

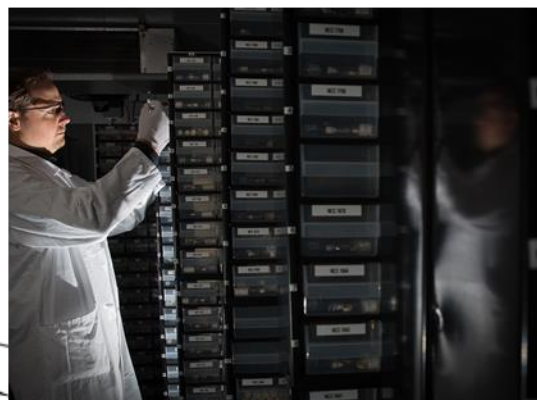


Nestlé Good food, Good life

Early life microbiome and biotic research @ Nestle Research

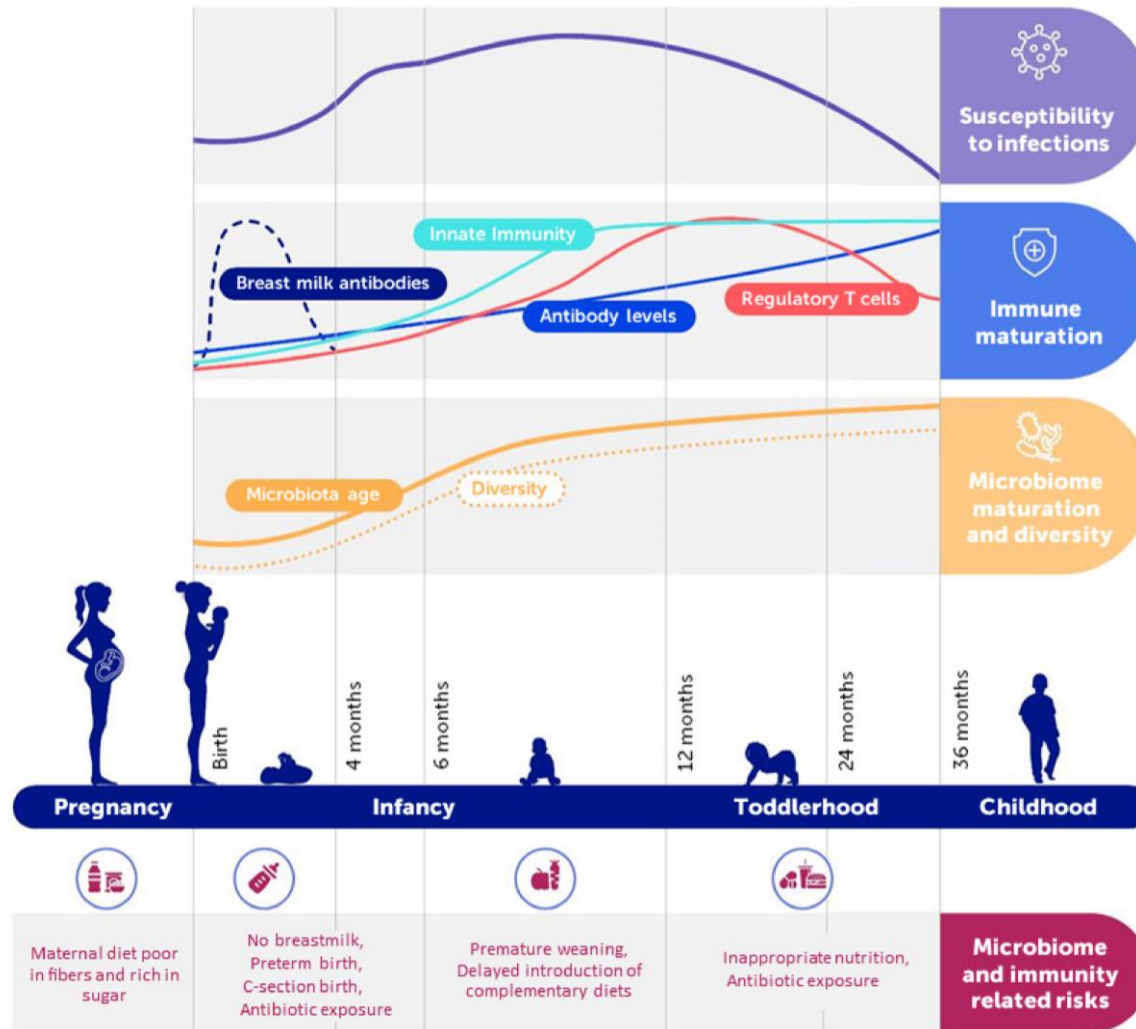


0.8 Mbp



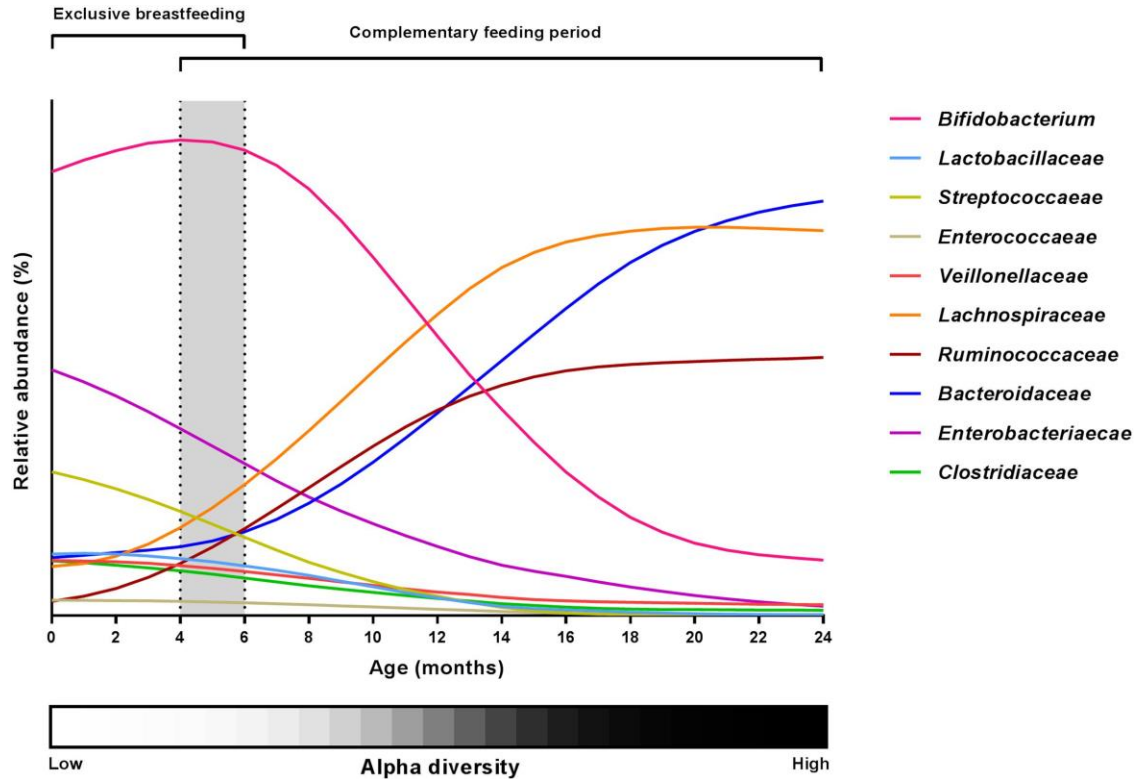
Biopharmaceutical biotechnology course
EPFL, 8th of October 2025
Stéphane Duboux, PhD

Infancy is a critical developmental phase for long term immune health

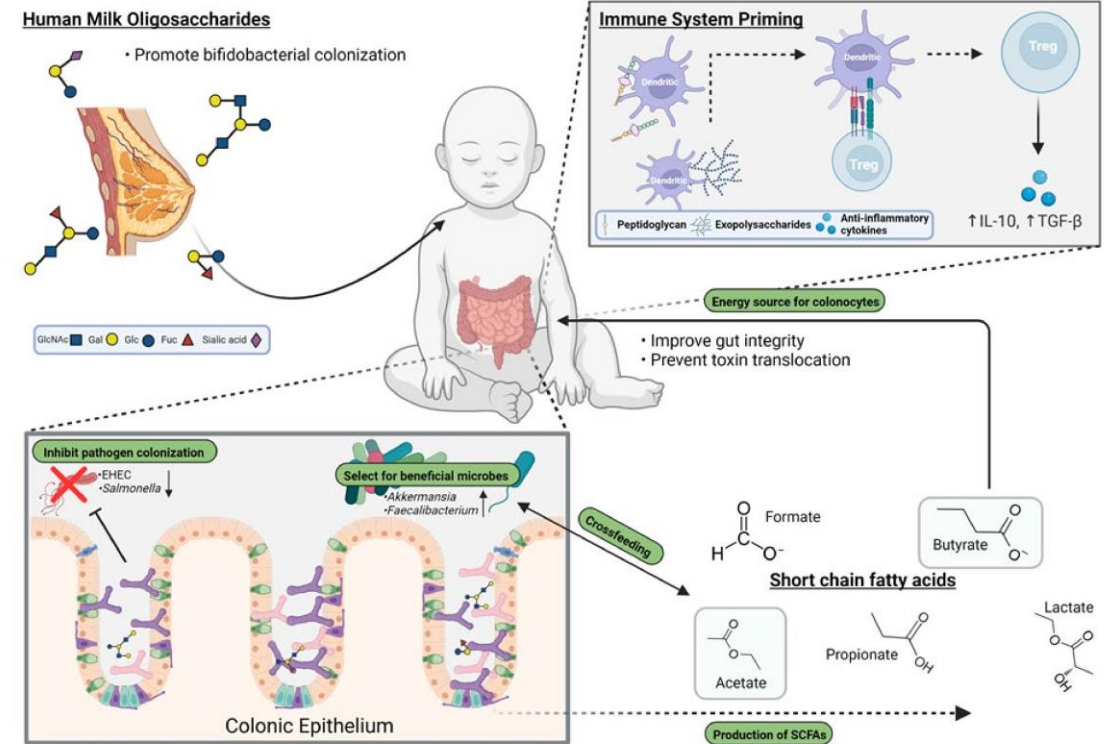


Adapted from Dogra et al. "Nurturing the Early Life Gut Microbiome and Immune Maturation for Long Term Health". *Microorganisms* 2021, 9, 2110. <https://doi.org/10.3390/microorganisms9102110>

Bifidobacteriaceae are prevalent in the infant gut microbiome and play a key role during this period

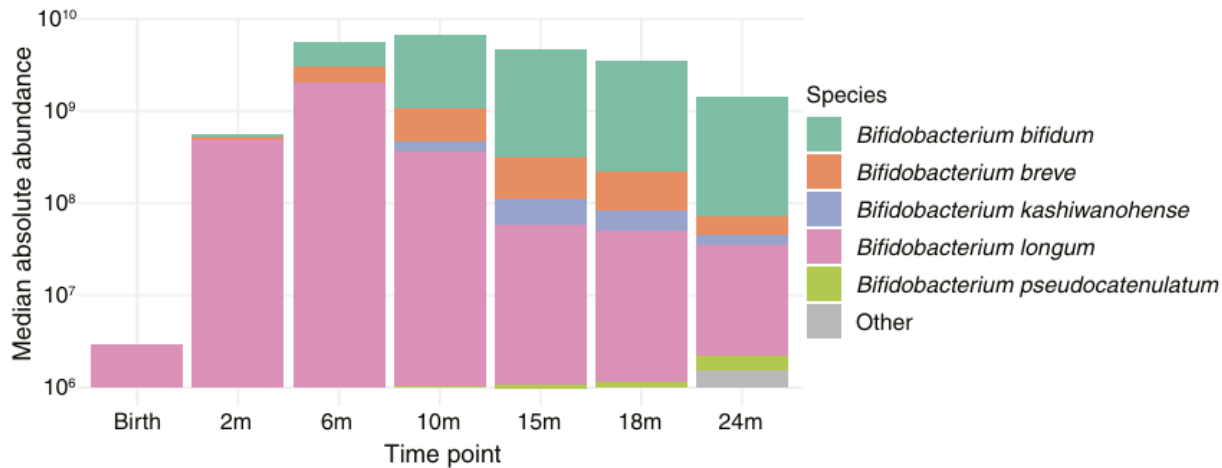
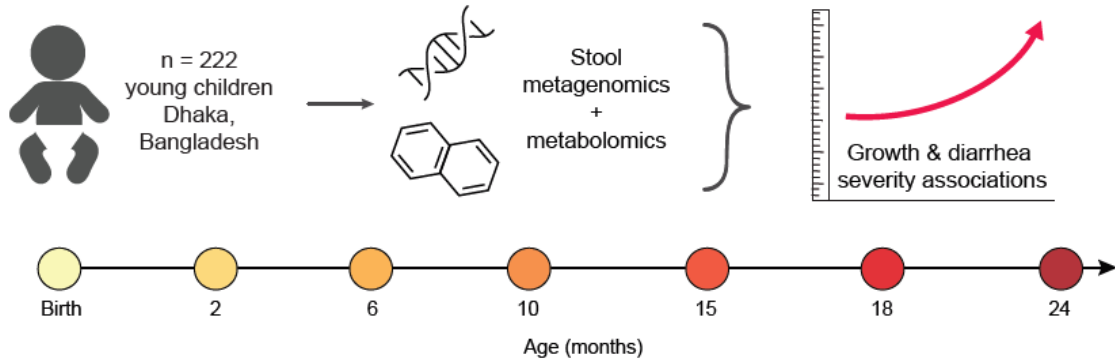


Laursen et al. 2017 "First foods and Gut microbes"
 Front. Microbiol., 06 March 2017, Volume 8 - 2017 |
<https://doi.org/10.3389/fmicb.2017.00356>

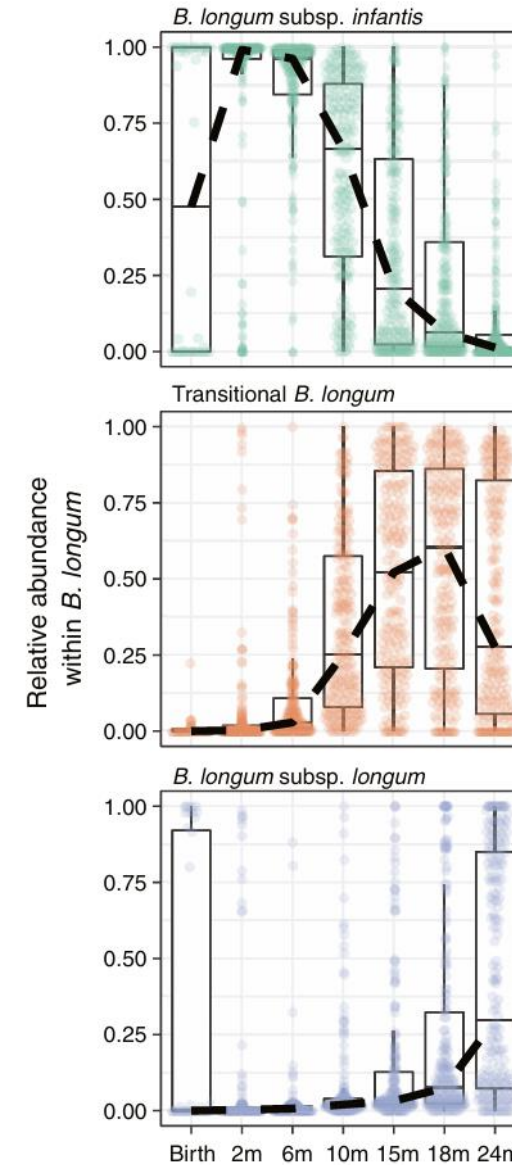


Stuivenberg et al. "Why Are Bifidobacteria Important for Infants?" *Microorganisms* 2022, 10, 278.
<https://doi.org/10.3390/microorganisms10020278>

Understanding the *Bifidobacteriaceae* succession in the infant gut

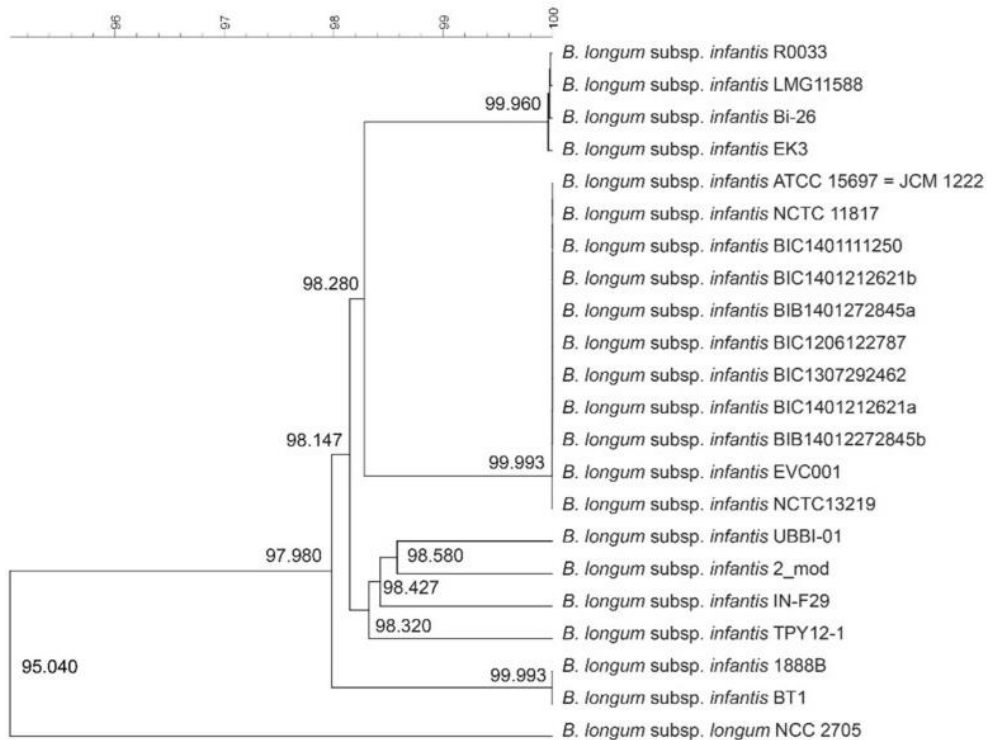


Vatanen, Duboux et al. "A distinct clade of *Bifidobacterium longum* in the gut of Bangladeshi children thrives during weaning". *Cell*. 2022 Nov 10;185(23):4280-4297.e12. doi: 10.1016/j.cell.2022.10.011. Epub 2022 Nov 1. PMID: 36323316.

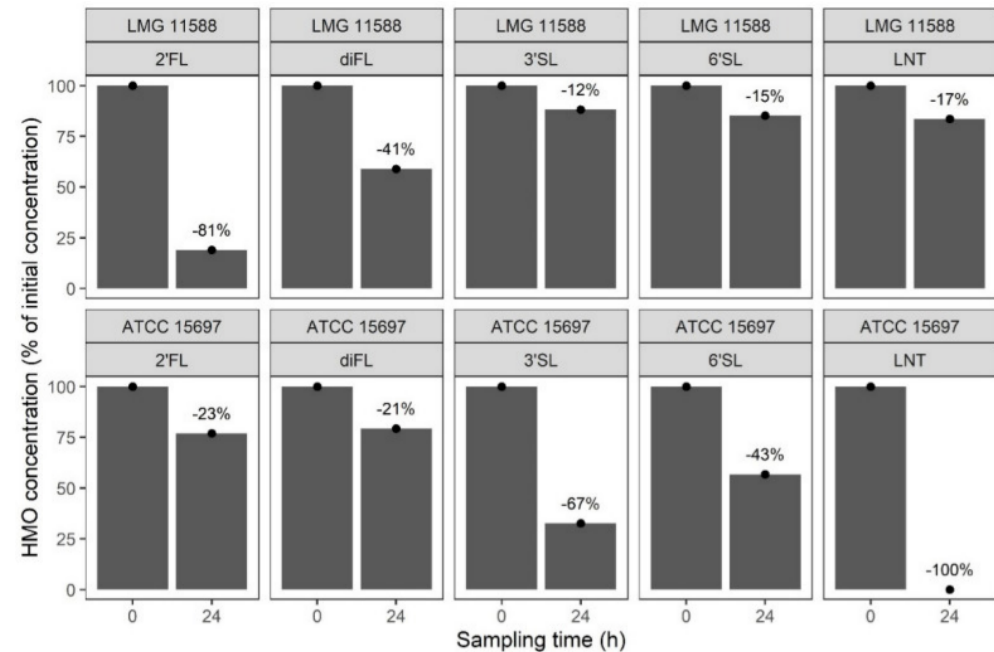


Exploring *B. I. infantis* diversity and related functionality

B. longum subsp. *infantis* diversity contains two large strain clusters...



... with different human milk oligosaccharides consumption patterns



Duboux et al. "Phylogenetic, Functional and Safety Features of 1950s *B. infantis* Strains" *Microorganisms*. 2022 Jan 18;10(2):203. doi: 10.3390/microorganisms10020203. PMID: 35208658; PMCID: PMC8879182.

B. I. iuvenis – a newly discovered subspecies with capacities to use both human milk oligosaccharides and food derived glycan fibers



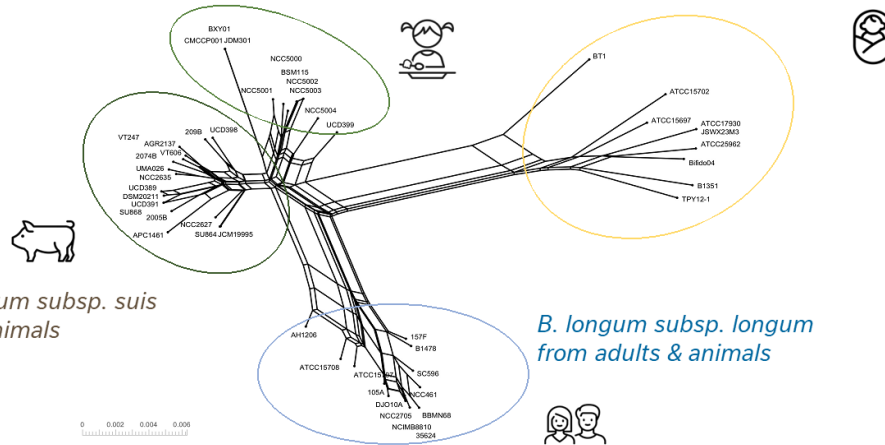
ALMA MATER STUDIORUM
UNIVERSITÀ DI BOLOGNA

B. longum subsp. *iuvenis* nov
from weaning infants

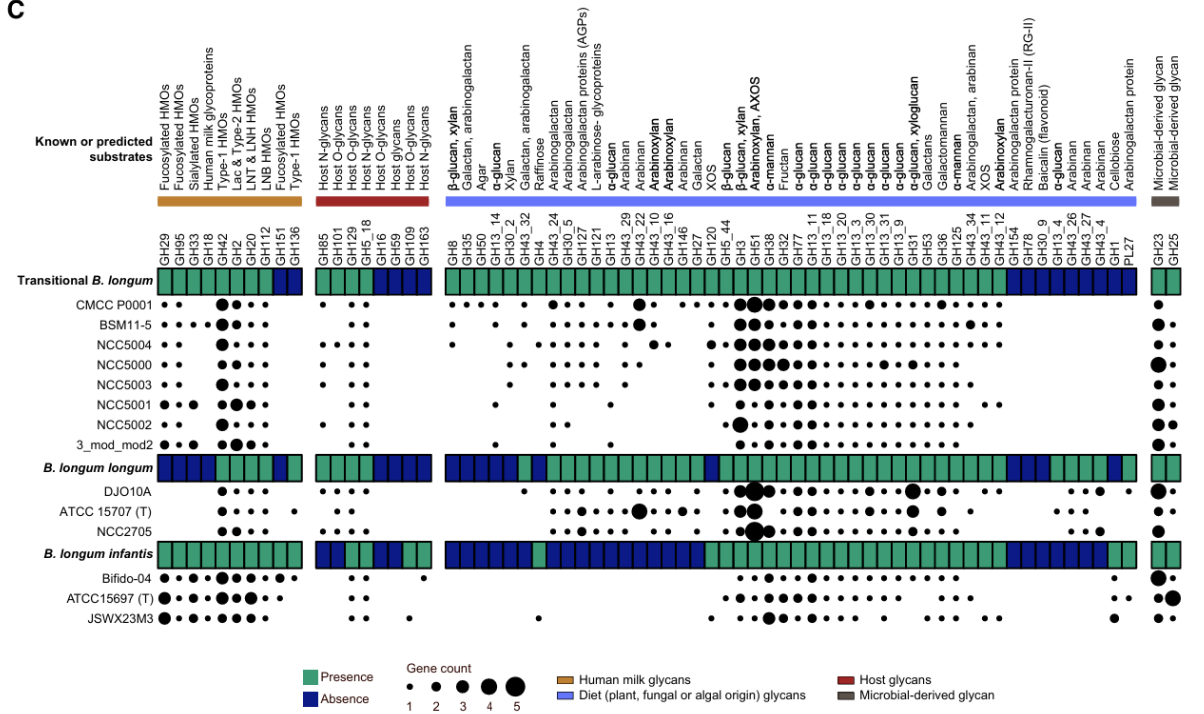
B. longum subsp. *infantis*
from young infants

B. longum subsp. *suis*
from animals

B. longum subsp. *longum*
from adults & animals



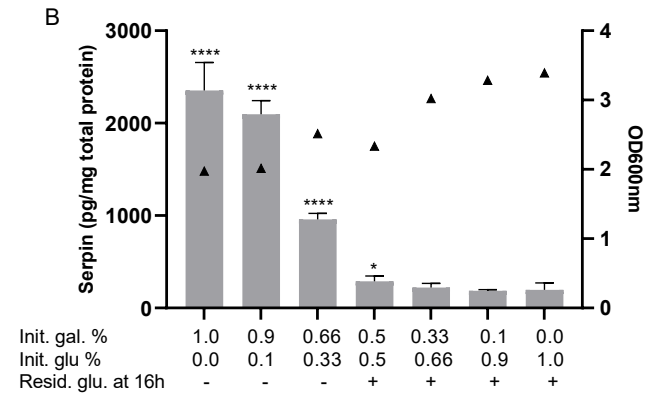
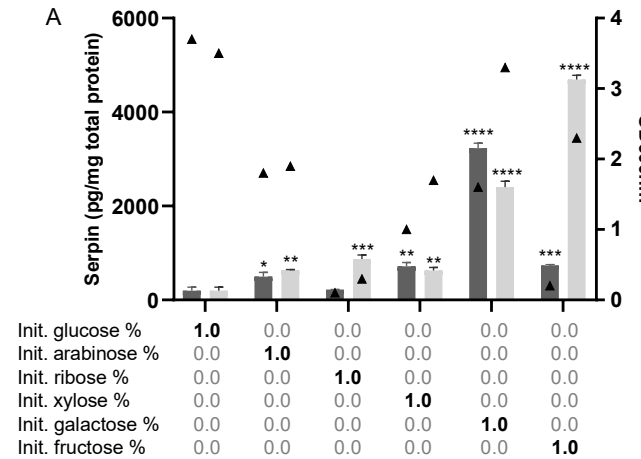
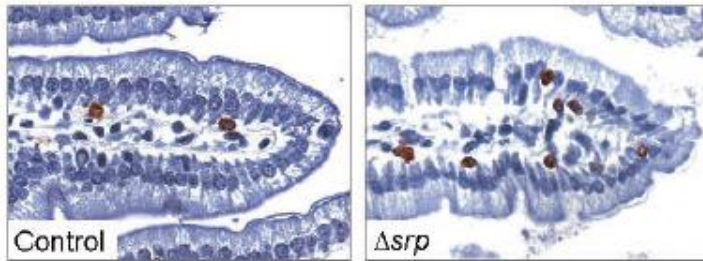
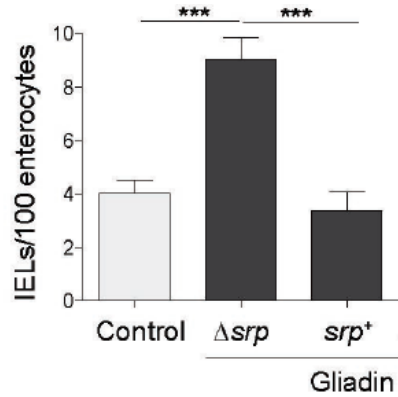
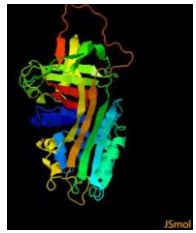
C



Modesto, Duboux et al. “*Bifidobacterium longum* subsp. *iuvenis* subsp. nov., a novel subspecies isolated from the faeces of weaning infants”. *Int J Syst Evol Microbiol.* 2023 Oct;73(10). doi: 10.1099/ijsem.0.006013. PMID: 37851001.

Vatanen, Duboux et al. “A distinct clade of *Bifidobacterium longum* in the gut of Bangladeshi children thrives during weaning”. *Cell.* 2022 Nov 10;185(23):4280-4297.e12. doi: 10.1016/j.cell.2022.10.011. Epub 2022 Nov 1. PMID: 36323316.

An important effector molecule mediating *Bifidobacterium* immune response is regulated by carbohydrates



- NCC 2705 serpin (*srp*) inhibits human serine protease (elastase) ¹
- NCC 2705 protects celiac mouse from gluten induced reaction through the production serpin ²

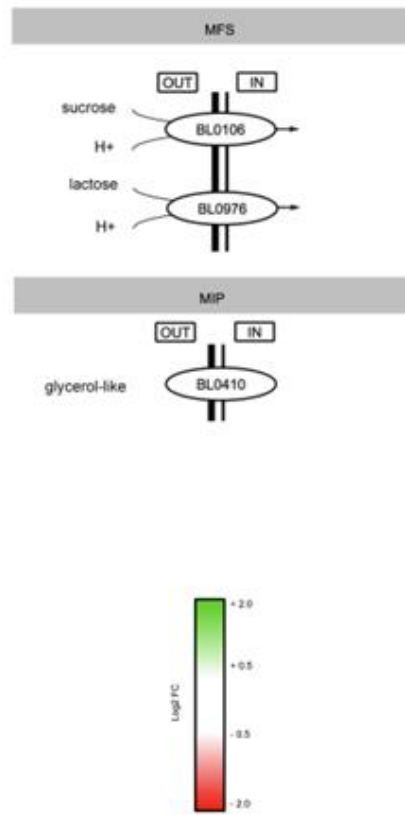
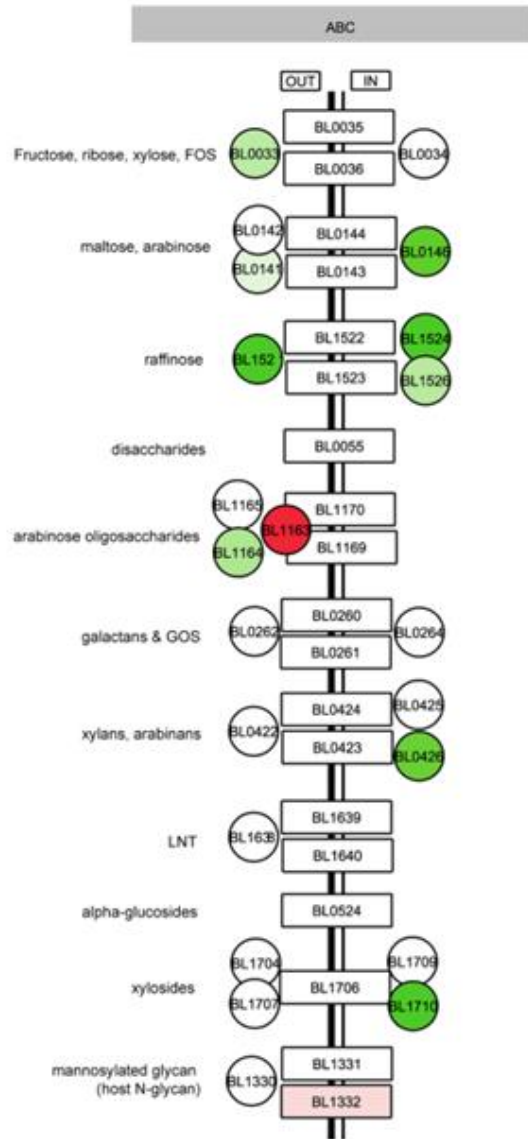
- NCC 2705 serpin is controlled by carbohydrates ³:
 - induced by galactose and fructose
 - repressed by glucose

¹ Ivanov et al, THE JOURNAL OF BIOLOGICAL CHEMISTRY VOL. 281, NO. 25, pp. 17246–17252, June 23, 2006

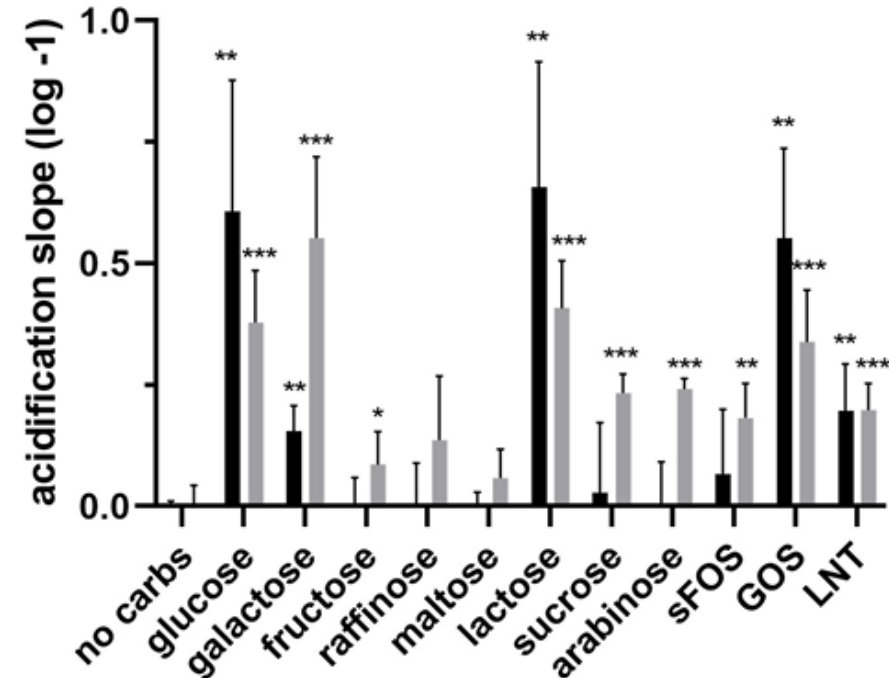
² McCarville & Dong, Duboux et al, Appl. Environ. Microbiol. doi:10.1128/AEM.01323-17

³ Duboux et al., Sci- Rep. 2021 Mar 31;11(1):7236.

Galactose drives key metabolic changes in *B. I. longum* NCC 2705



	GLUCOSE		GALACTOSE	
	OD-Based	CFU-Based	OD-Based	CFU-Based
MAX CELL DENSITY ± SEM (OD600; CFU/ML)	5.87 ± 0.12	2.80 × 10 ⁸ ± 1.86 × 10 ⁷	3.80 ± 0.06	7.80 × 10 ⁸ ± 1.22 × 10 ⁸
AVERAGE MAX GROWTH RATE μ ± SEM (1/H)	0.67 ± 0.05	-	0.35 ± 0.05	-
ESTIMATED AVERAGE DOUBLING TIME (1/H)	-	1.05	-	2.06
AVERAGE ± SEM CFU:OD	5.93 × 10 ⁷ ± 1.81 × 10 ⁷		2.54 × 10 ⁸ ± 4.28 × 10 ⁷	
AVERAGE CELL LENGTH ± SEM (μM)	2.47 ± 0.06		1.57 ± 0.03	
MAX ACIDIFICATION SLOPE (1/H)	-0.57 ± 0.07		-0.39 ± 0.03	
AVERAGE FINAL PH ± SEM	4.51 ± 0.04		4.50 ± 0.05	



Duboux et al. "The Pleiotropic Effects of Carbohydrate-Mediated Growth Rate Modifications in *Bifidobacterium longum* NCC 2705". *Microorganisms*. 2023 Feb 26;11(3):588. doi: 10.3390/microorganisms11030588.

Key take away messages

- Infant gut microbiome changes are highly dynamic during the first two years of life – and can be influenced by extrinsic factors
- *Bifidobacteriaceae* are highly prevalent in early infancy – and follows specific succession
- Different *B. longum* subspecies have different functionalities :
 - *B. l. infantis* is adapted to human milk oligosaccharides (HMOs) present in human milk
 - *B. l. iuvenis* – a newly described subspecies – can metabolize both HMOs and food fibers
- Carbohydrate drive metabolic changes in *B. longum*, which are relevant both from a functionality and manufacturing perspective



Nestlé Good food, Good life

Thank you !

