DTU

Uddannelses- og Forskningsstyrelsen

Food & Bio Cluster Denmark

Webinar om Mikrobiota, kost og sundhed

30. maj 2023

Kostens betydning for tarmens mikrobiom efter fødslen og i de første år

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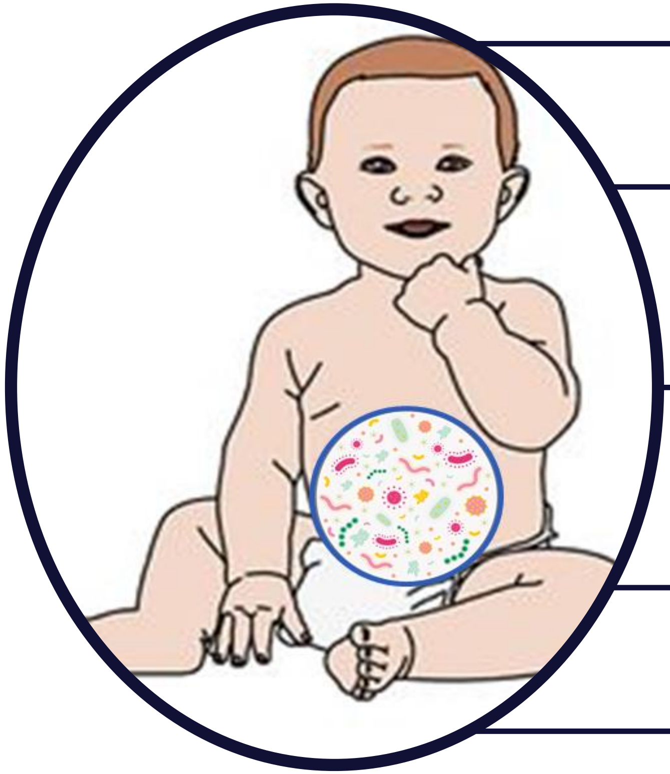
Hvorfor forske i tarmmikrobiotaen?



Undernutrition
(Subramanian *et al.*, 2014 – Nature)
(Blanton *et al.*, 2016 – Science)
(Raman *et al.*, 2019 – Science)
(Gehrig *et al*, 2019 – Science)
(Chen *et al.*, 2021 -NEJM)

Type 1 diabetes
(Giongo et al., 2011 – ISME)
(Kostic *et al.*, 2015 – Cell Host & Microbe)
(Vatanen *et al.*, 2018 – Nature)
(Steward *et al.*, 2018 – Nature)

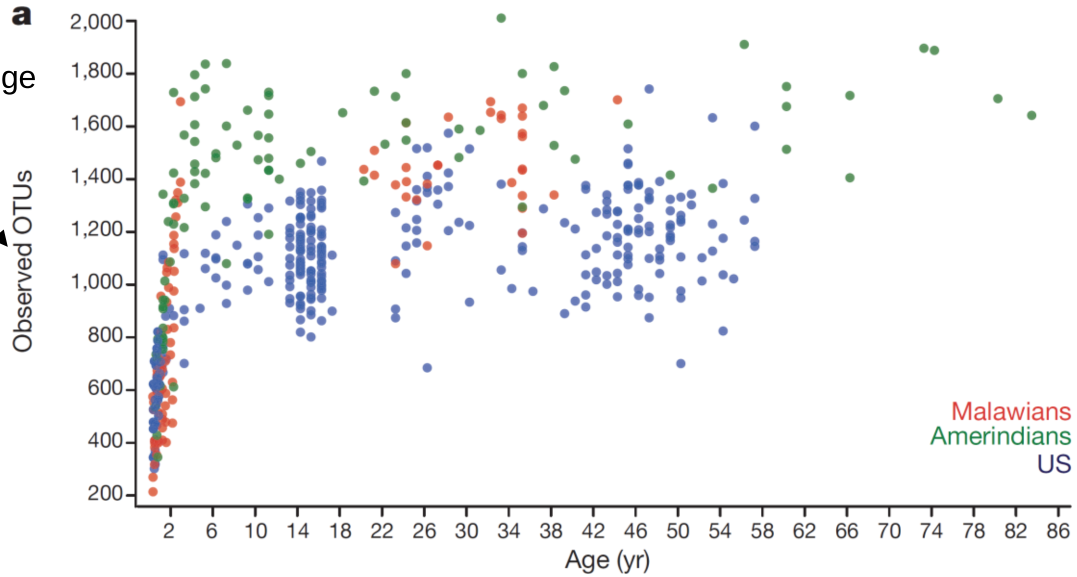
Inflammatory bowel diseases
(Michail et al., 2012 – Inflamm Bowel Dis)
(Grevers *et al.*, 2014 – Cell Host & Microbe)
(Torres *et al.*, 2020 – Gut)

Asthma and allergies
(Arrieta *et al.*, 2014 – Sci Trans Med)
(Fujimura *et al.*, 2016 – Nat Med)
(Stokholm *et al.*, 2018 – Nat Comn)
(Feehley *et al.*, 2019 - Nat Med)

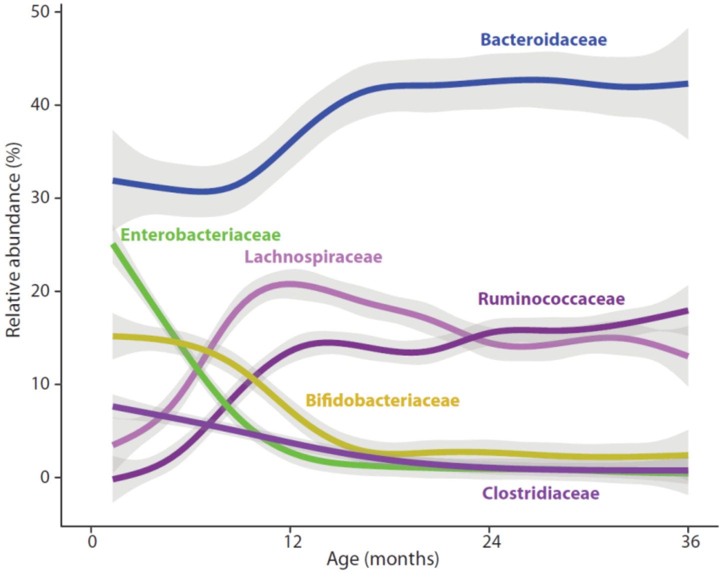
Obesity
(Riva *et al.*, 2016 – Envion Micro)
(Korpela *et al.*, 2017 – Microbiome)
(Laursen *et al.*, 2021 – FEMS Micro Eco)

Udviklingen af tarm-mikrobiomet i det tidlige liv

Antallet af forskellige bakterier i tarmen (α-diversity)

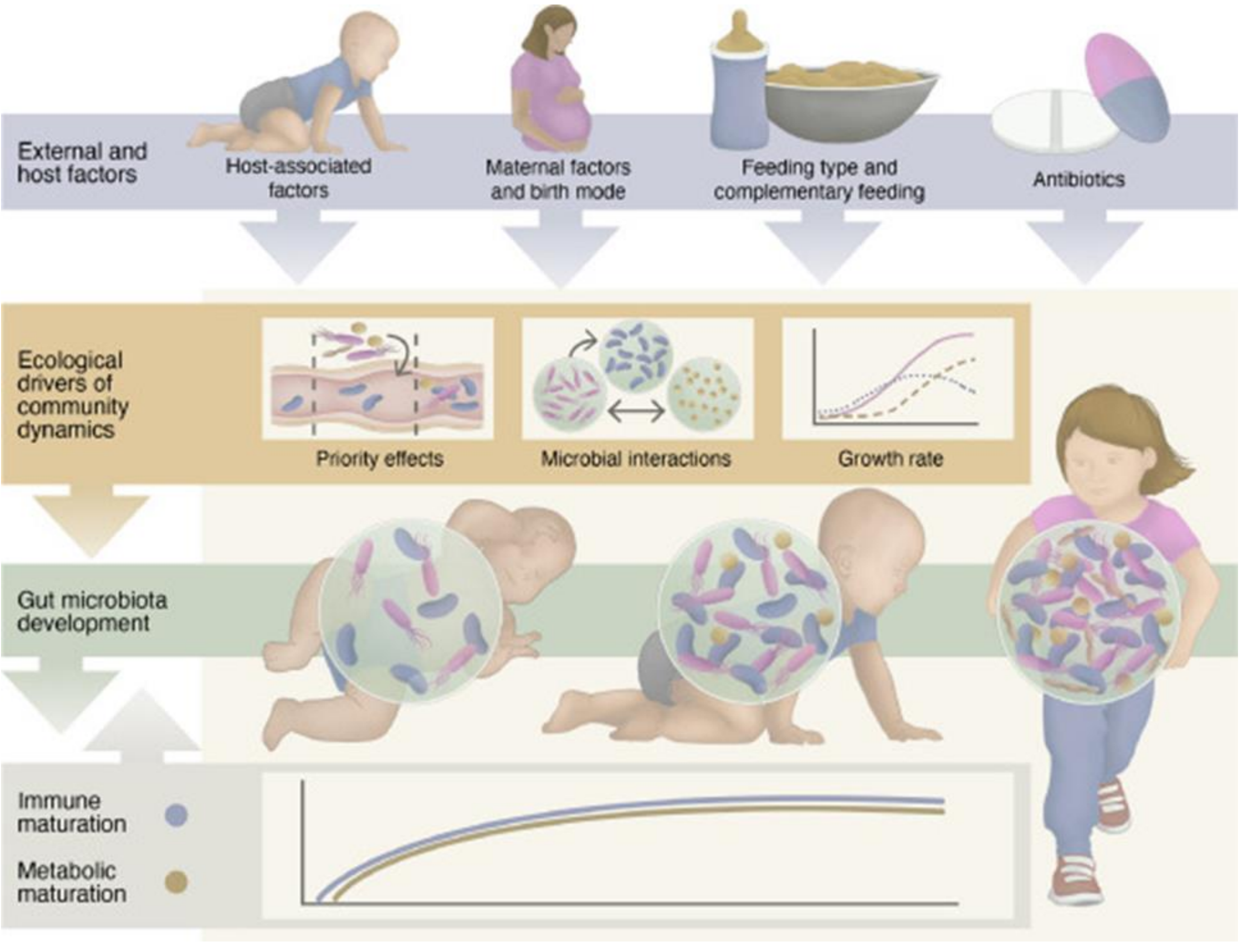


Yatsunenko *et al.*, 2012 - Nature



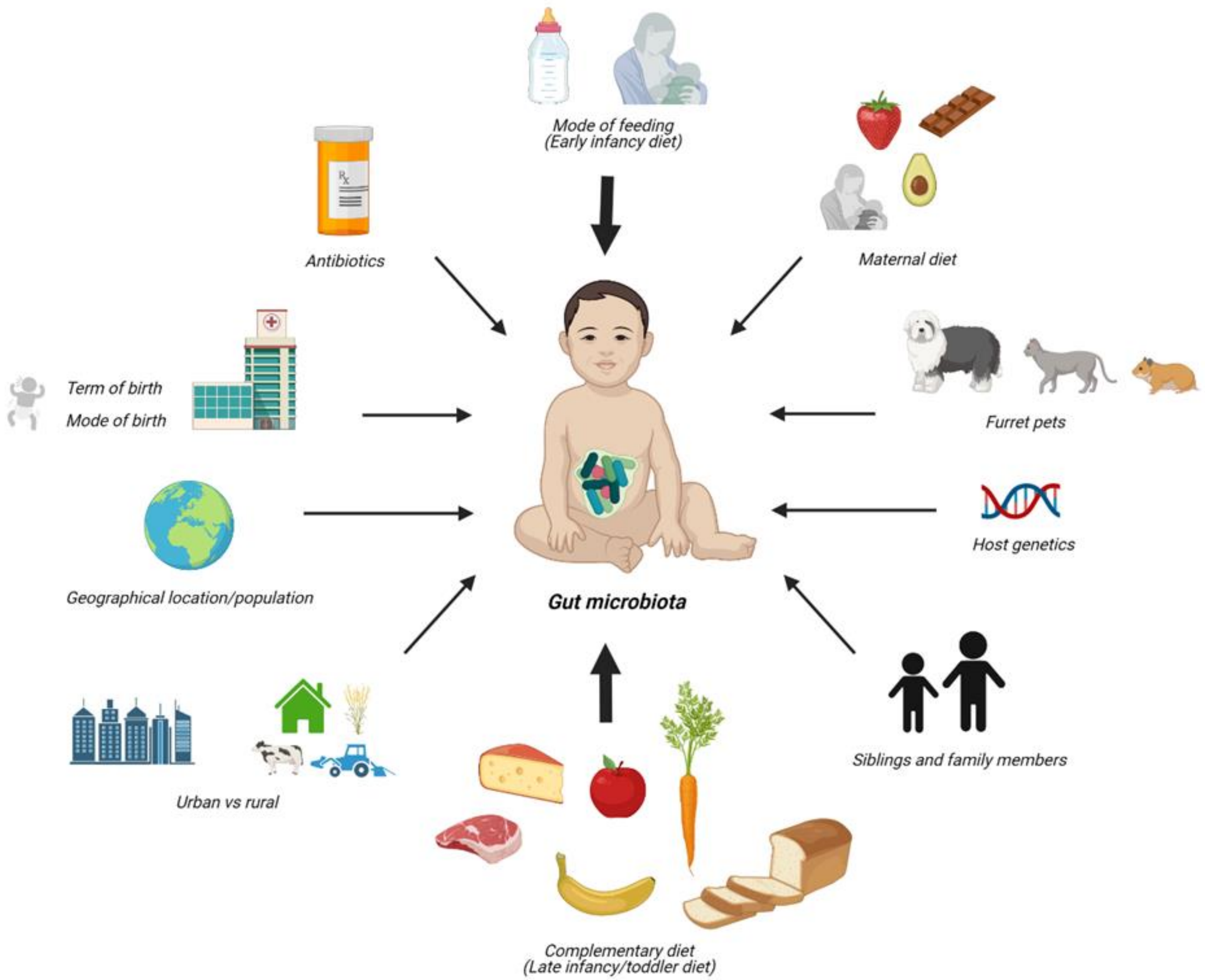
Yassour *et al.*, 2016 – SciTransMed

Tarm-mikrobiotaen udvikles sideløbende med immunsystemet og stofskiftet



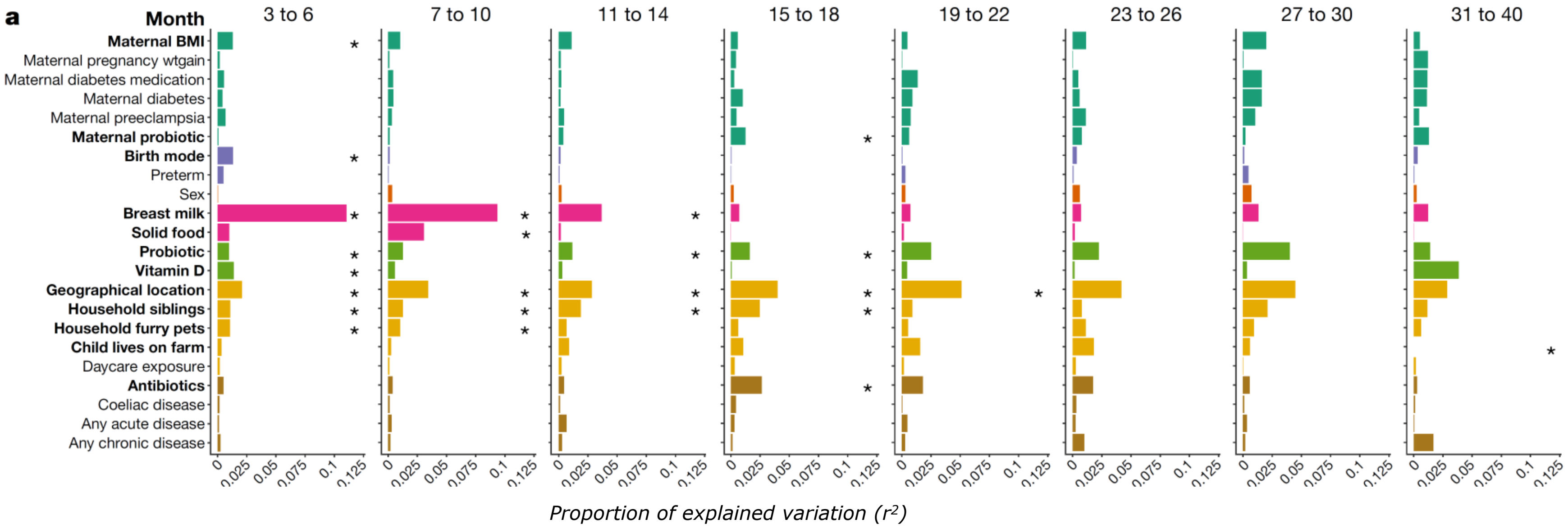
Jian et al., 2021 EBioMedicine

Faktorer der påvirker tarm-mikrobiotaens udvikling



Laursen *et al.*, 2021 – Annals of Nutrition and Metabolism

Amning påvirker i høj grad tarmmikrobiota i det tidlige liv

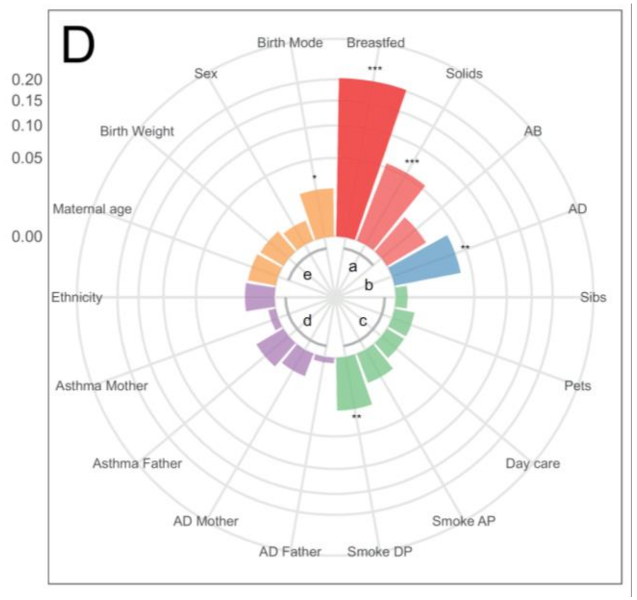


$N_{children}$ > 900

$N_{samples}$ > 11000

Steward *et al.*, 2018 - Nature

7 months af age

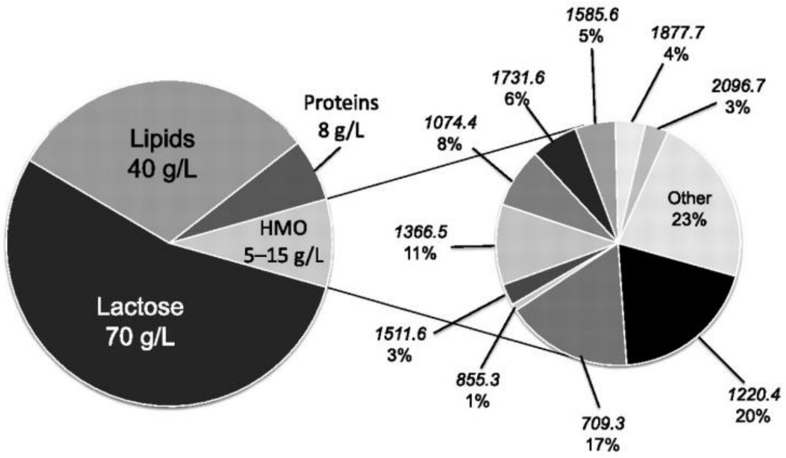


$N_{children}$ > 300

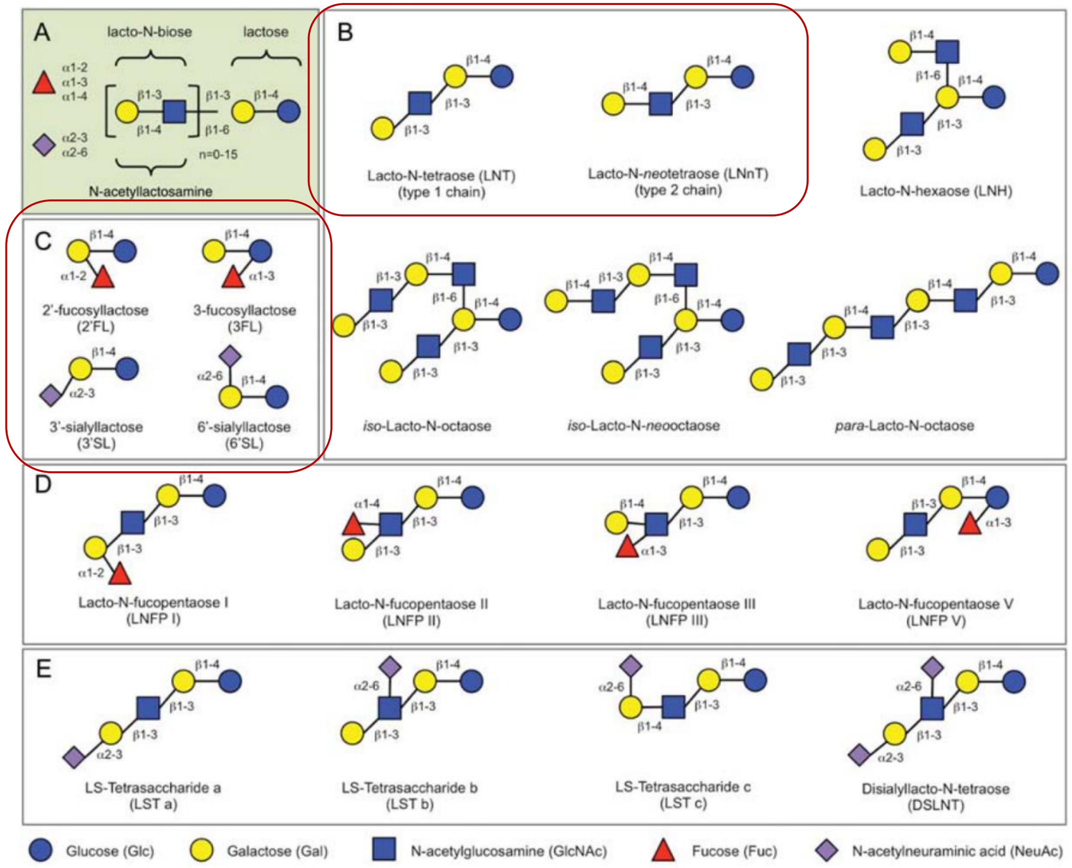
$N_{samples}$ > 900

Galazzo et al., 2020 - Gastroenterology

Modermælk indeholder HMO’er

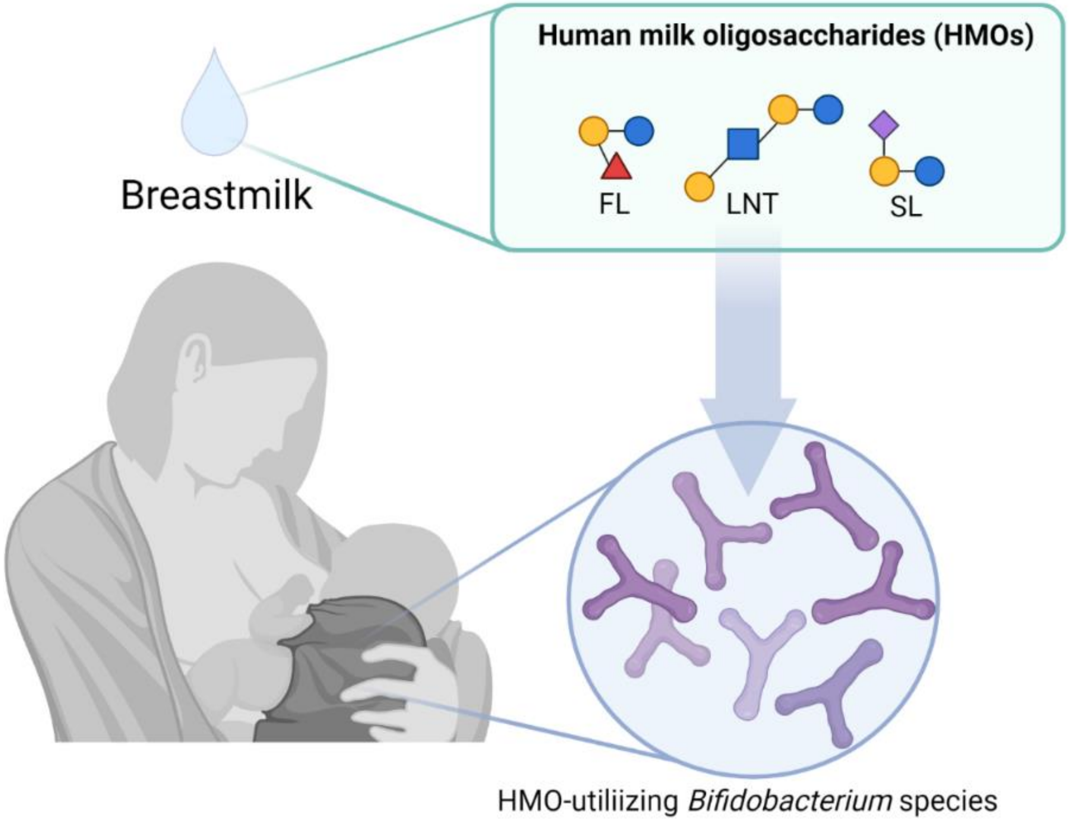


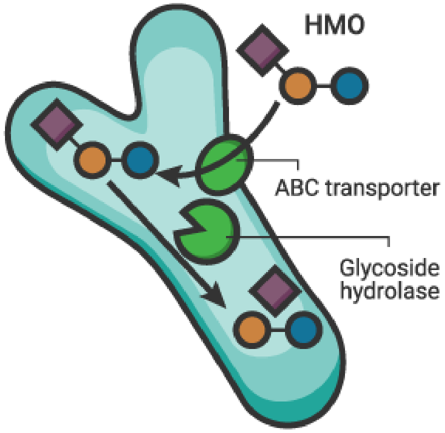
Zivkovic et al, 2010 PNAS

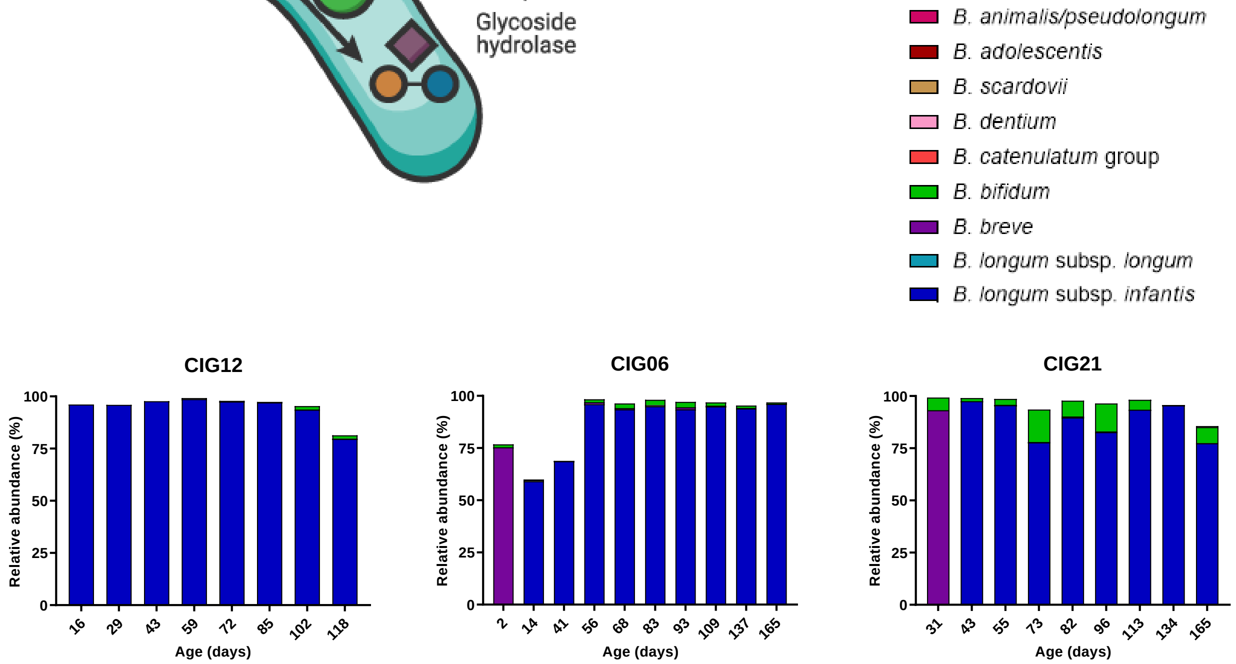


Bode L., 2012 - Glycobiology

Speficikke *Bifidobacterium* arter udnytter modermælkens indhold af HMO'er til at dominere mikrobiotaen i spædbarnets tarm







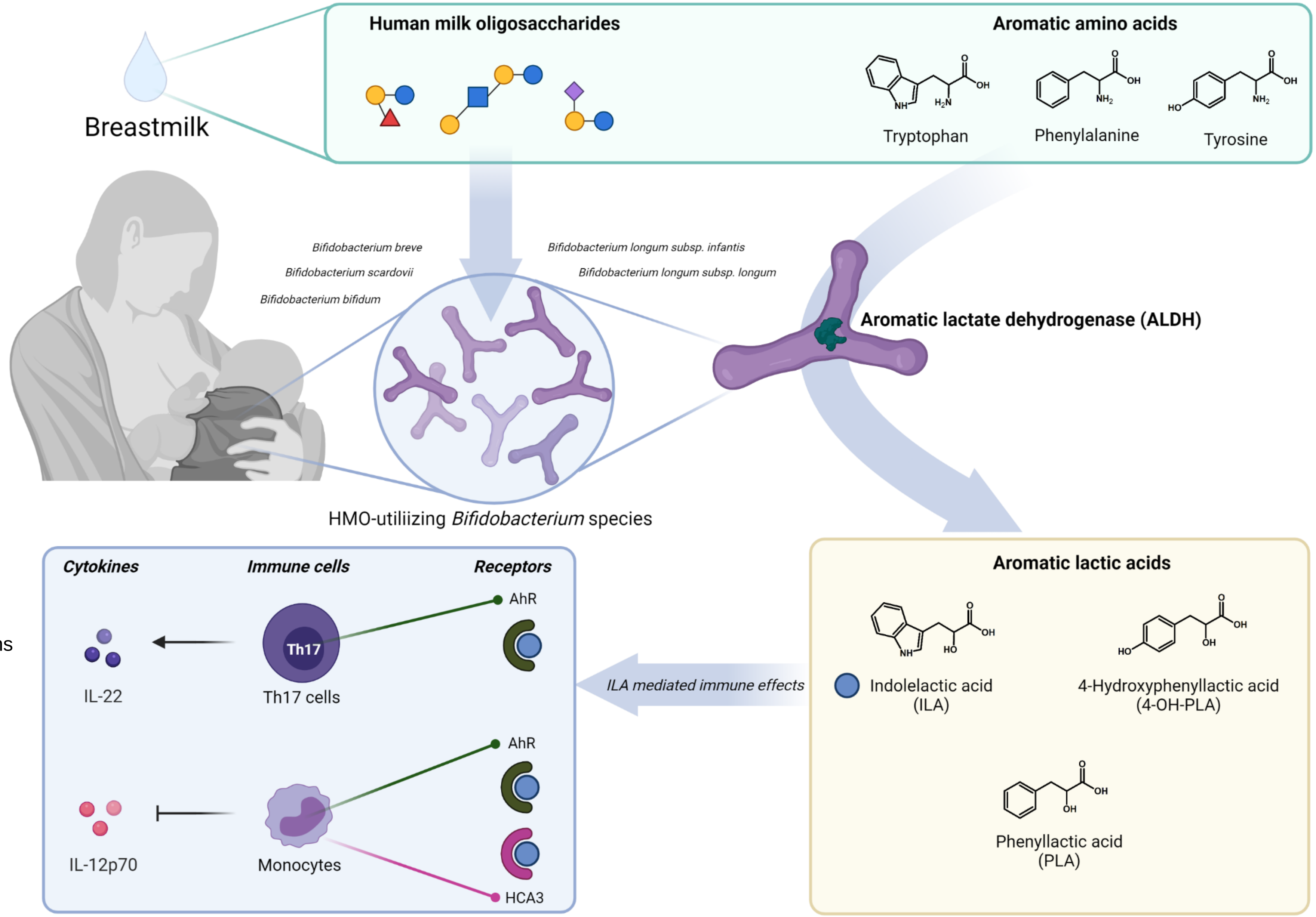
Laursen et al., 2021 – Nature Microbiology

Reduceret risiko for:

- Infektionssygdomme?
- At udvikle immun-relaterede sygdomme?
- At udvikle inflammatoriske tarmsygdomme?

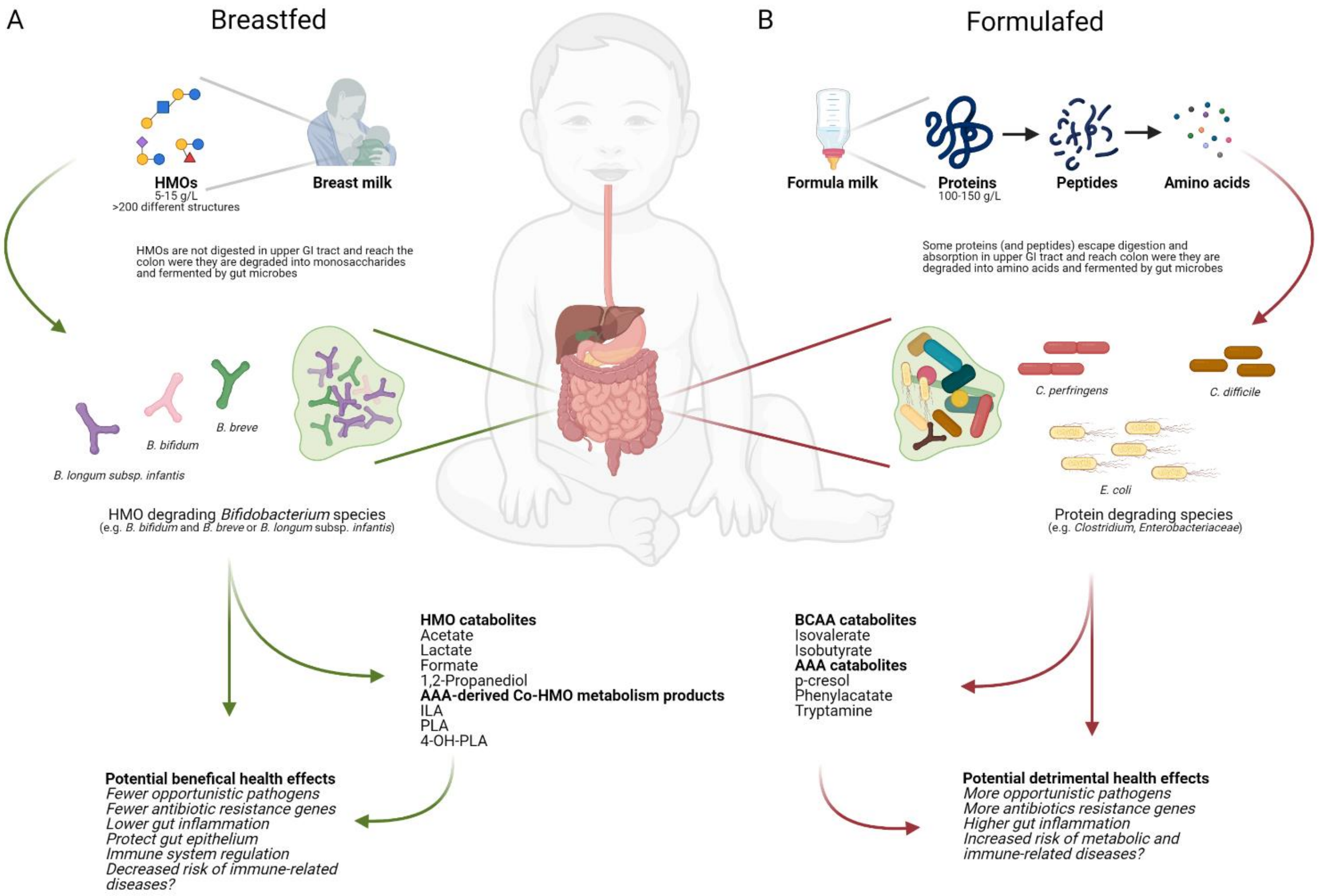
Cytokin som styrker tarmslimhindens forsvar imod patogener

Pro-inflammatorisk cytokin



Laursen et al., 2021 – Nature Microbiology

Amning og modermælkserstatning



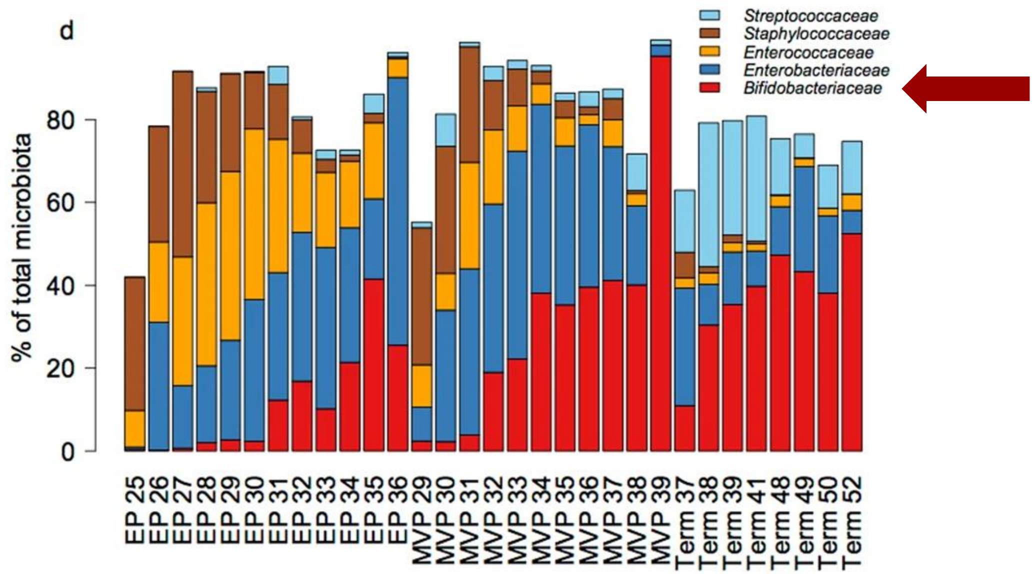
Laursen, 2021 – Annals of Nutrition and Metabolism

Modermælkserstatning tilsat FOS/GOS

Modermælkserstatning tilsat HMO'er

(2'FL, LNnT)

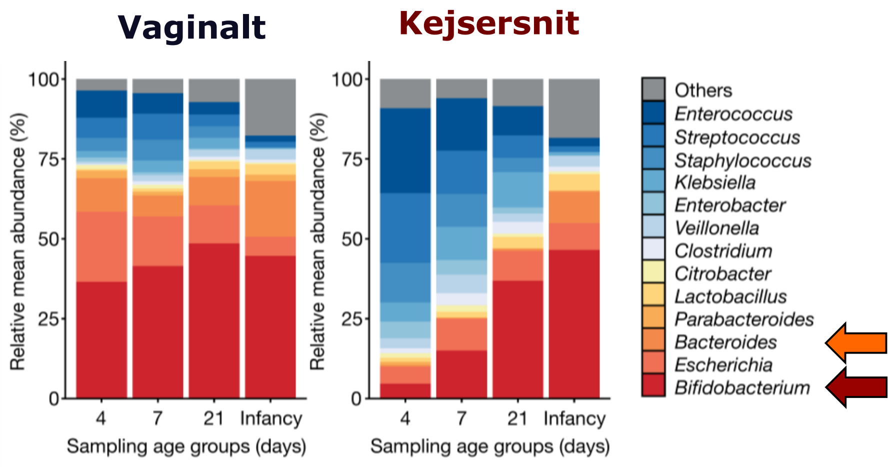
For tidlig fødsel og fødsel ved kejsersnit forsinker tarmmikrobiotamens udvikling (på trods af amning)

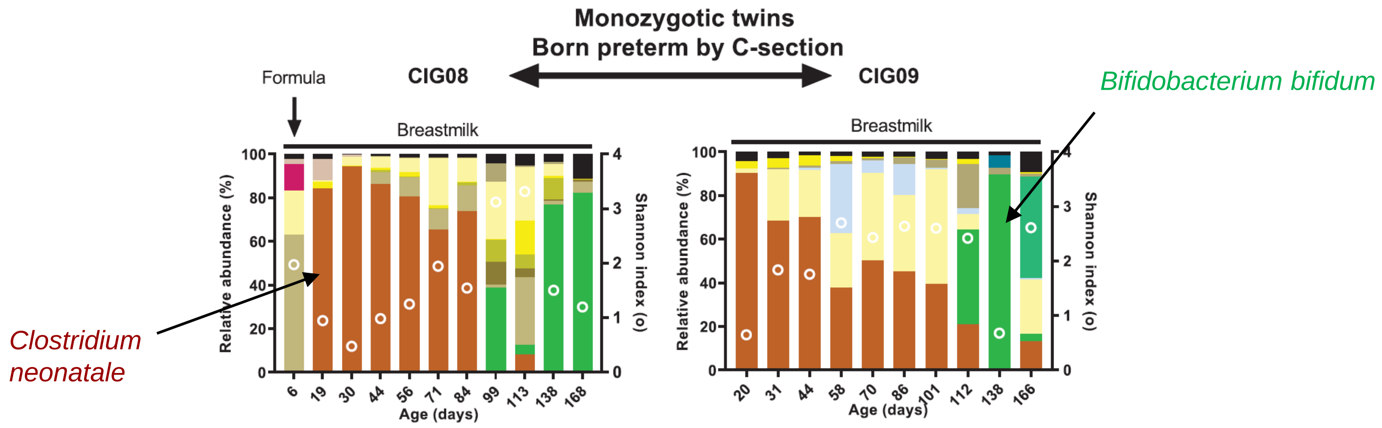


Korpela *et al.*, 2018 – Scientific Reports

EP = extremely premature

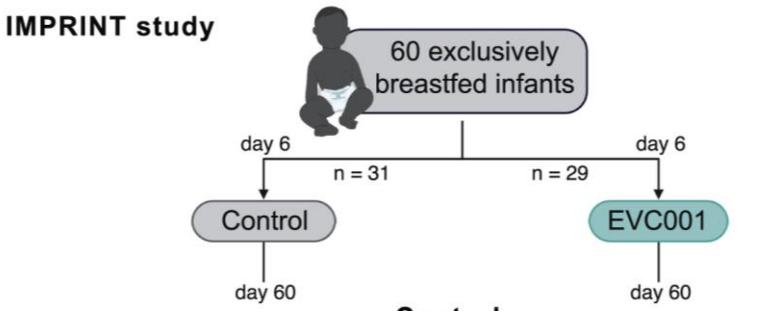
MVP = moderately or very premature

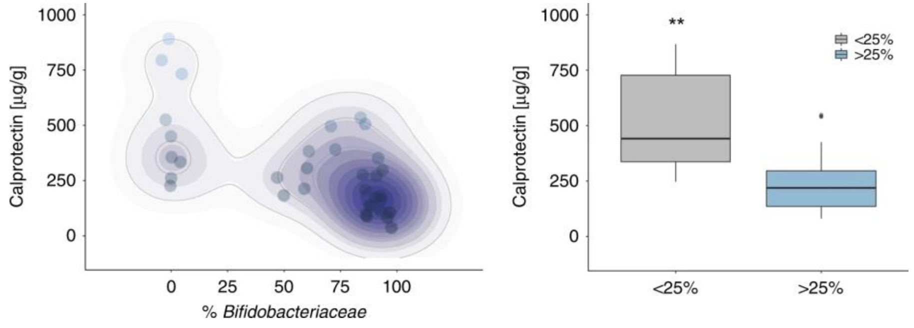




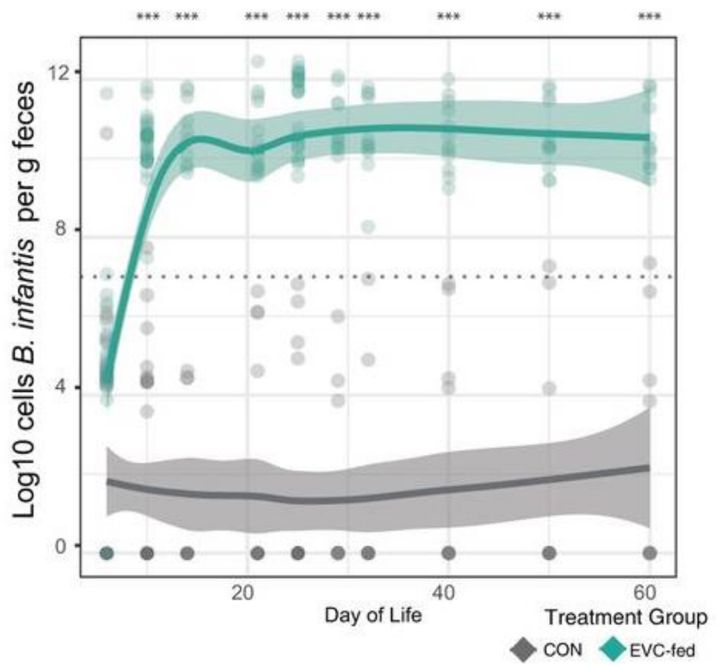
Laursen et al., 2021 – Nature Microbiology

B. infantis EVC001 intervention reducerer inflammation i tarmen og nedsætter mængden af cytokiner der spiller en rolle i allergi og autoimmunitet

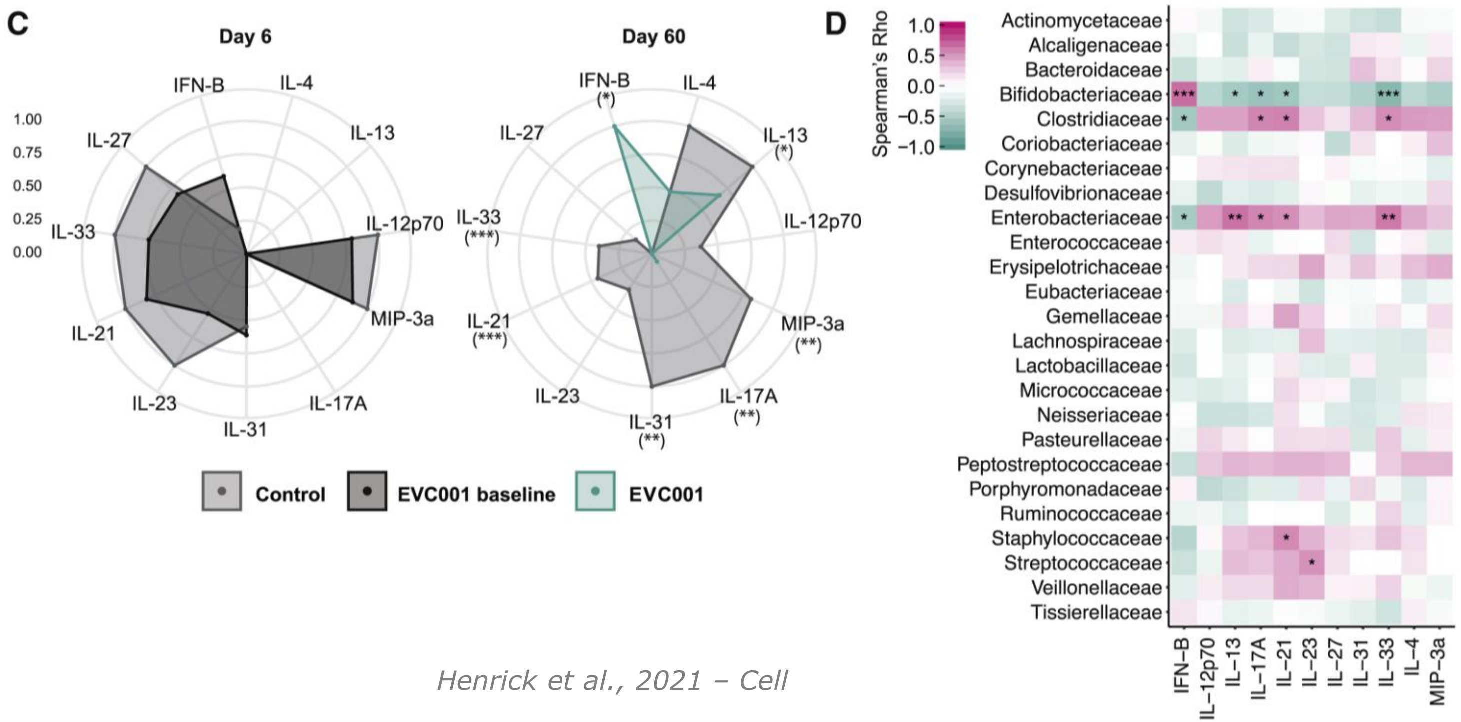




Henrick et al., 2019 – Pediatric Research



Frese et al., 2017 – mSphere

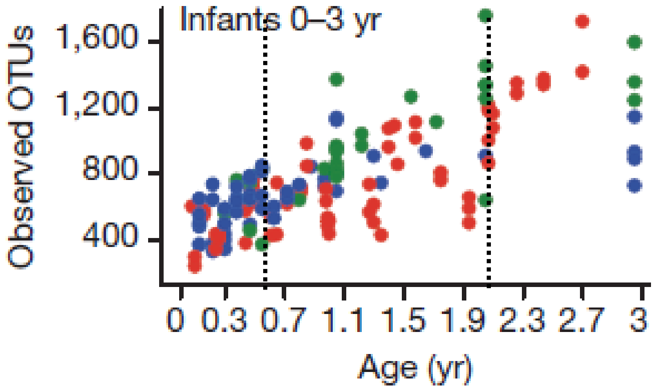


Henrick et al., 2021 – Cell

Overgangkost

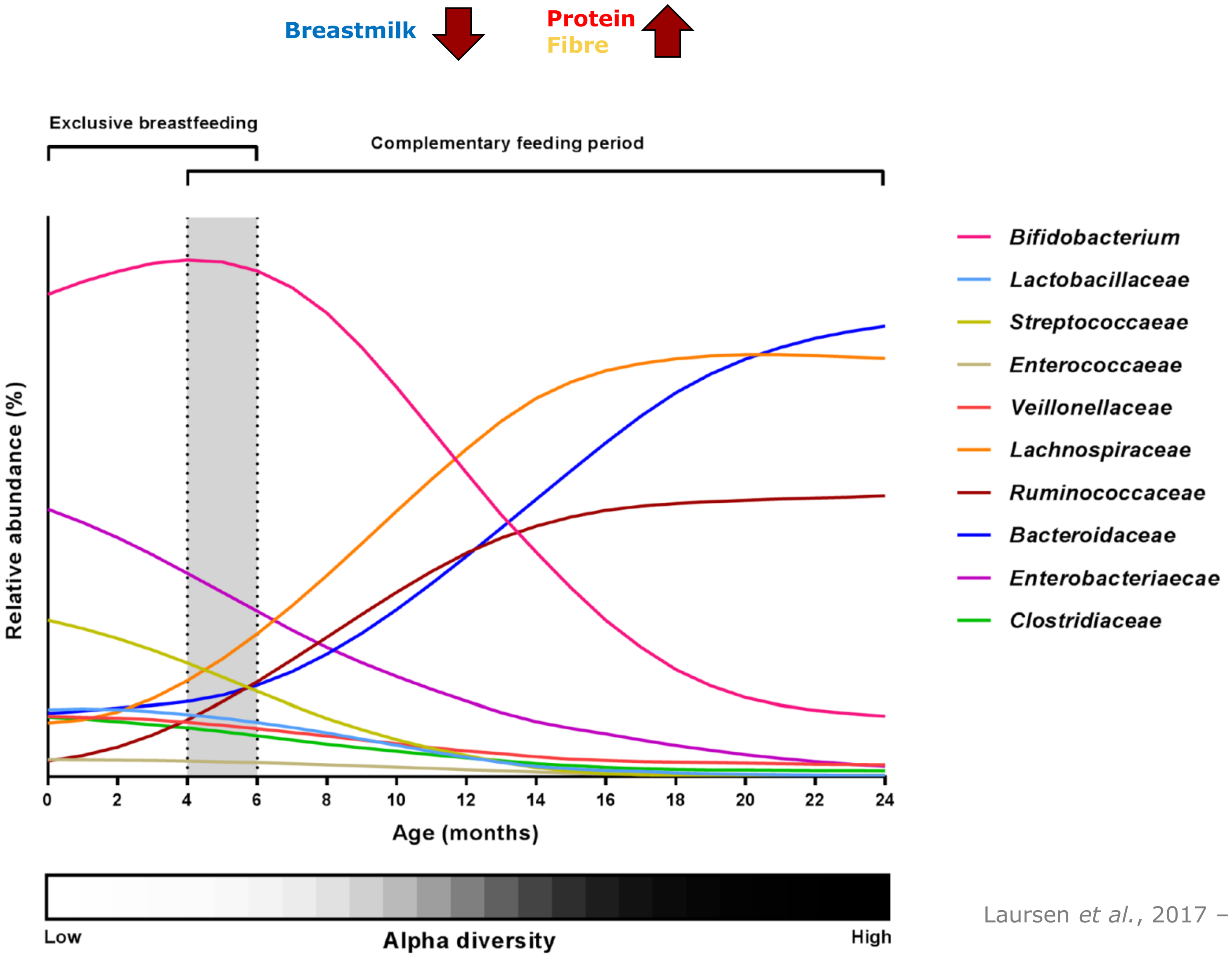
WHO

"Complementary feeding is defined as the process starting when breast milk alone is no longer sufficient to meet the nutritional requirements of infants, and therefore other foods and liquids are needed, along with breast milk. The transition from exclusive breastfeeding to family foods – referred to as complementary feeding – typically covers the period from ***6 - 24 months of age****…"*



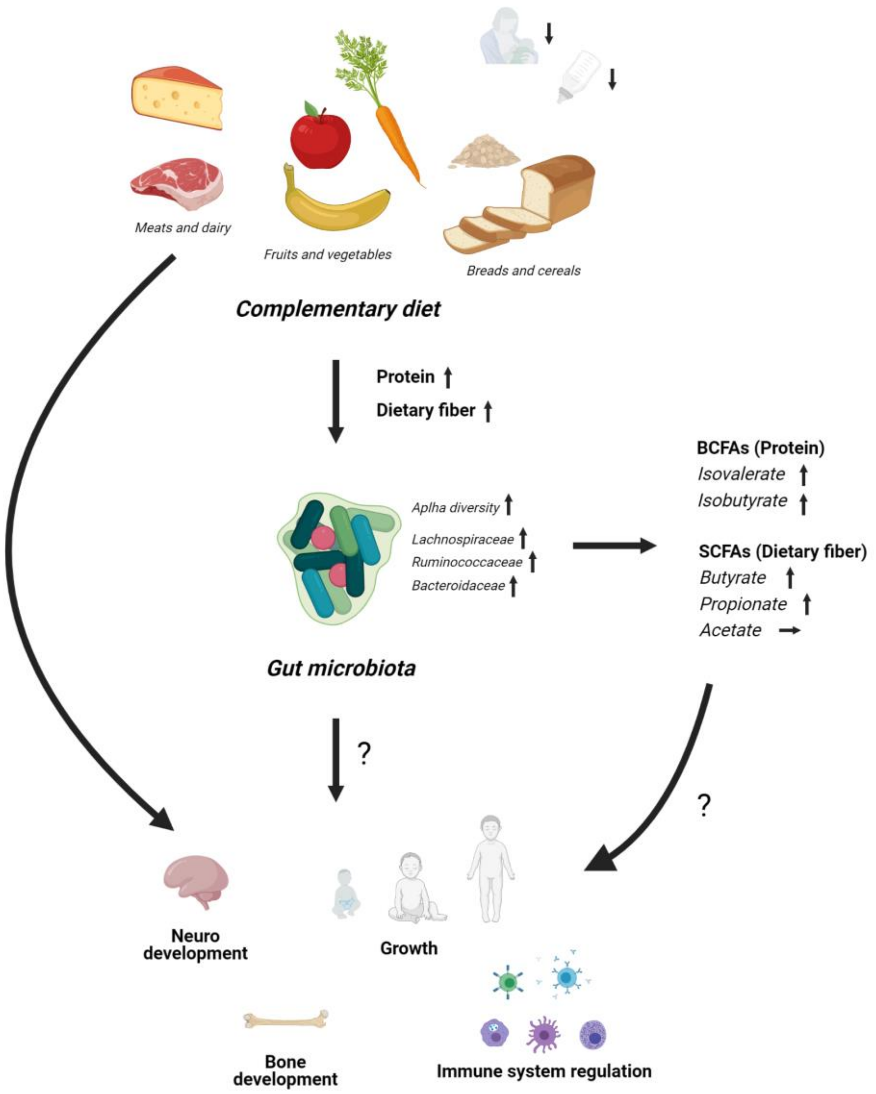
Yatsunenko *et al.*, 2012 - Nature

Overgangskosten ændrer på tarmmikrobiotaens sammensætning og giver øget diversitet



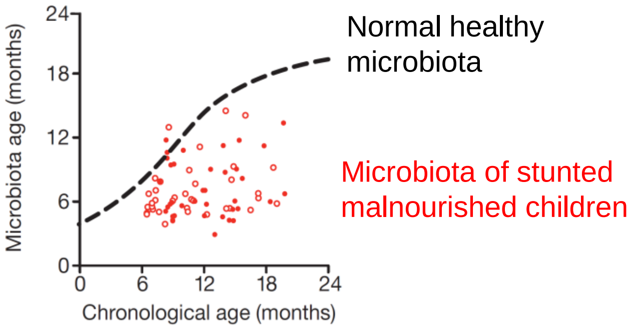
Laursen *et al.*, 2017 – *Frontiers in Microbiology*

Påvirker overgangskosten vækst of udvikling via tarmmikrobiotaen?



Laursen, 2021 – Annals of Nutrition and Metabolism

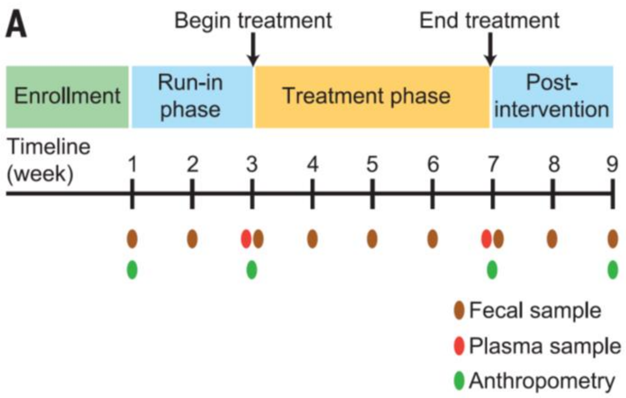
MDCF = ”microbiota directed complementary foods”



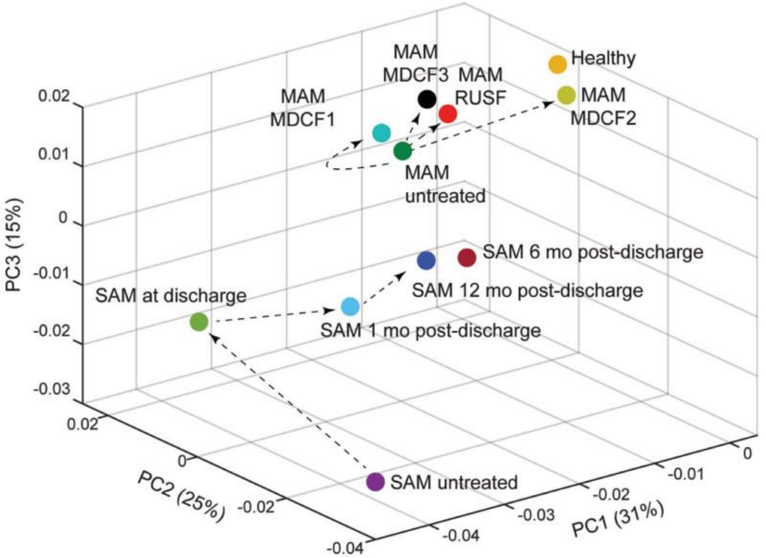
Subramanian *et al*,. 2014 - *Nature*

Component (g/100g)	RUSF	MDCF-1	MDCF-2	MDCF-3
Chickpea flour	–	8	10	30
Peanut flour	–	7	10	–
Soy flour	–	5	8	14
Raw banana	–	19	19	–
Rice	18.9	–	–	–
Lentil	21.5	–	–	–
Powdered skimmed milk	10.5	11.5	–	–
Sugar	17	24.3	29.9	30.9
Soybean oil	29	22	20	22
Micronutrient premix	3.14	3.1	3.14	3.1
Protein	10.2	12.4	11.8	13.9
Fat	29.5	22.8	20.8	24.1
Carbohydrate	31.8	18.6	16.3	22
Fiber	4.7	3.3	4.5	5.6
Protein energy ratio (PER)	8.3	11.9	11.6	11.7
Fat energy ratio (FER)	53.6	49.3	46.2	45.7
Total calories per 100g	494.6	416.1	406.8	475.8

Gehrig *et al*,. 2019 - *Science*



Gehrig *et al*,. 2019 - *Science*



Raman *et al*,. 2019 - *Science*

3 mrd kostintervention med MDCF-2 forbedrer underernærede børns (12-18m) vækst sammenlignet med standard behandling (RUSF)

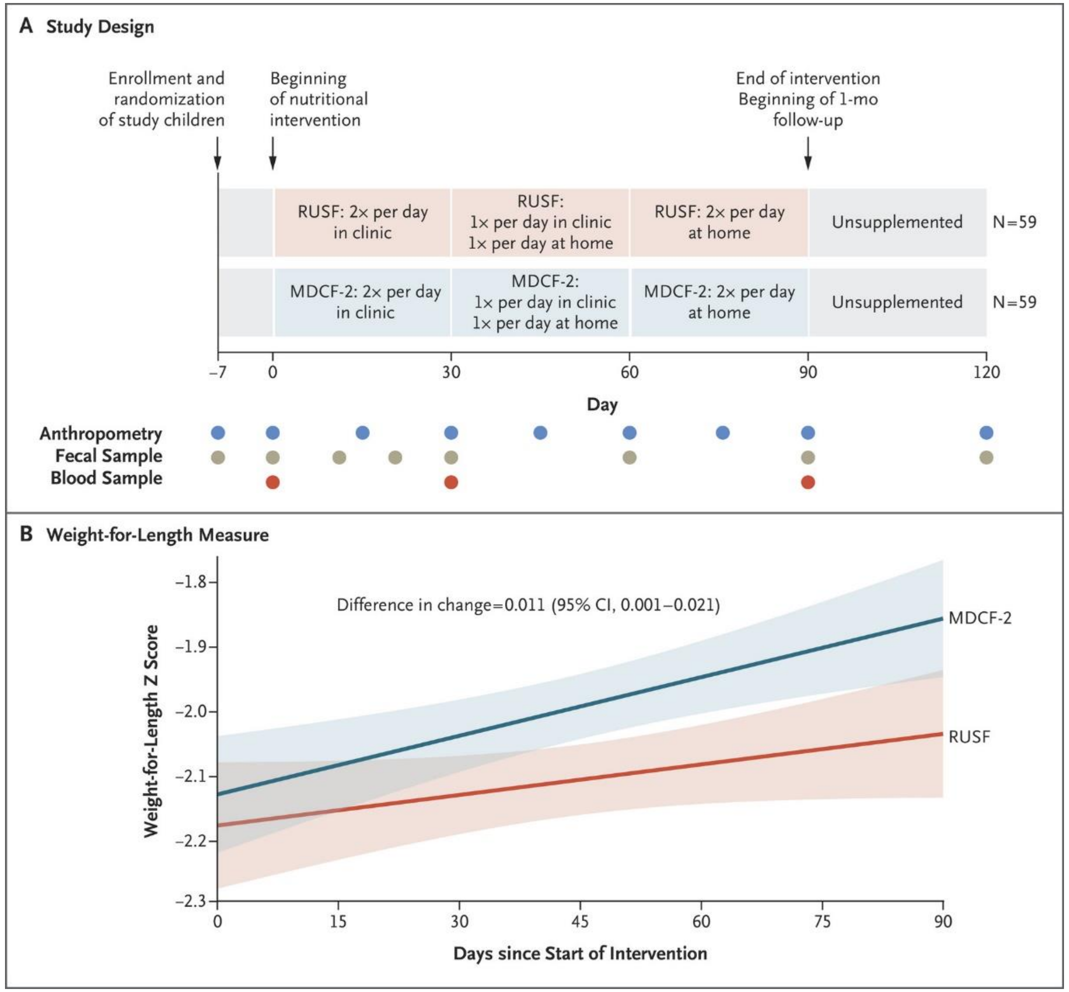


Table 2. Clinical Response to MDCF-2 or RUSF Supplementation.*

Anthropometric Feature	MDCF-2 (N=59)	RUSF (N=59)	Difference (95% CI)†
At baseline			
Weight-for-length z score	−2.22±0.39	−2.29±0.36	0.086 (−0.056 to 0.228)
Weight-for-age z score	−2.66±0.67	−2.71±0.64	0.036 (−0.213 to 0.285)
Length-for-age z score	−2.14±1.14	−2.13±1.13	−0.044 (−0.467 to 0.380)
MUAC — cm	12.8±0.51	12.7±0.44	0.077 (−0.100 to 0.254)
Mean rate of growth per week during 3-mo treatment (95% CI)‡			
Weight-for-length z score	0.021 (0.014 to 0.029)	0.010 (0.003 to 0.017)	0.011 (0.001 to 0.021)
Weight-for-age z score	0.017 (0.012 to 0.022)	0.010 (0.004 to 0.015)	0.008 (0.001 to 0.015)
Length-for-age z score	0.004 (0.002 to 0.007)	0.005 (0.003 to 0.008)	−0.001 (−0.005 to 0.003)
MUAC — cm	0.031 (0.029 to 0.034)	0.029 (0.025 to 0.032)	0.003 (−0.001 to 0.007)
Mean rate of growth per week during treatment plus 1-mo follow-up (95% CI)‡			
Weight-for-length z score	0.010 (0.005 to 0.016)	0.000 (−0.005 to 0.006)	0.010 (0.002 to 0.018)
Weight-for-age z score	0.009 (0.005 to 0.013)	0.001 (−0.003 to 0.005)	0.008 (0.002 to 0.013)
Length-for-age z score	0.004 (0.002 to 0.006)	0.003 (0.001 to 0.006)	0.000 (−0.003 to 0.003)
MUAC — cm	0.028 (0.026 to 0.031)	0.024 (0.022 to 0.027)	0.004 (0.000 to 0.007)

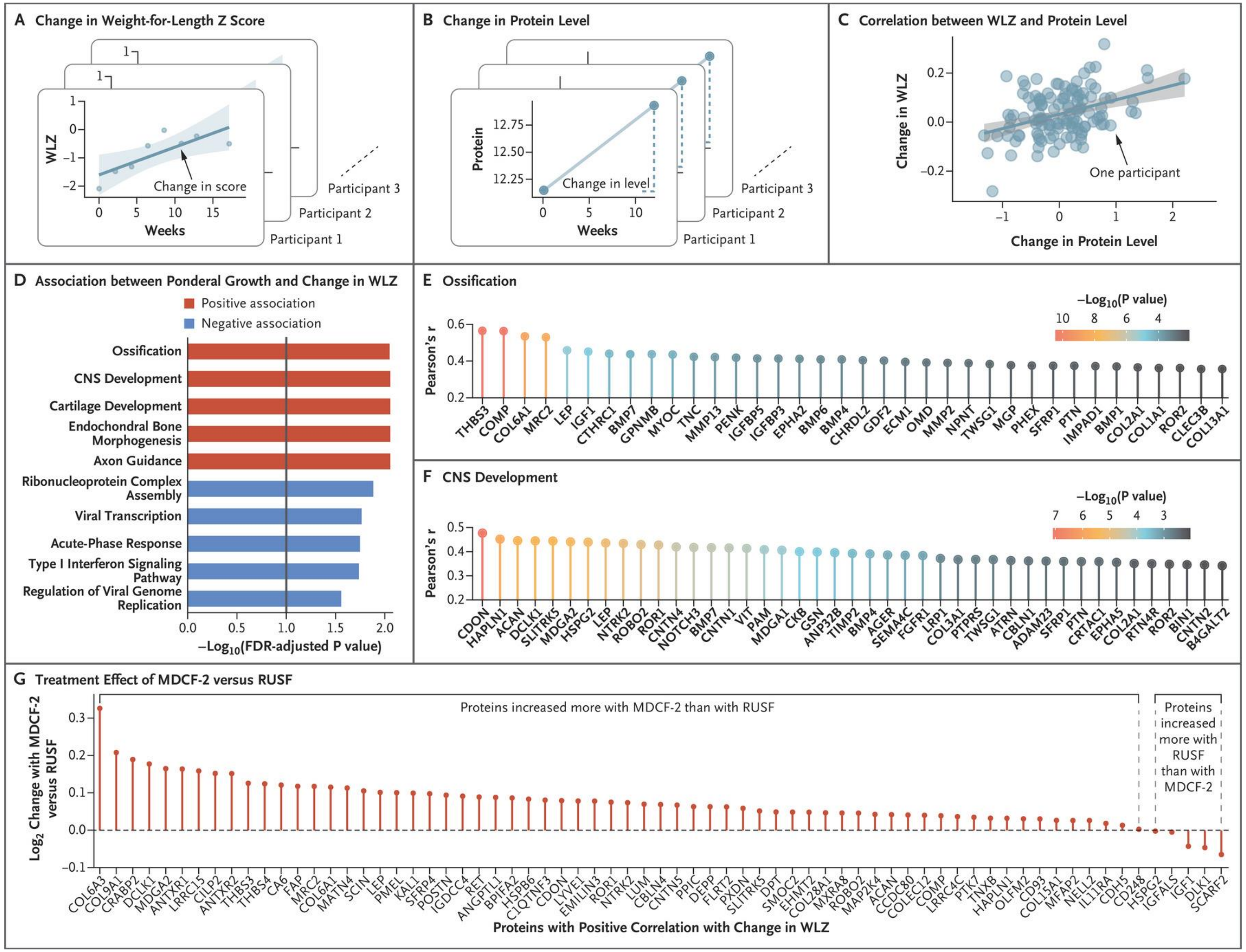
* Plus–minus values are means ±SD. MUAC denotes mid–upper-arm circumference.

† Values for the between-group difference at baseline were derived from a linear model predicting anthropometric features at the start of treatment as a function of treatment group after adjustment for age, sex, and any illness within 7 days before treatment initiation. Values for the between-group difference in the growth rate per week during the 3-month treatment period and during treatment plus 1-month follow-up were derived from a mixed-effects linear model predicting anthropometric features as a function of the interaction between treatment group and the number of weeks since the initiation of nutritional supplementation after adjustment for the baseline variables plus the number of weeks of treatment, the treatment group, and a random intercept for each participant to account for the within-participant correlation. Positive values indicate a faster growth rate in children receiving MDCF-2.

‡ Values for the rate of growth per week during the treatment period and during treatment plus follow-up were derived from a mixed-effects linear model. This model predicts anthropometric features as a function of the number of weeks since the initiation of nutritional supplementation after adjustment for the baseline variables plus a random intercept for each participant to account for the within-participant correlation.

Chen et al., 2021 – New England Journal of Medicine

Forbedret vækst kobles til højere niveauer af proteiner i blodet, som er vigtige for knogle og central nervesystemets udvikling



Chen et al., 2021 – New England Journal of Medicine

Opsummering

- Barnets tarmmikrobiota gennemgår en drastisk udvikling i de første leveår, sideløbende med at vores immunsystem og stofskifte udvikles

- Udviklingen af barnets tarmmikrobiota påvirkes af en lang række faktorer
  - Fødsel ved kejsersnit og for tidlig fødsel forsinker udviklingen
  - Amning og passende overgangskost (fx. kostfibre) er vigtige for en sund udvikling

- Amning og etablering af HMO-nedbrydende *Bifidobacterium* arter i den tidlige spædbarndom beskytter imod inflammation og påvirker immunsystemet i en gavnlig retning i forhold til tolerance

- Underernærede børn har en umoden tarmmikrobiota som kan modnes med rationelt designet overgangskost, hvilket også forbedre vækst og markører for knoglevækst og centralnervesystemets udvikling.