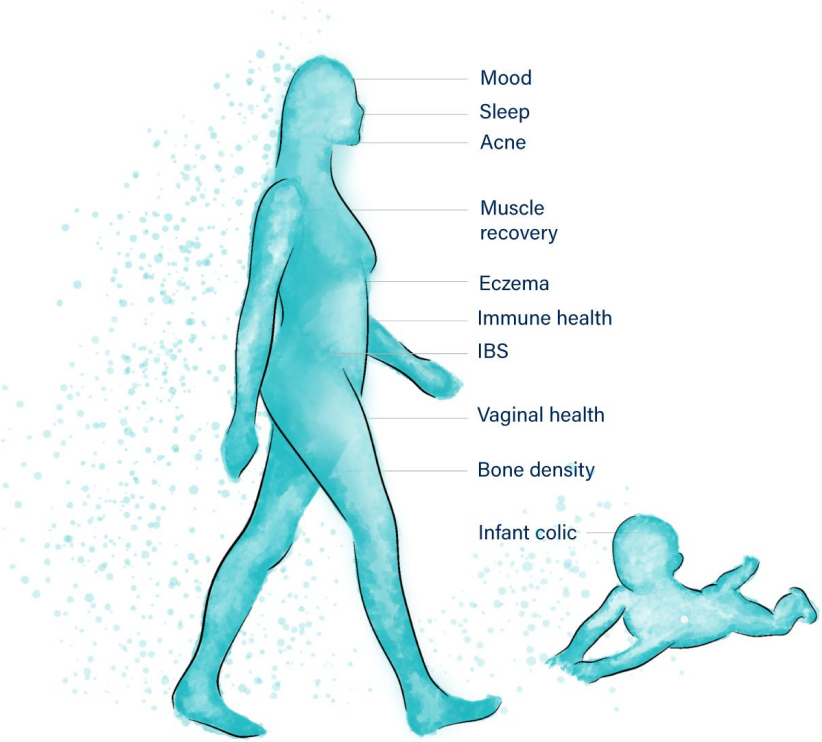
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Certified B Corporations are leaders in the global movement for an inclusive, equitable and regenerative economy by committing and demonstrating:

- Responsible social and environmental practices that benefit employees and the wider community
- A corporate governance structure that emphasises accountability
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Activated Probiotics paediatric range





The microbiome through the life stages

It's becoming more and more evident that our microbiota influence every aspect of human health. But who are these bugs, where do they come from, and how do they change as we grow and age?

The foetal microbiome begins to develop in utero, and is seeded significantly during the process of birth. Breast milk delivers both live microorganisms and fibre, and is a major influence on the development of a healthy neonatal microbiome.

For the first six or so months, a healthy infant microbiome is heavily dominated by bifidobacteria. As the infant takes in increasing solid food, the microbiome diversifies.



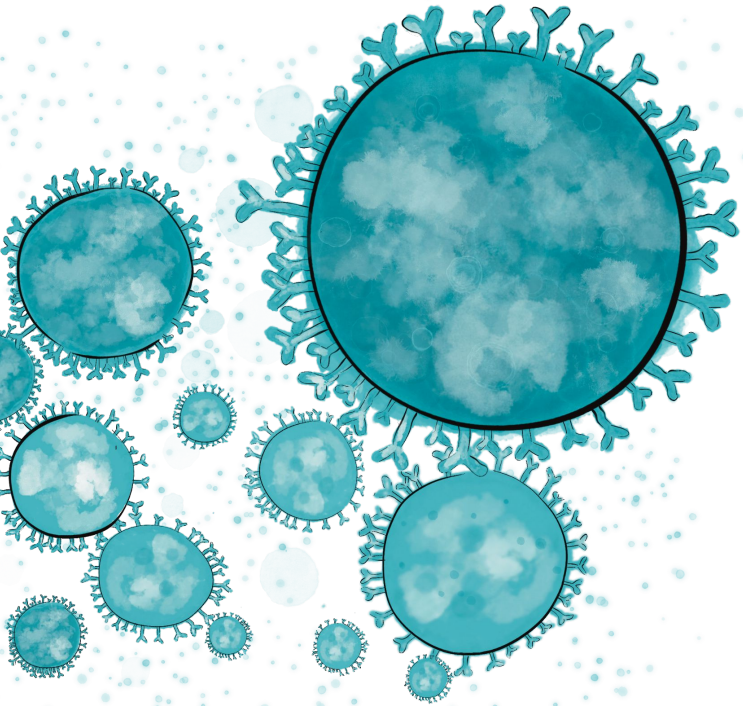
The microbiome through the life stages

Diversity is the most widely recognised marker of microbiome health. Travel, interpersonal connection, eating a wide variety of plant foods, living in the country or with animals—these factors all enhance microbial diversity.

The microbiome becomes less diverse with age, correlating with a decrease in digestive secretions and a slowing of metabolism. Diversity significantly decreases after menopause.

Our microbiota may succeed us, assisting in decomposition and altering the soil.

The microbiota and the developing immune system



Distribution of immune cells

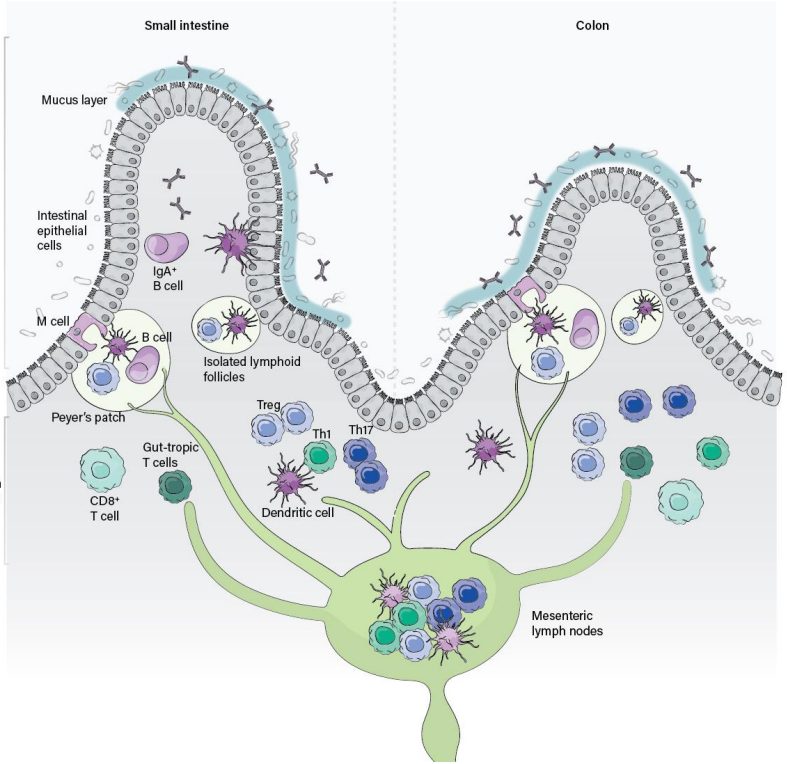
Lymphoid tissue lines the mucous membranes of the:

- Gastrointestinal tract
- Respiratory tract
- Urogenital tracts
- Conjunctiva of the eyes
- Inner ears

~80% of all immune cells accumulate within and transit between this network of mucosa-associated lymphoid tissues (MALT)

REFERENCE

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Mucosa-associated lymphoid tissue (MALT)

The mucosal immune system is responsible for identifying pathogenic microorganisms and mounting a defensive response against them to **protect the body from infection**.

It is also responsible for suppressing the immune response to:

- Non-harmful antigens from the body's own cells
- The commensal microbiota
- Ingested foods and airborne matter

This is called **'oral tolerance'** - it helps to avoid unnecessary immune responses and prevent chronic inflammatory diseases such as food allergies

Holmgren et al. Nat Med. 2005;11(4 Suppl):S45–53.

The role of the microbiota in the developing immune system

Colonisation of these mucosal surfaces with a community of microorganisms, known as microbiota, plays a significant role in the functional maturation of underlying immune tissue after birth.

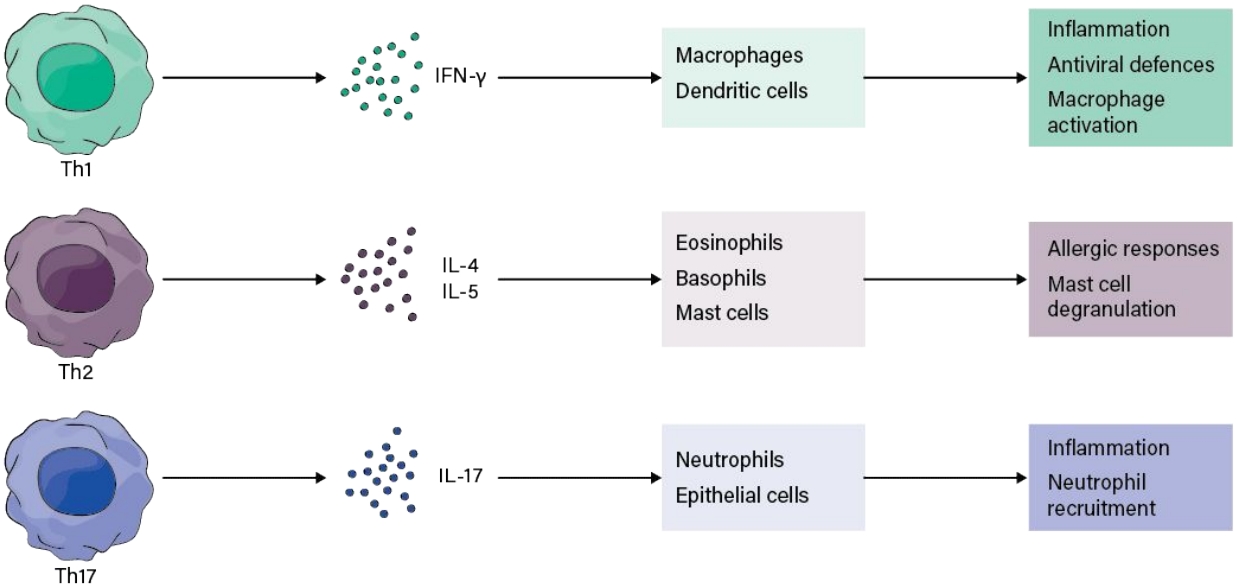
While infants born at term have structurally-developed MALT, these tissues must undergo functional maturation by interacting with the microorganisms beginning to colonise the mucosal surfaces in order to impart:

- Oral tolerance
- Infection resistance

Gut microbiota colonisation also promotes the closure of tight gap junctions and supports intestinal epithelial barrier (IEB) integrity.

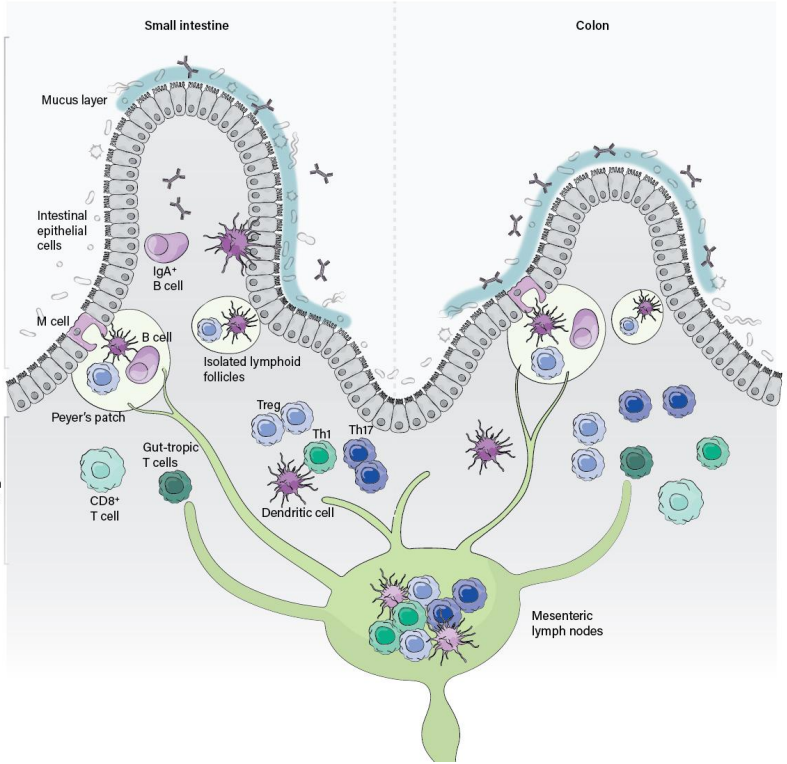
Kasarello et al. *Open J Pediatr Child Health*. 2019;4(1):040–6.

An overview of key T cell subtypes and their functions



Lee. *Immune Netw.* 2023;23(1):e4.

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The gut microbiome and oral tolerance

The neonatal immune system is primed towards a T-helper 2 (Th2) immune response, increasing the risk of allergies after birth.

Stimulation from the commensal gut microbiome is needed to increase T-helper 1 and 17 (Th1/Th17) activity and reduce Th2 dominance.

Th1/Th17 cells are activated in response to bacteria and fungi, and suppress Th2 immune cell responses.

The presence of a diverse and abundant microbial community promotes the Th1/Th17 response in infancy and helps to reduce the risk of allergies.

Prescott et al. *J Immunol*. 1998;160(10):4730–7.
Walker et al. *Nat Rev Immunol*. 2018;18(2):121–33.

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The gut microbiome and infection resistance

After birth, conditions which protected health in-utero (e.g. suppressed Th1 immunity, increased gut permeability) increase susceptibility to infection.

The colonisation of the gut with the right balance of microorganisms after birth helps to improve infection resistance by:

- Stimulating Th1/Th17 immune system function
- Promoting the closure of tight gap junctions to create a fully formed epithelial barrier

Breastfeeding helps to favour the proliferation of these beneficial microorganisms, particularly bifidobacteria, which stimulate the maturation of intestinal immune defences.

Kasarello et al. *Open J Pediatr Child Health*. 2019;4(1):040–6.

Ongoing infection resistance afforded by the gut microbiome

A healthy microbiota helps to enhance the immune system's response against pathogenic bacteria and the body's natural defences through a range of different mechanisms, including:

- Elevation of IgA production
- Maintenance of the epithelial cell lining and mucus layer
- Stimulation of Th1/Th17 immune responses
- Colonisation resistance
- Secretion of antimicrobial substances

Forchielli et al. *Br J Nutr.* 2005;93(Suppl 1):S41–8.
Khan et al. *Front Cell Infect Microbiol.* 2021;11:716299.
Walker et al. *Nat Rev Immunol.* 2018;18(2):121–33.

Major factors influencing the neonatal and paediatric microbiome

Mode of feeding and the microbiome

Breastfeeding is the single most important determinant of gut microbial colonisation after birth.

In a study of 91 infants who were either exclusively breast-fed or formula-fed:

- *Bifidobacterium* dominated in all groups, but was significantly higher in breast-fed infants at 40 days (46% vs 32-33% in formula groups)
- *Bacteroides* was significantly higher in breast-fed infants
- Potentially less beneficial genera, *Streptococcus, Enterococcus, Veillonella, Clostridioides,* were significantly lower in breast-fed infants

Human milk oligosaccharides (HMOs) selectively feed *Bifidobacterium* and *Bacteroides*, but cannot be used by potential pathogens like *Veillonella* or *Enterococcus.*

Ma et al. *Sci Rep.* 2020;10:15792.
Liu et al. *Front Microbiol.* 2019;10:598.
Jiang et al. *Nat Commun.* 2026;17:4594.

Mode of feeding and the microbiome

Counterintuitively, breast-fed infants had lower α-diversity than formula-fed infants at 40 days.

- Breast milk selectively promotes infant-type *Bifidobacteria t*hat specialise in degrading HMOs
- This creates a low-diversity but protective environment
- Diversity rises naturally with solid food introduction around 6 months

"More diversity = better" is an adult framework that doesn't apply to young infants

It's the right microbes at the right time that matters

Ma et al. Sci Rep. 2020;10:15792.
Liu et al. Front Microbiol. 2019;10:598.
Jiang et al. Nat Commun. 2026;17:4594.

Mode of delivery and the microbiome

Cesarean delivery significantly alters the early gut microbial community structure.

At 6 weeks of age, compared to vaginally-delivered infants, CS-born infants showed:

- Significantly decreased *Bifidobacterium*
- Increased *Klebsiella* (a hospital-associated opportunistic pathogen)
- Increased *Veillonella* and *Lactobacillus*
- Altered overall community structure

This disruption contrasts with normal microbial establishment, which has been linked to increased risk of chronic diseases such as asthma and obesity in later life.

Ma et al. Sci Rep. 2020;10:15792.
Liu et al. Front Microbiol. 2019;10:598.
Jiang et al. Nat Commun. 2026;17:4594.

Breastfeeding & the CS-perturbed microbiome

Using vaginally-born, exclusively breastfed (VB) infants as the "reference":

- CS-born, exclusively breastfed (CB) infants resembled VB infants
- CS-born, mixed-fed (CM) infants diverged significantly

Three genera explained much of the difference between CB and CM infants:

- Enterococcus: lower in CB and VB; higher in CM
- Veillonella: lower in CB and VB; higher in CM
- Faecalibacterium: higher in CB and VB; lower in CM

Exclusive breastfeeding can partially compensate for the microbial disruption caused by cesarean delivery

Ma et al. Sci Rep. 2020;10:15792.
Liu et al. Front Microbiol. 2019;10:598.
Jiang et al. Nat Commun. 2026;17:4594.

Microbial restoration

A CS-perturbed gut microbiome doesn't always stay perturbed.

Some infants' microbiomes "restore" by 1 year of age, resembling those of vaginally-delivered infants.

In two independent birth cohorts (Danish COPSAC, n=700; Canadian CHILD, n=325):

- Children whose microbiomes successfully restored by age 1 had asthma risk comparable to vaginally-delivered children
- Children who retained a CS-like microbiome at age 1 had elevated asthma risk at age 5-6

Delivery mode sets the trajectory, but the trajectory is modifiable within the first weeks and months.

Ma et al. Sci Rep. 2020;10:15792.
Liu et al. Front Microbiol. 2019;10:598.
Jiang et al. Nat Commun. 2026;17:4594.

Factors contributing to microbial restoration

A CS-perturbed microbiome composition can be influenced by environmental exposures or ecological interactions

The strongest predictors of successful 1-year restoration was associated with the gut microbiome at just 1 week of age (not 1 month)

Bacteria positively associated with restoration:

- *Bifidobacterium longum*
- *Bacteroides* species
- *Parabacteroides distasonis*
- *Sutterella wadsworthensis*

Clostridium perfringens was the strongest negative predictor

Ma et al. Sci Rep. 2020;10:15792.
Liu et al. Front Microbiol. 2019;10:598.
Jiang et al. Nat Commun. 2026;17:4594.

Factors contributing to microbial restoration

Environmental factors associated with restoration:

- Having older siblings (the closer in age, the stronger the effect)
- Rural birth area
- Cats at home

Maternal intrapartum antibiotics had a negative effect:

- Vaginally delivered babies whose mothers received antibiotics had a gut microbiota that resembles CS babies

Ma et al. Sci Rep. 2020;10:15792.
Liu et al. Front Microbiol. 2019;10:598.
Jiang et al. Nat Commun. 2026;17:4594.

Prevalence and impact of antibiotics in children

According to the The Royal Australian College of General Practitioners:

- Antibiotics are prescribed at 4–9× the rate recommended by Therapeutic Guidelines
- The majority of antibiotics used in children are for upper respiratory tract infections (URTIs)
- Reducing antibiotic use in children for URTIs is a priority for action

57% of children aged 0-4 received at least one course of antibiotics in a 12 month period

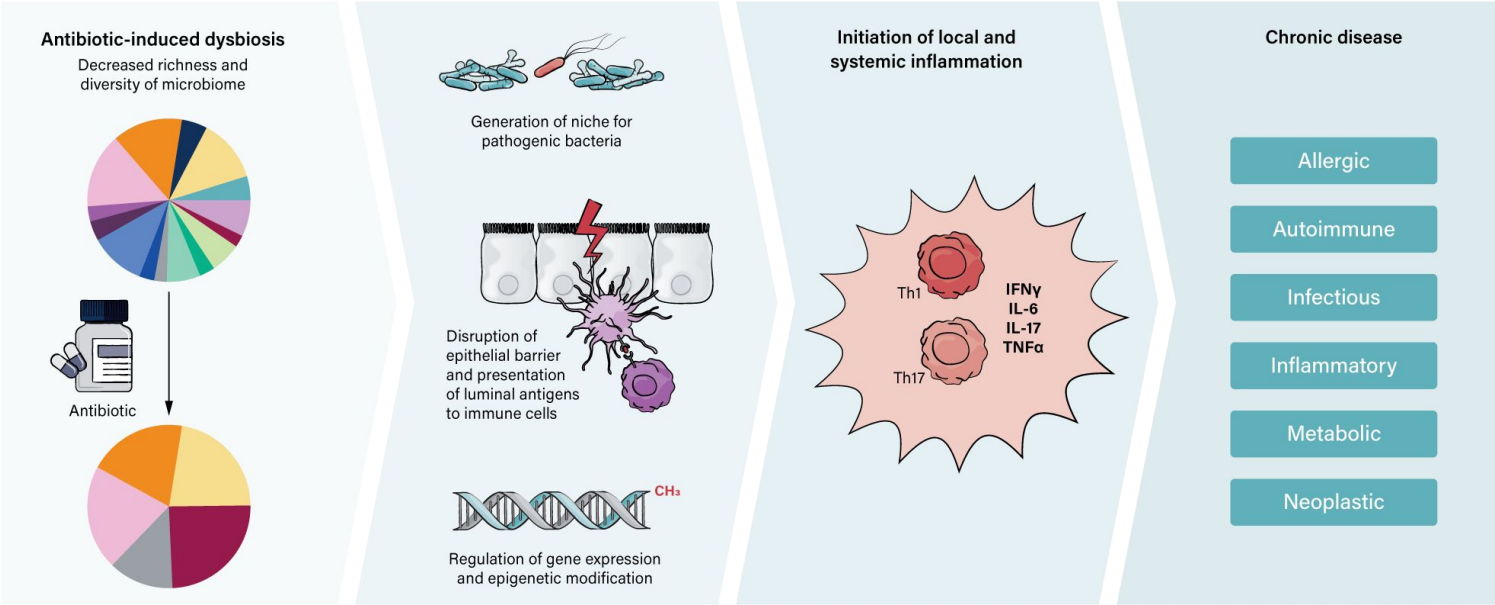
2x higher use of antibiotics in Australia than comparable high-income countries

1.75x greater risk of developing asthma by age 7.5 associated with early-life antibiotic use

Australian Commission on Safety and Quality in Health Care. AURA 2016. Australian Commission on Safety and Quality in Health Care; 2016.

Queen et al. *Gut Microbes.* 2020;11(4):1092–103.

Long-term impacts of dysbiosis



Queen et al. *Gut Microbes.* 2020;11(4):1092–103.

The shrinking gut microbiome and its consequences

The shrinking microbiome

An infant's 'first 1000 days of life' is a critical development window, with the microbial genome programing an infant's health and future risk of disease.

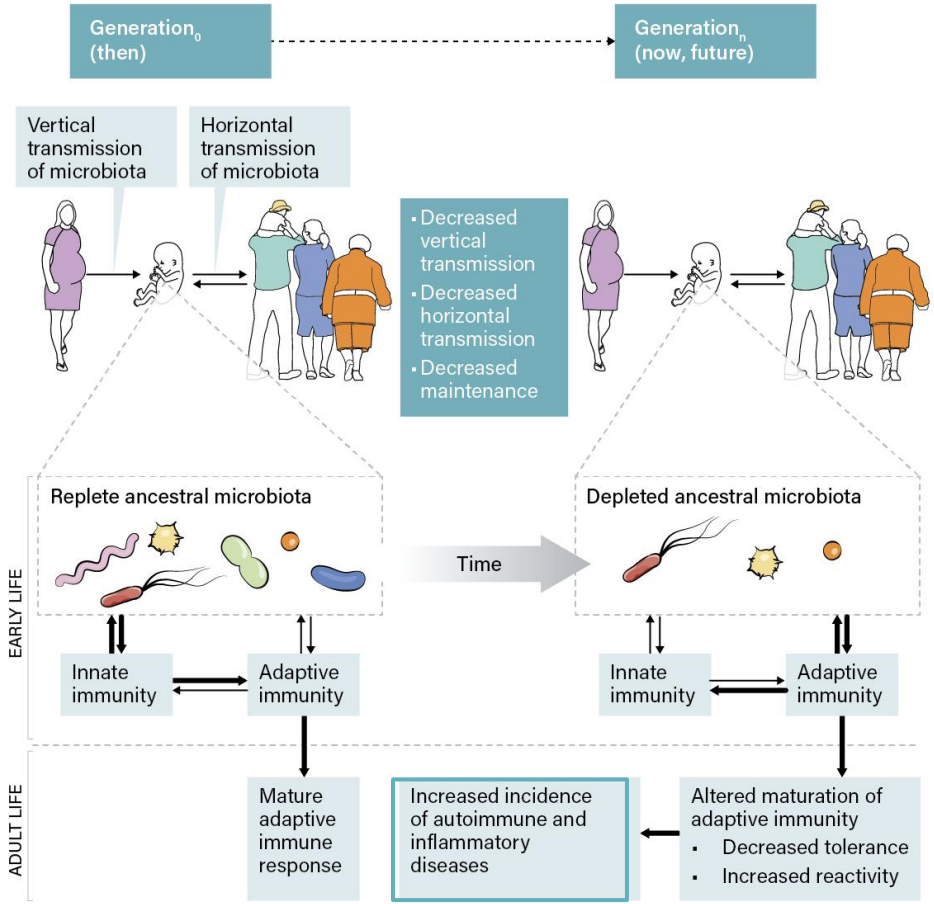
Increased use of antimicrobials, formula feeding, caesarean sections and changing living conditions are believed to be shrinking the diversity and density of beneficial microorganisms in the infant microbiome.



Selma-Royo et al. *Adv Exp Med Biol.* 2019;1125:3–24.

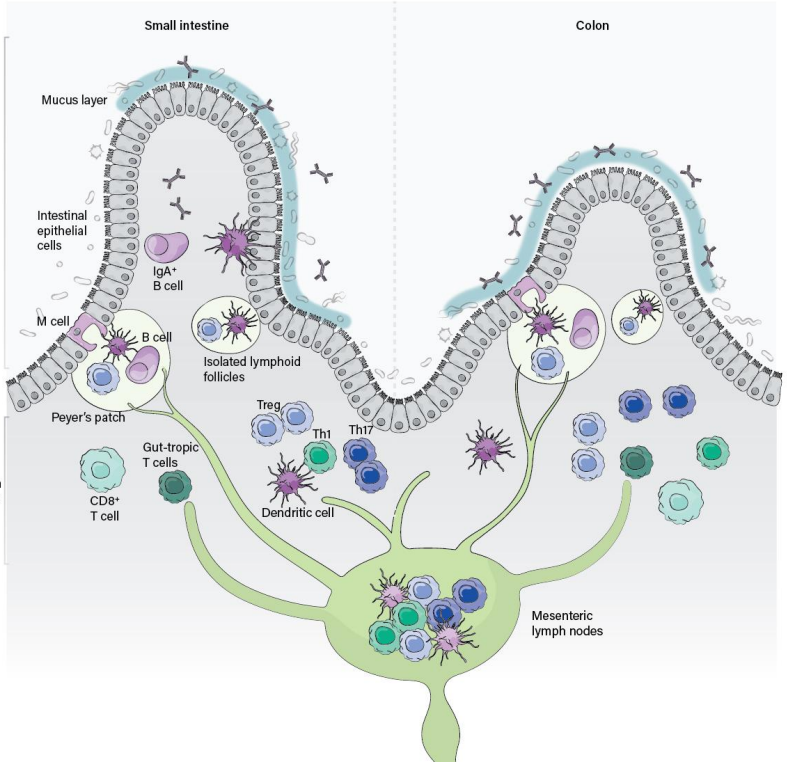
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The theory of disappearing microbiota



Blaser MJ. *Nat Rev Immunol [Internet]*. 2017;17(8):461–3.

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Gut dysbiosis and atopy

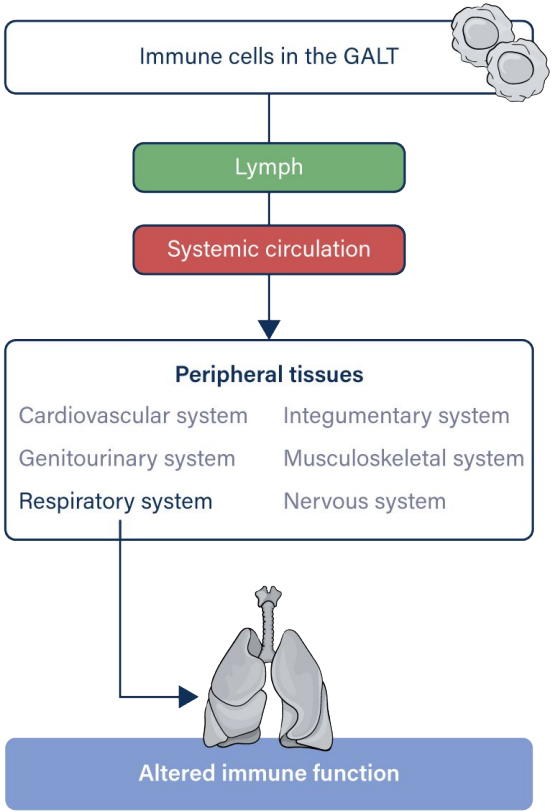
The gut microbiota influences the manifestation of allergic disease by calibrating Th1/Th2 balance for ‘oral tolerance’ and maintaining IEB integrity.

When the gut microbiota is disturbed, there is potential for:

- Persistent Th2 dominance due to insufficient microbial stimulation of Th1/Th17 responses
- IEB dysfunction allowing increased antigen translocation and contact with the immune system
- IgE-mediated sensitisation to innocuous antigens

Vighi et al. *Clin Exp Immunol.* 2008;153 Suppl 1(Suppl 1):3-6.
Holmgren et al. *Nat Med.* 2005;11(Suppl 4):S45–S53.
Zhou et al. *Front. Immunol.* 2021;12:639902.

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Gut dysbiosis and the atopic march

Deviation of the immune system to a Th2 phenotype begins in the gut and is transferred to all mucosa-associated lymphoid tissue in the body.

We can see this impact spreading to other parts of the body through the manifestation of the atopic march:

- The skin and atopic dermatitis
- The gastrointestinal tract and food allergies
- The nasal cavity and allergic rhinitis
- The lungs and allergic asthma

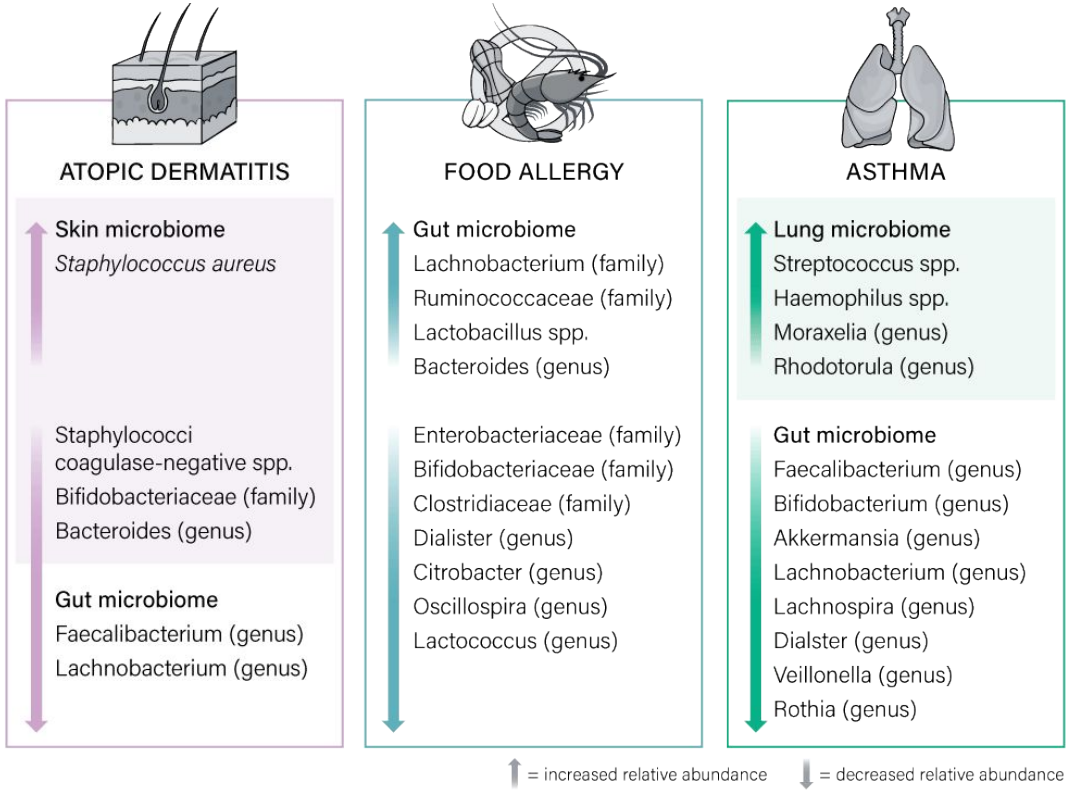
Infantile gut dysbiosis increases immune hyperreactivity to respiratory, food-borne, and contact antigens.

Hufnagl et al. *Semin Immunopathol [Internet]*. 2020;;42(1):75–93.

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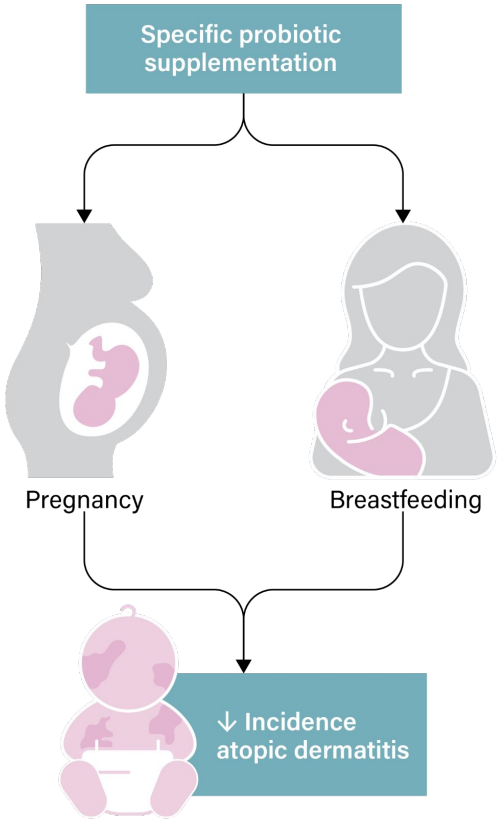
Patterns of dysbiosis

Evidence is building for the causal relationship between early life microbial perturbation in the gut, skin, and airways, and the development of allergic diseases.



Frati et al. *Int J Mol Sci.* 2019;20(1):123.
Cahenzli et al. *Cell Host Microbe.* 2013;14(5):559–570.
Russell et al. *EMBO Rep.* 2012;13(5):440–447.
Arrieta et al. *Gut Microbes.* 2016;7(4):342–352.
Drago et al. *J Clin Gastroenterol.* 2012;46(S1):56–63.
Peroni et al. *Front Immunol.* 2020;11.

Targeted probiotic strains for paediatric immune health



The maternal microbiome and foetal immune development

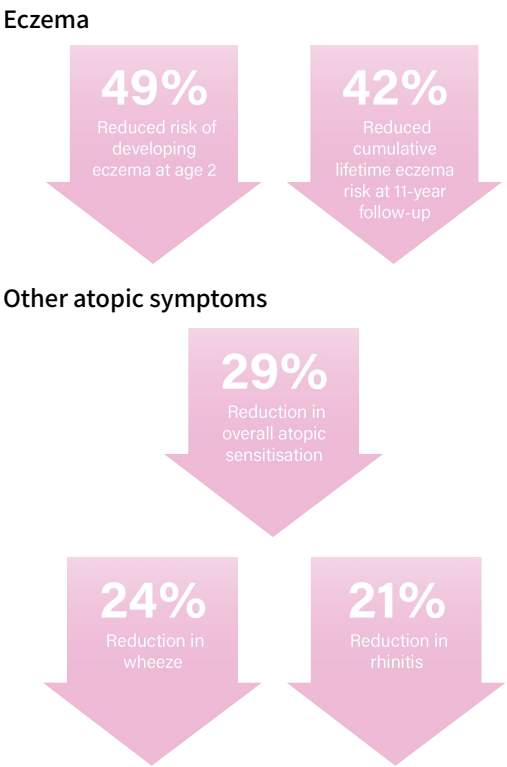
Since the discovery of bacterial DNA in the placenta, umbilical cord and amniotic fluid, the transfer and/or influence of the maternal microbiota in-utero is thought to impact foetal immune development.

The maternal microbiota may therefore determine the predisposition of the future child to immune dysregulation and pediatric allergies.

It has been clinically shown that supplementation of specific probiotic strains during pregnancy and breastfeeding can help reduce the incidence of atopic dermatitis in infants.

Selma-Royo et al. Adv Exp Med Biol. 2019;1125:3–24.
Kalliomäki et al. *J Allergy Clin Immunol.* 2007;119:1019–1021.
Foolad et al. JAMA Dermatol. 2013;149(3):350–355.

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Maternal probiotics and atopy in infants

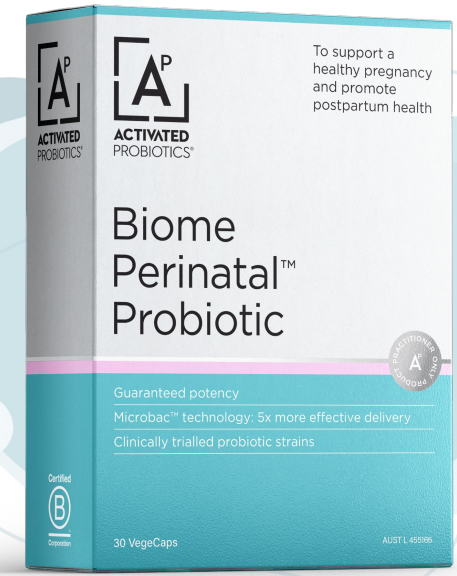
A series of studies assessed cumulative lifetime risk of eczema over 11 years in children whose mothers and themselves received *L. rhamnosus* HN001, HN019, or placebo from 35 weeks' gestation to 6 months postpartum and until 2 years of age.

Children in the *L. rhamnosus* HN001 group had a 49% reduced risk of developing eczema at age 2, and at the 11-year follow-up, a cumulative lifetime eczema risk reduction of 42% was observed.

Significant protection against other atopic symptoms with *L. rhamnosus* HN001 use across the first 11 years of life included 29% reduction in overall atopic sensitisation, 24% reduction in wheeze, and 21% reduction in rhinitis.

Wickens et al. *Pediatr Allergy Immunol.* 2018;29(8):808–14.

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Practitioner-only product

Biome Perinatal™ Probiotic

To support a healthy pregnancy and promote postpartum health

- Guaranteed potency
- Microbac™ technology: 5x more effective delivery
- Clinically trialled probiotic strains

Formulation

Lactobacillus rhamnosus GG (ATCC 53103)	5 BLB*
Lactobacillus rhamnosus HN001 (ATCC SD5675)	6 BLB*
Lactobacillus crispatus LCR01 (DSM 24619)	1 BLB*
Bifidobacterium breve BR03 (DSM 16604)	5 BLB*
Bifidobacterium animalis subsp. *lactis* BA05 (DSM 18352)	3 BLB*
Total live bacteria (BLB=Billion Live Bacteria)	**20 BLB***

Probiotic strains for the relief of eczema

In a randomised double-blind placebo-controlled trial, *L. salivarius* LS01 significantly improved outcomes versus placebo:

- SCORAD: 53% reduction ($p < 0.001$)
- DLQI: 55% improvement ($p = 0.021$)

Benefits were maintained for 4 weeks after treatment cessation.

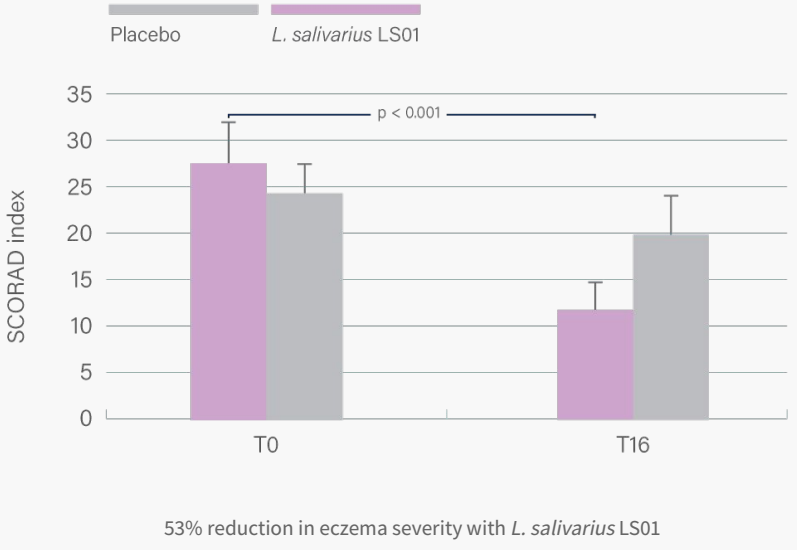


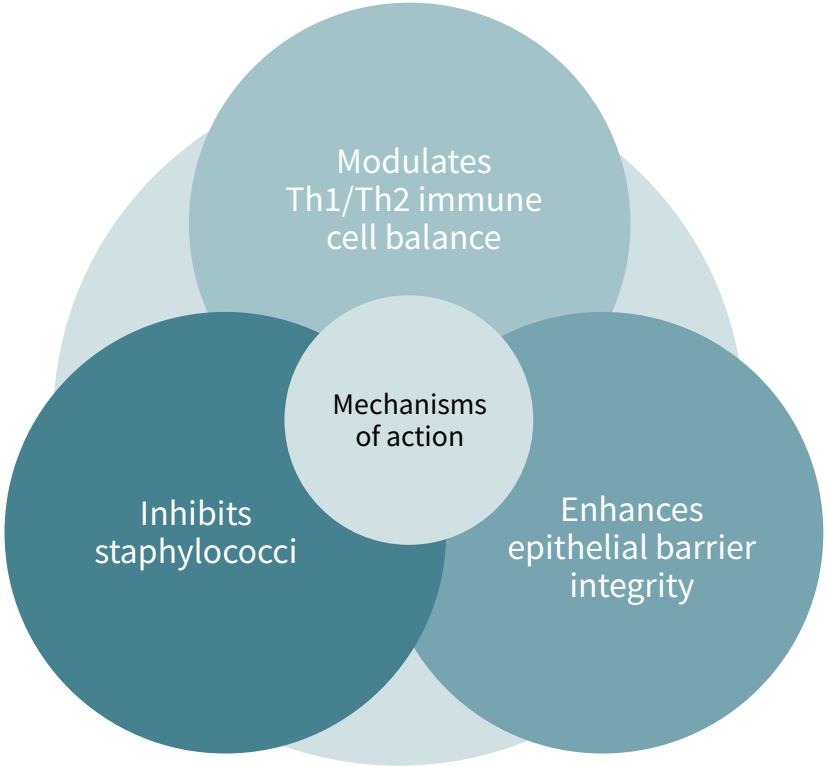
Figure 1: *Lactobacillus salivarius* LS01 significantly reduced SCORAD index after 16 weeks of treatment compared to placebo ($p<0.001$). Those taking the probiotic experienced a 53% reduction in the severity of their symptoms.

Drago et al. *J Clin Gastroenterol.* 2012;46 Suppl:S56-S63.

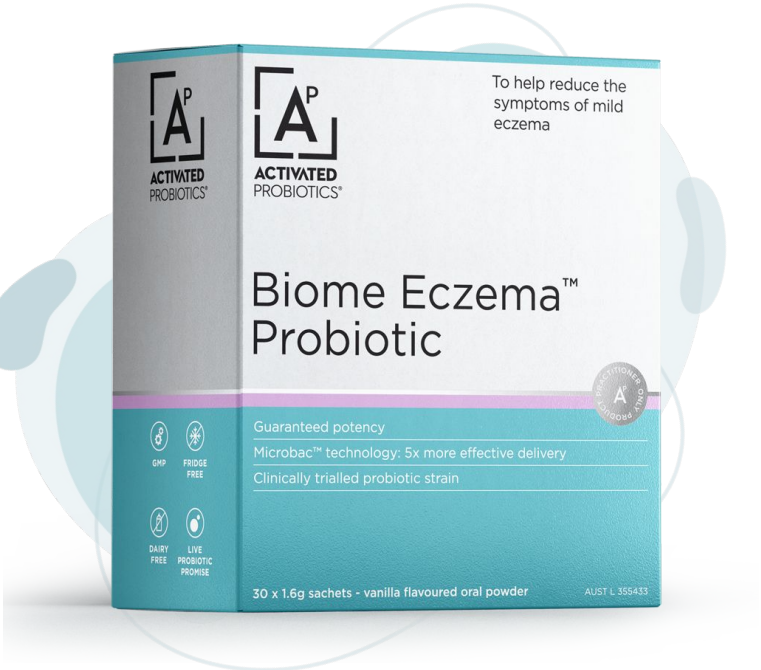
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L. salivarius LS01 mechanisms of action for atopic dermatitis

LS01 has been the subject of much mechanistic investigation to understand how it is benefiting atopic dermatitis.



Drago et al. *J Clin Gastroenterol.* 2012;46(S1):56–63
Drago et al. *Allergy Asthma Immunol Res.* 2015;7(4):409–43.
Drago et al. *Int J Immunopathol Pharmacol.* 2011;24(4):1037–48.



Practitioner-only product

Biome Eczema™ Probiotic

To help reduce the symptoms of mild eczema

- Relieves itchy skin associated with mild eczema
- Guaranteed potency
- Microbac™ technology: 5x more effective delivery
- Clinically trialled probiotic strain

Formulation

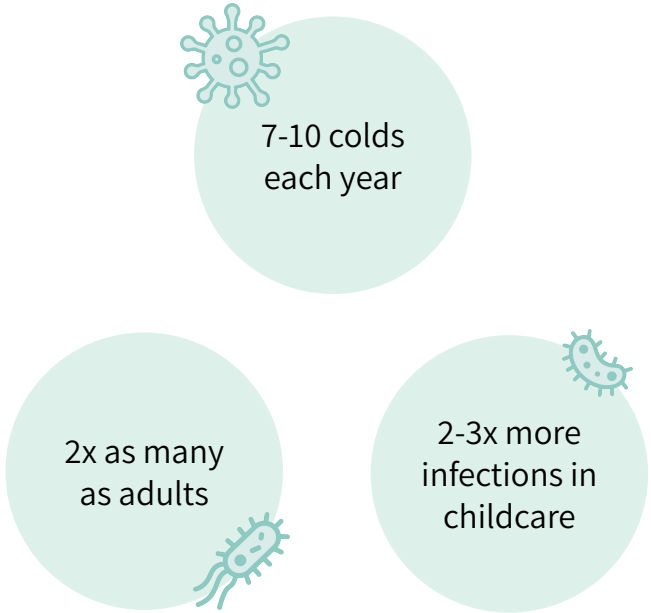
Lactobacillus salivarius LS01 (DSM 22775)	2 BLB*
Total live bacteria (BLB=Billion Live Bacteria)	**2 BLB***

Prevalence of paediatric infections

Contributing factors:

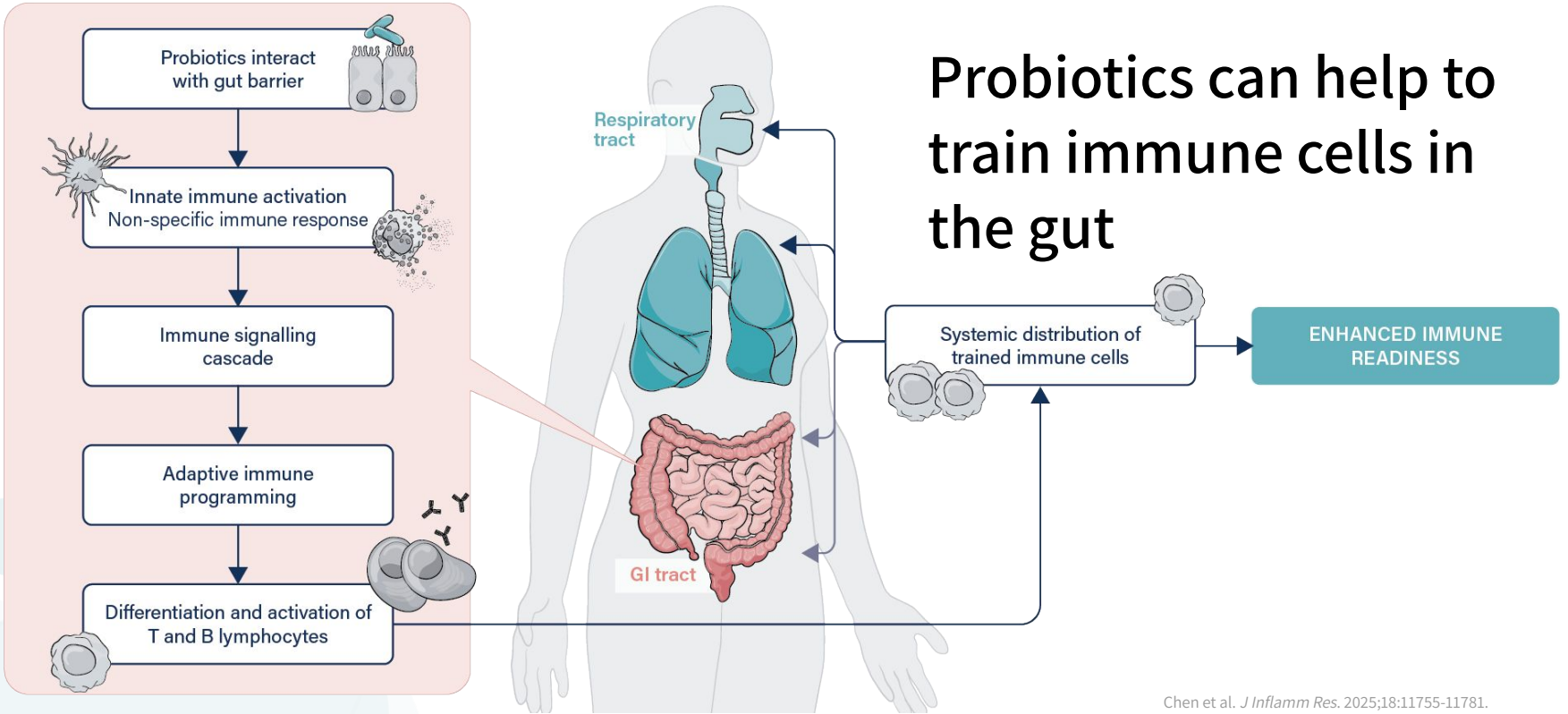
- Immature immune system
- High pathogen exposure
- Antibiotic-driven microbiome disruption

Supporting infection resistance is particularly relevant in early life



Troullos et al. *J Med Internet Res.* 2014;16(6):e144. doi:10.2196/jmir.2868
Silverstein et al. *Pediatrics.* 2003;111(4):e371–75. doi:10.1542/peds.111.4.e371

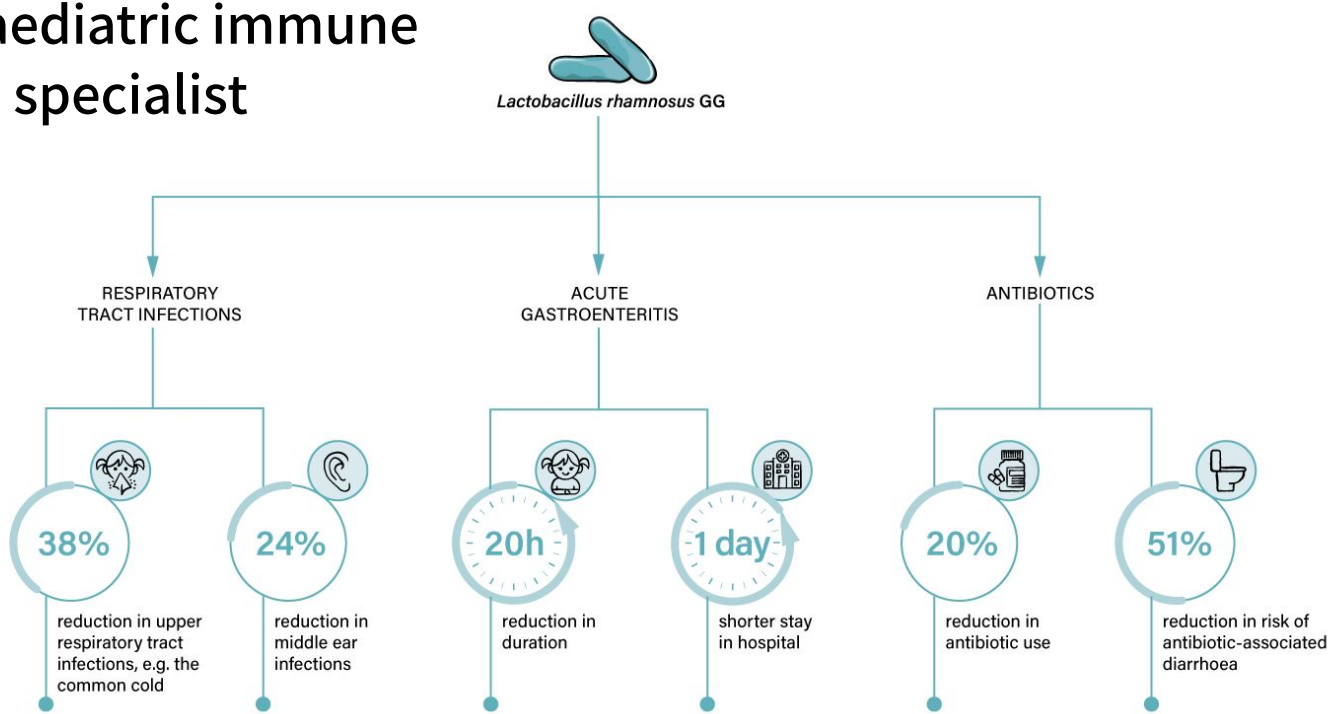
Probiotics can help to train immune cells in the gut



Chen et al. *J Inflamm Res.* 2025;18:11755-11781.

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The paediatric immune health specialist



Liu et al. *Indian Pediatr.* 2013;50(4):377–81.
Szajewska et al. *Aliment Pharmacol Ther.* 2015;42(10):1149–57.

ACTIVATED PROBIOTICS®



Practitioner-only product

Biome Baby™ Probiotic

To help support digestive and immune health in infants

- Supports gut health and immunity in infants
- Guaranteed potency
- Microbac™ technology: 5x more effective delivery
- Clinically trialled probiotic strains

Formulation

Bifidobacterium breve BR03 (DSM 16604)	0.4 BLB*
Bifidobacterium breve B632 (DSM 24706)	0.4 BLB*
Lactobacillus rhamnosus GG (ATCC 53103)	1 BLB*
Total live bacteria (BLB=Billion Live Bacteria)	**1.8 BLB***

Prebiotic fructo-oligosaccharides (FOS) 1.5g

ACTIVATED PROBIOTICS®



Practitioner-only product

Biome Daily Kids™ Probiotic

- Helps enhance immune system function
- Helps reduce the occurrence
- and duration of common colds
- Supports good gut bacteria during antibiotic use

Formulation

Lactobacillus plantarum 6595 (DSM 6595)	3 BLB*
Lactobacillus rhamnosus GG (ATCC 53103)	2 BLB*
Bifidobacterium animalis subsp. *lactis* BS01 (LMG P-21384)	2 BLB*
Lactobacillus casei LC03 *(DSM 27537)*	1 BLB*
Bifidobacterium breve BR03 (DSM 16604)	2 BLB*
Total live bacteria (BLB=Billion Live Bacteria)	**10 BLB***

The oral microbiota and paediatric dental health



The oral microbiome

The oral cavity harbours more than 700 species of bacteria, fungi, viruses, etc.

The oral microbiome contributes to whole body homeostasis in a number of unique and unexpected ways.

The surface of teeth is home to one of the most important communities within the oral microbiome when it comes to health: ‘dental plaque’.

Peng et al. *Int J Oral Sci.* 2022;;14(1):14.

ACTIVATED PROBIOTICS®



Practitioner-only product

Biome Dental™ Probiotic

To help support dental health and a healthy oral microbiome

- Guaranteed potency
- Clinically trialled probiotic product

Formulation

Lactobacillus helveticus Rosell®-52 (CNCM I-1722)	3.4 BLB*
Lactobacillus rhamnosus Rosell®-11 (CNCM I-1720)	1.8 BLB*
B. longum Rosell®-175 (CNCM I-3470)	0.46 BLB*
Saccharomyces boulardii (CNCM I-1079)	0.65 BLB*
Total live bacteria (BLB=Billion Live Bacteria)	**6.3 BLB***

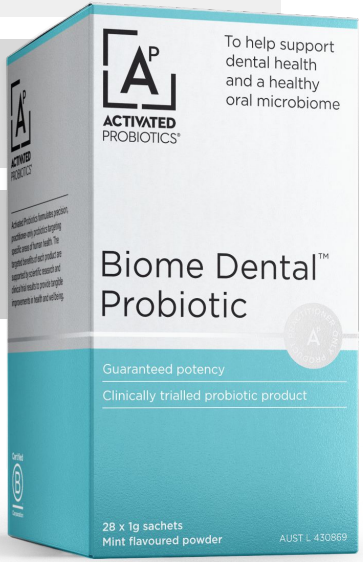
Who is Biome Dental™ Probiotic for?

Adults and children needing to reduce gum inflammation and dental plaque accumulation

Those with halitosis

Patients who are at increased risk of oral candidiasis

Adults and children looking to reduce risk of dental cavities



ACTIVATED PROBIOTICS®

ACTIVATED PROBIOTICS

Thank You

Practitioner Portal
https://activatedprobiotics.com.au/practitioner-login/

Technical Support
support@activated.co

The Activated Probiotics Practitioner Network on Facebook
https://www.facebook.com/groups/2707614249567886

Certified B Corporation
This company meets the highest standards of social and environmental impact

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