

IMMUNE IMPRINTING — LATEST EVIDENCE AND CLINICAL IMPLICATIONS

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IMPERIAL

**THE EFFECT OF INFECTIONS
ON SUSCEPTIBILITY TO AUTOIMMUNE
AND ALLERGIC DISEASES**

JEAN-FRANÇOIS BACH, M.D., D.Sc.

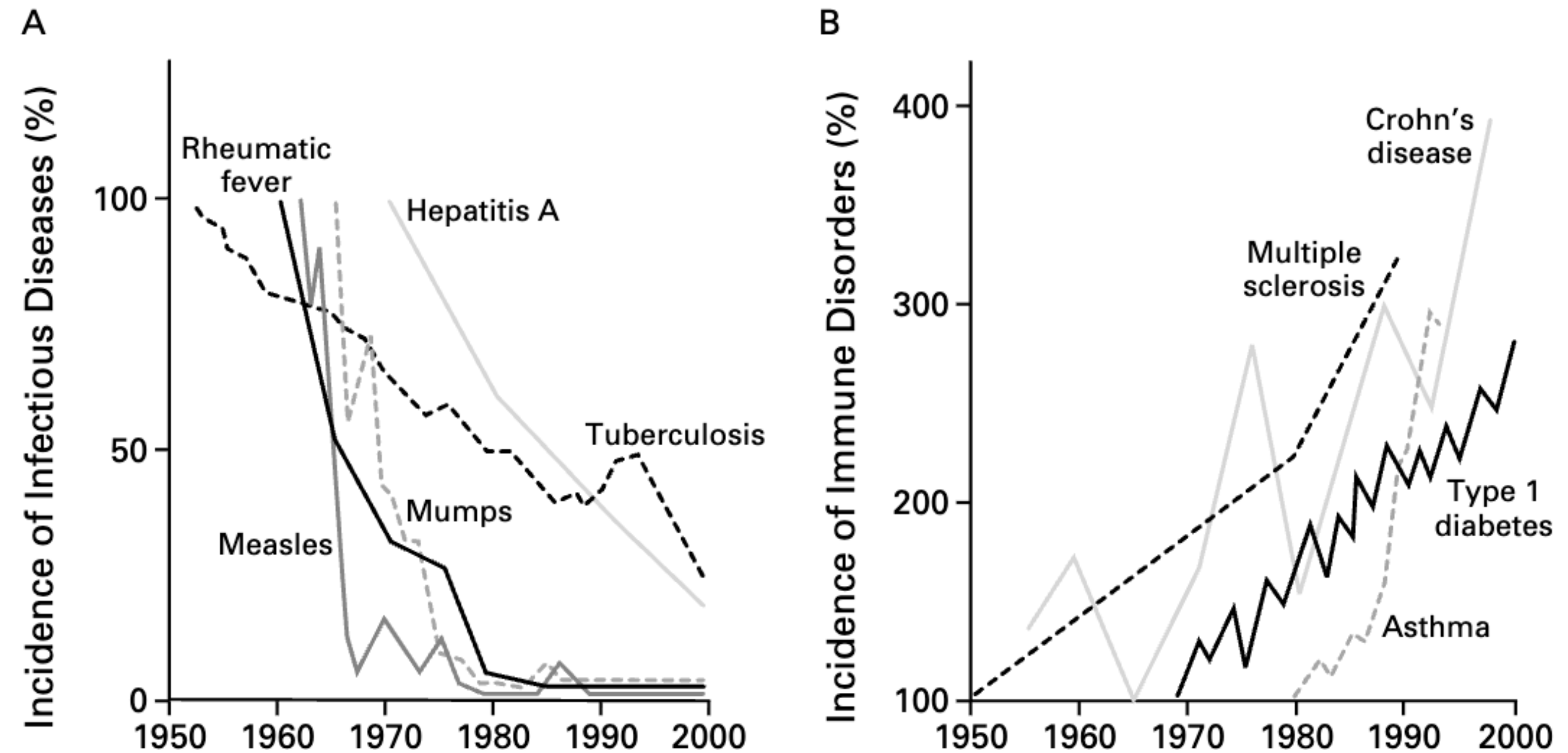


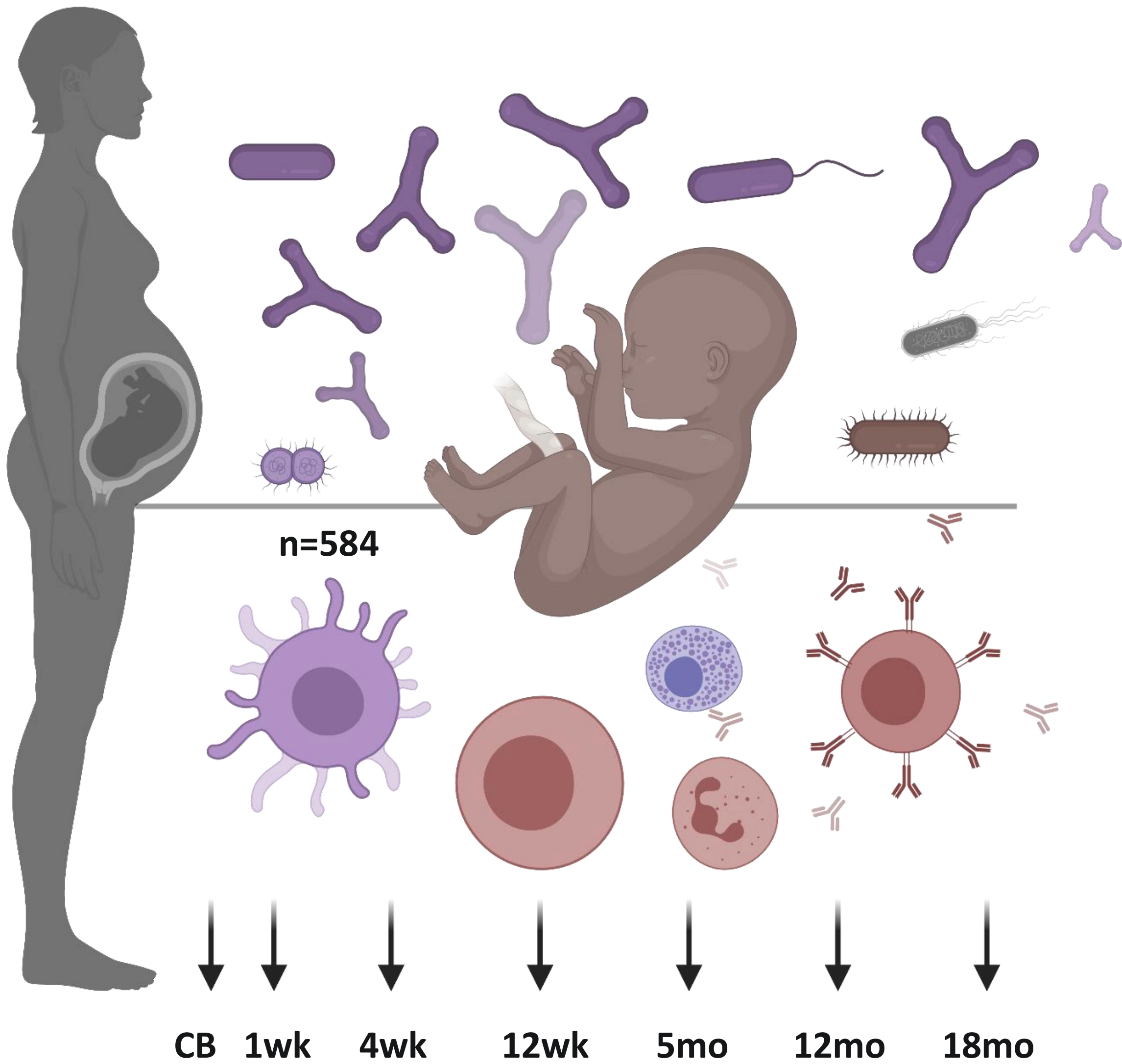
Figure 1. Inverse Relation between the Incidence of Prototypical Infectious Diseases (Panel A) and the Incidence of Immune Disorders (Panel B) from 1950 to 2000.



WHAT IS HEALTHY IMMUNE DEVELOPMENT IN HUMANS?

└ **LIMITED INFLAMMATORY RESPONSES
TO COLONIZING MICROBES**

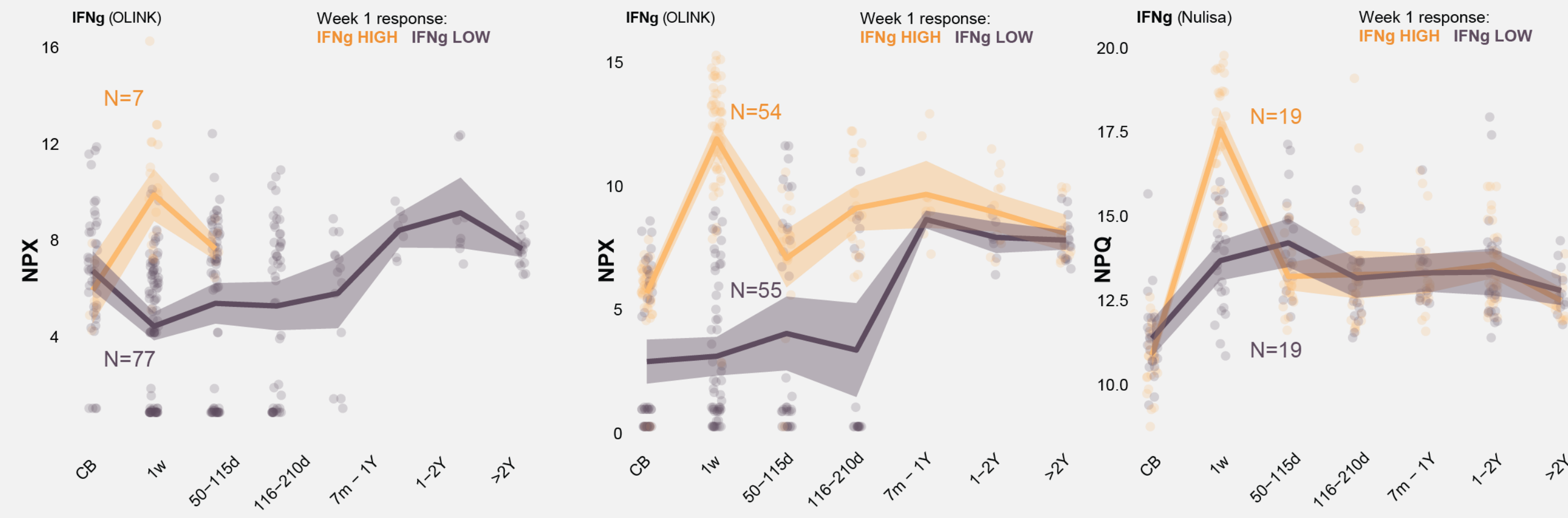
BORN IMMUNE COHORT (2016-)



Olin, et al, Cell, 2018
Pou et al, Nature Medicine, 2019
Henrick et al, Cell, 2021
Olin et al, Allergy, 2022
Brodin P, Science, 2022



SYSTEMIC CYTOKINE RESPONSES AFTER BIRTH



$N_{\text{term}}=150, N_{\text{preterm}}=84$

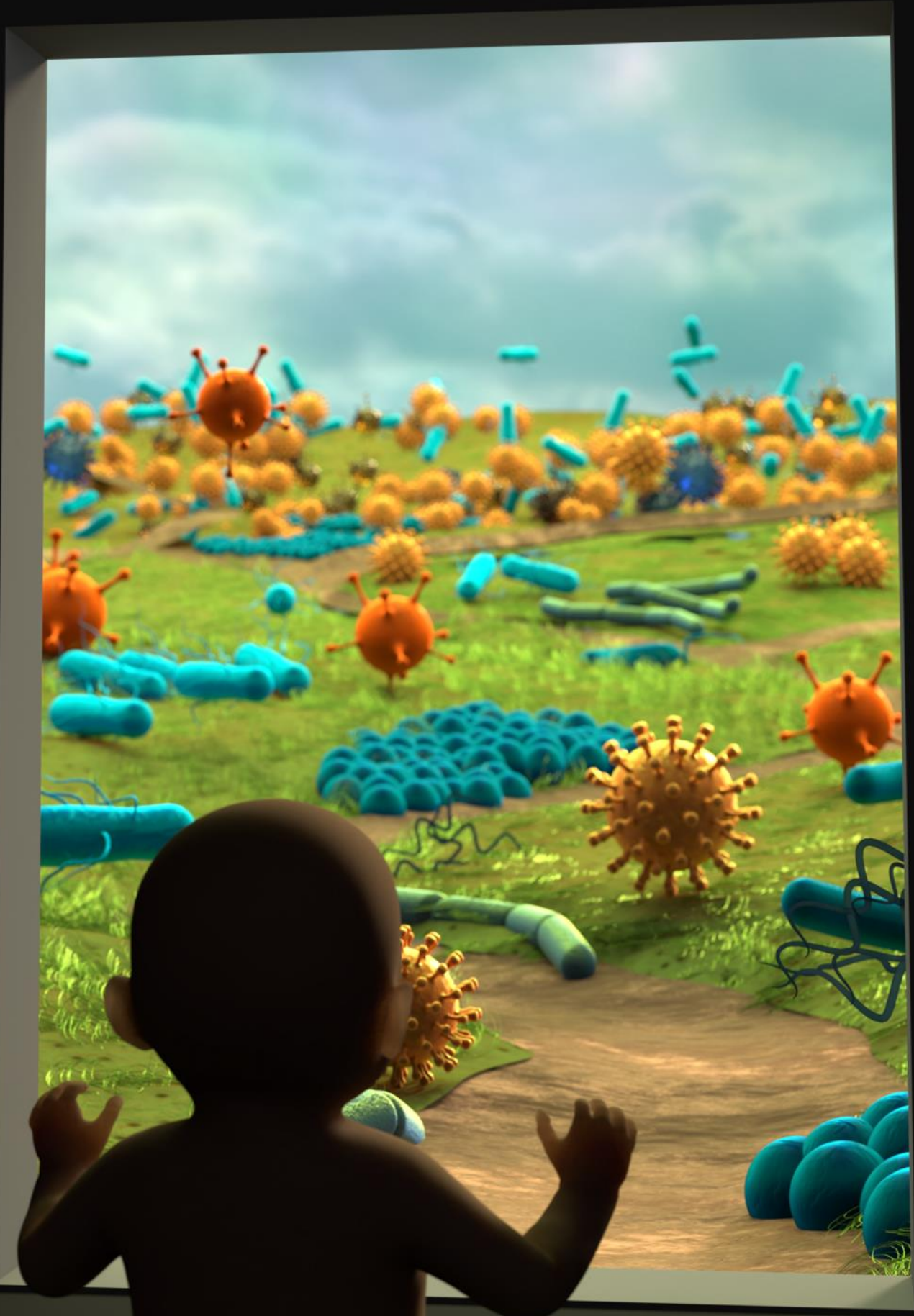
2200 blood samples (100μL/sample)

384 plasma proteins

“A SEEDING REACTION”

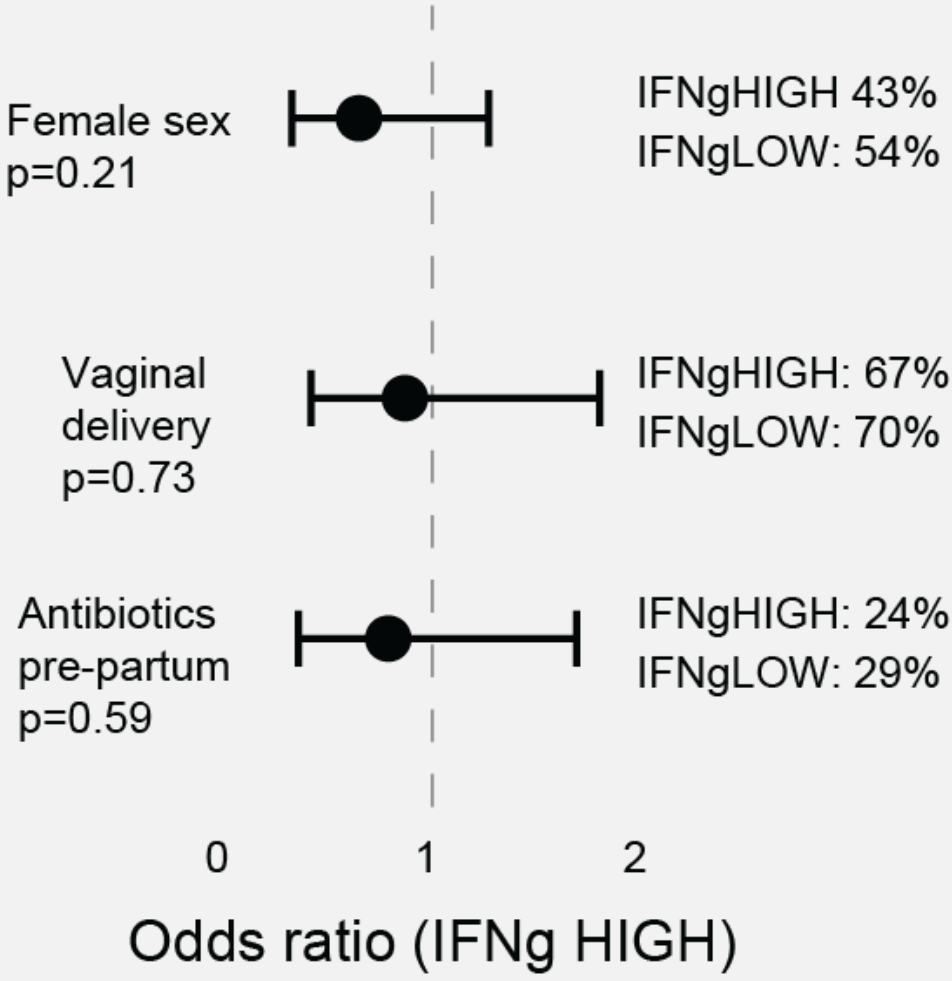
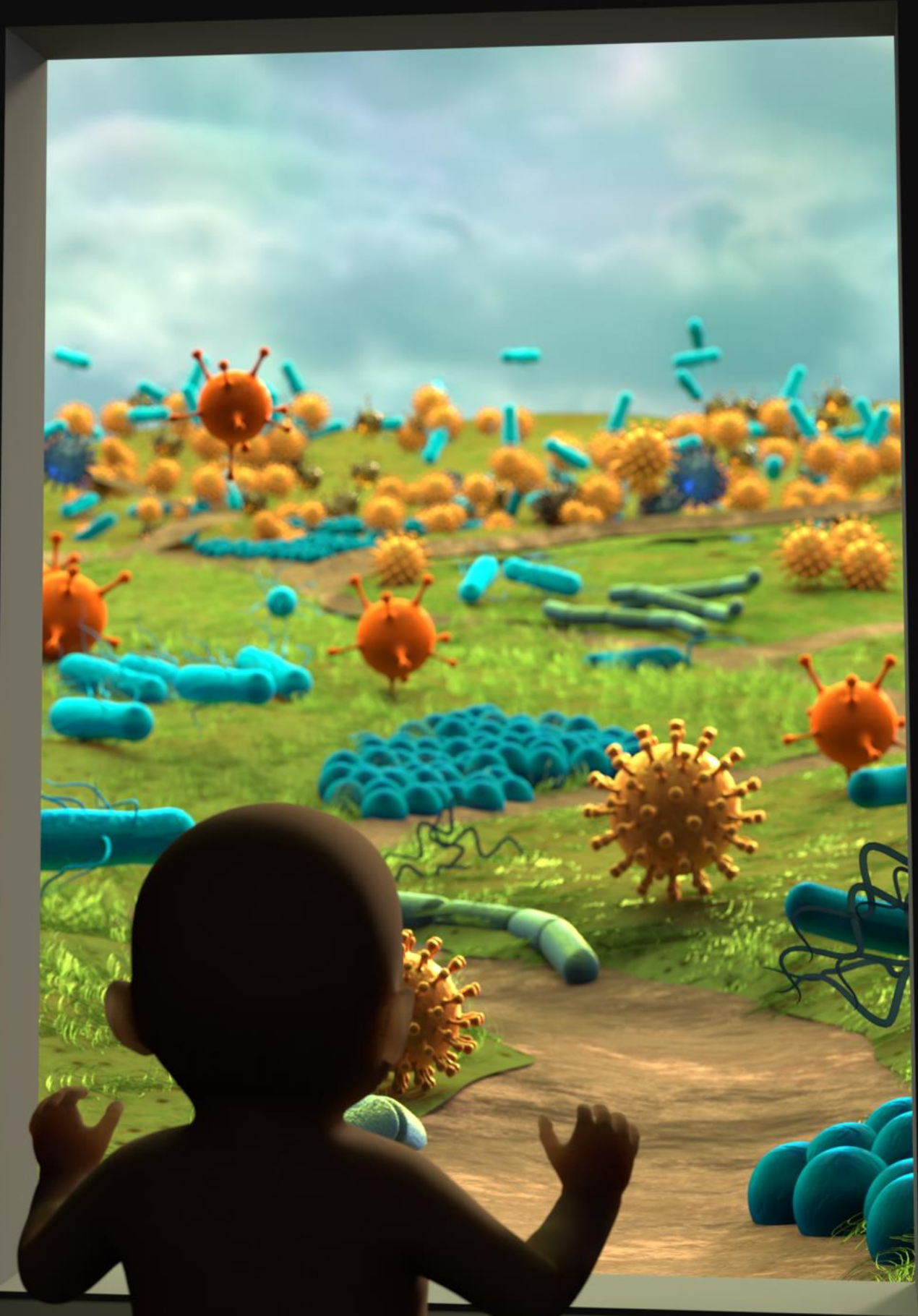


Aron Arzoomand M.D, PhD-student



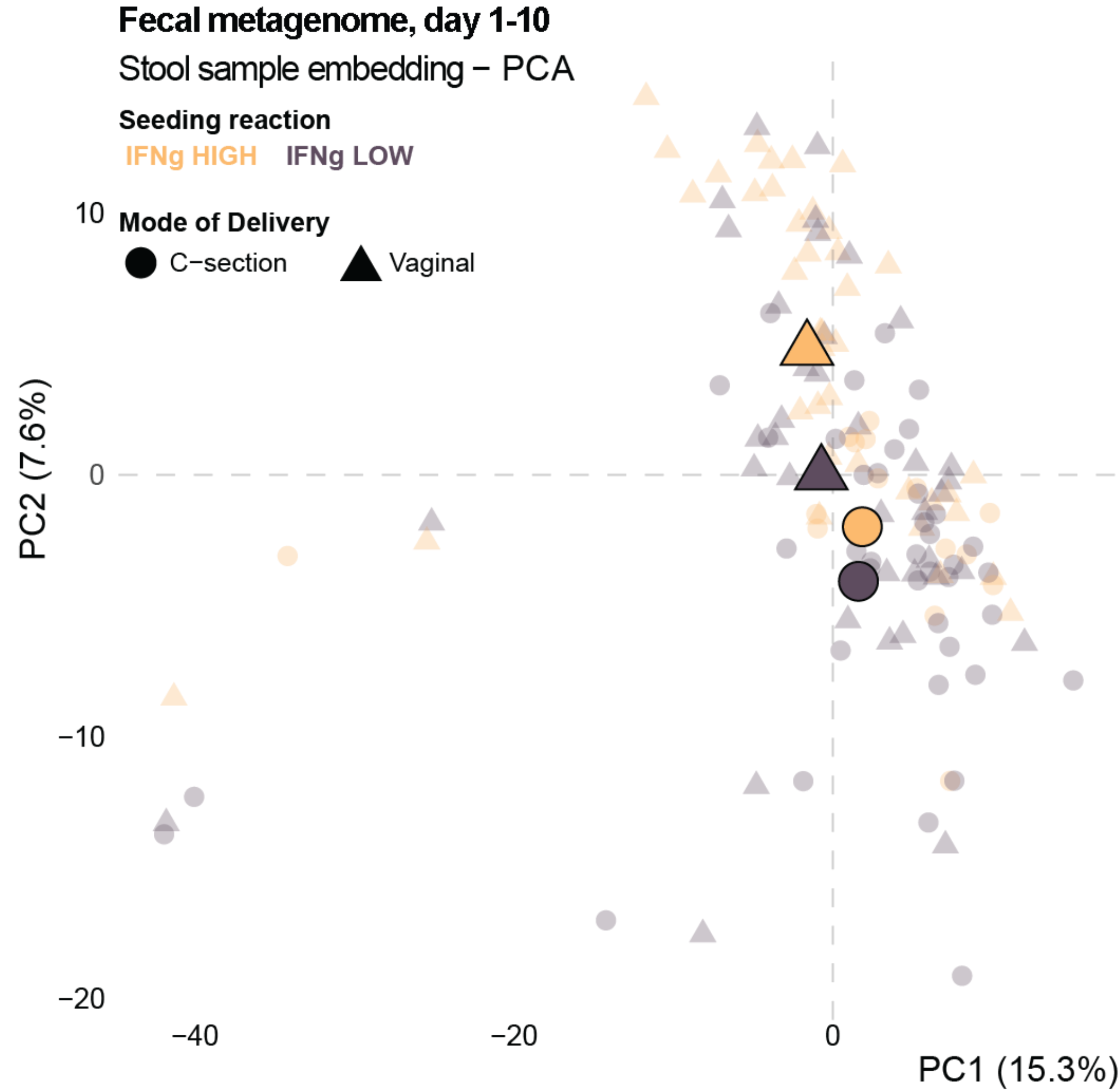
DETERMINANTS OF STRONG SEEDING REACTIONS

Metadata & Seeding reactions

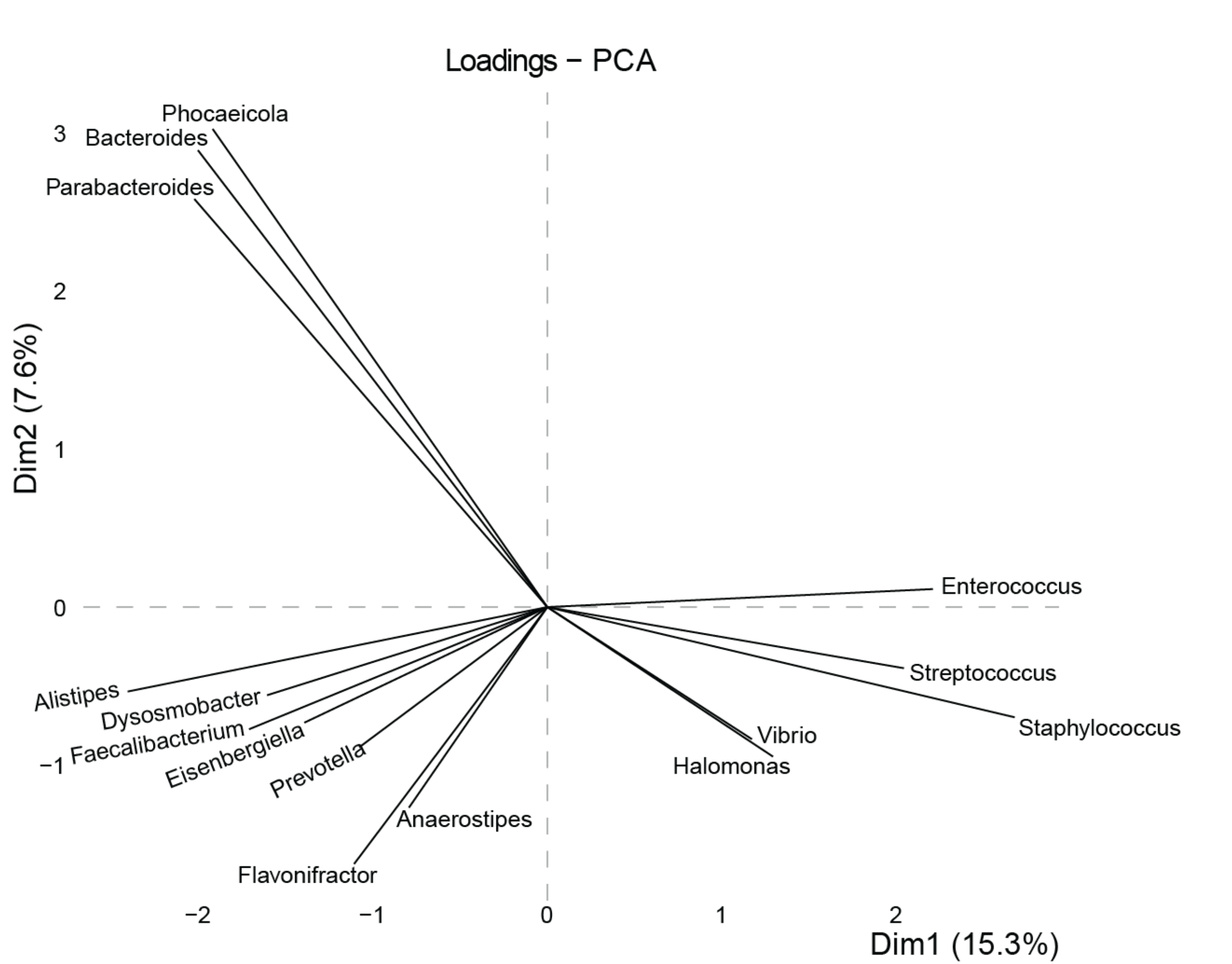


PIONEER MICROBES CORRELATE WITH VARIABLE SEEDING REACTIONS

A



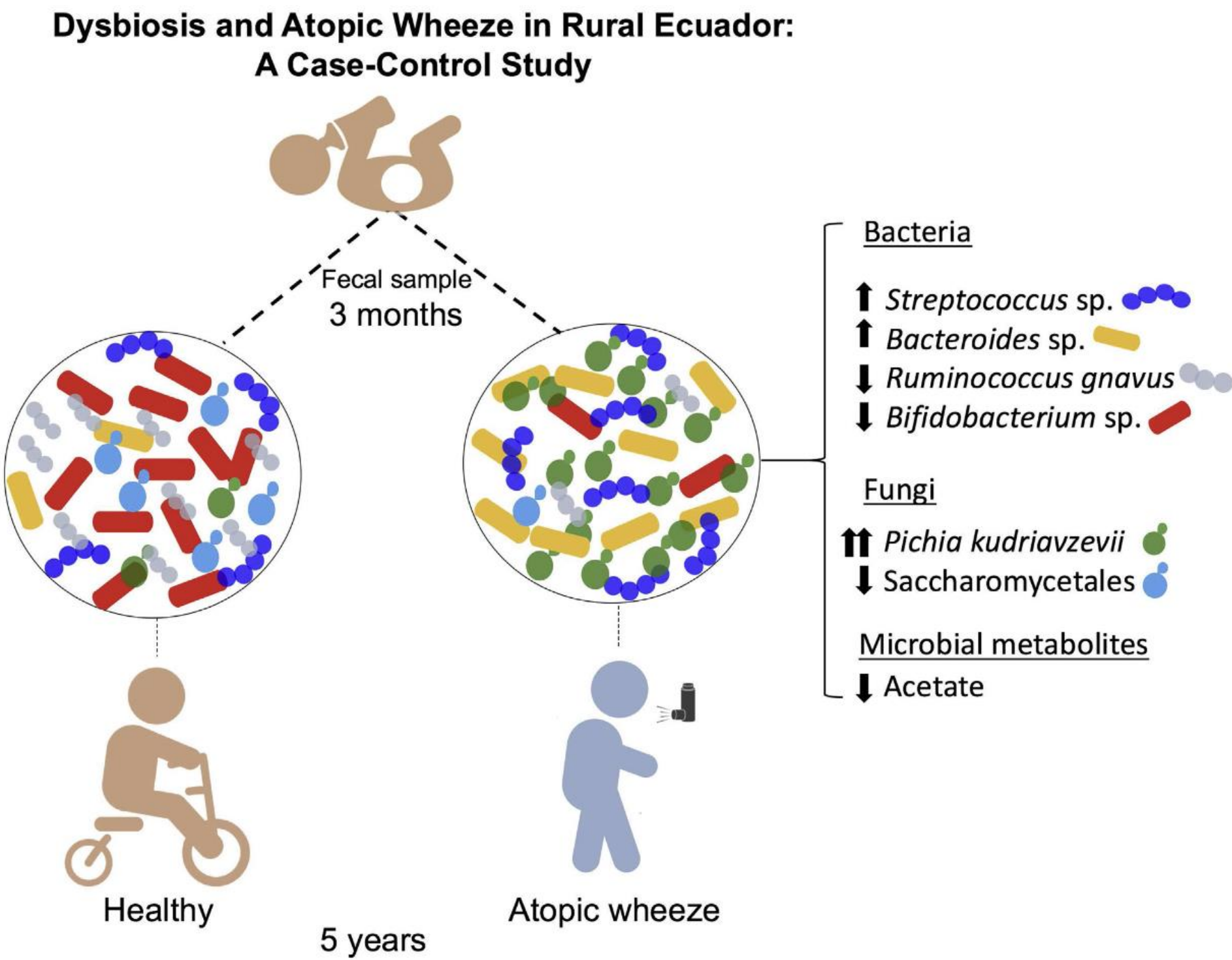
B



INDIVIDUAL MICROBES AND THEIR ASSOCIATIONS WITH DISEASE

Associations between infant fungal and bacterial dysbiosis and childhood atopic wheeze in a nonindustrialized setting

Marie-Claire Arrieta, PhD,^{a,b,c} Andrea Arévalo, MSc,^d Leah Stiemsma, PhD,^{e,f} Pedro Dimitriu, PhD,^g Martha E. Chico, MD,^h Sofia Loor, BSc,^h Maritza Vaca, MD,^h Rozlyn C. T. Boutin, BSc,^a Evan Morien, MSc,ⁱ Mingliang Jin, PhD,^j Stuart E. Turvey, MBBS, DPhil,^e Jens Walter, PhD,^j Laura Wegener Parfrey, PhD,ⁱ Philip J. Cooper, PhD,^{d,h,k,*} and Brett Finlay, PhD^{a,g,l,*}



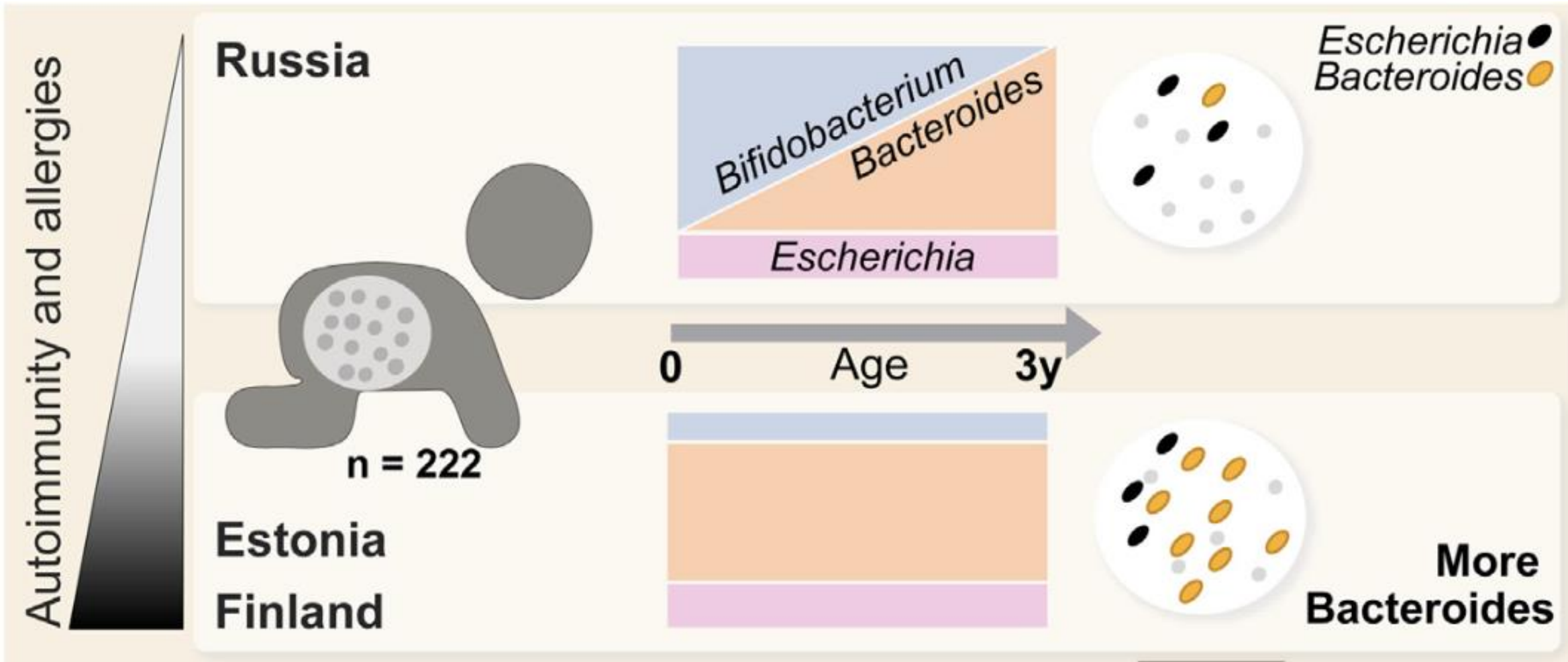
2017

Cell

Article

Variation in Microbiome LPS Immunogenicity Contributes to Autoimmunity in Humans

Tommi Vatanen,^{1,2,22} Aleksandar D. Kostic,^{1,3,4,22} Eva d’Hennezel,^{5,22} Heli Siljander,^{6,7,8} Eric A. Franzosa,^{1,4} Moran Yassour,¹ Raivo Kolde,³ Hera Vlamakis,¹ Timothy D. Arthur,¹ Anu-Maaria Hämäläinen,⁹ Aleksandr Peet,¹⁰ Vallo Tillmann,¹⁰ Raivo Uibo,¹¹ Sergei Mokurov,¹² Natalya Dorshakova,¹³ Jorma Ilonen,^{14,15} Suvi M. Virtanen,^{16,17,18} Susanne J. Szabo,⁵ Jeffrey A. Porter,⁵ Harri Lähdesmäki,² Curtis Huttenhower,^{1,4} Dirk Gevers,^{1,23} Thomas W. Cullen,^{5,23} Mikael Knip,^{6,7,8,19,23} on behalf of the DIABIMMUNE Study Group, and Ramnik J. Xavier^{1,3,20,21,23,*}



2016

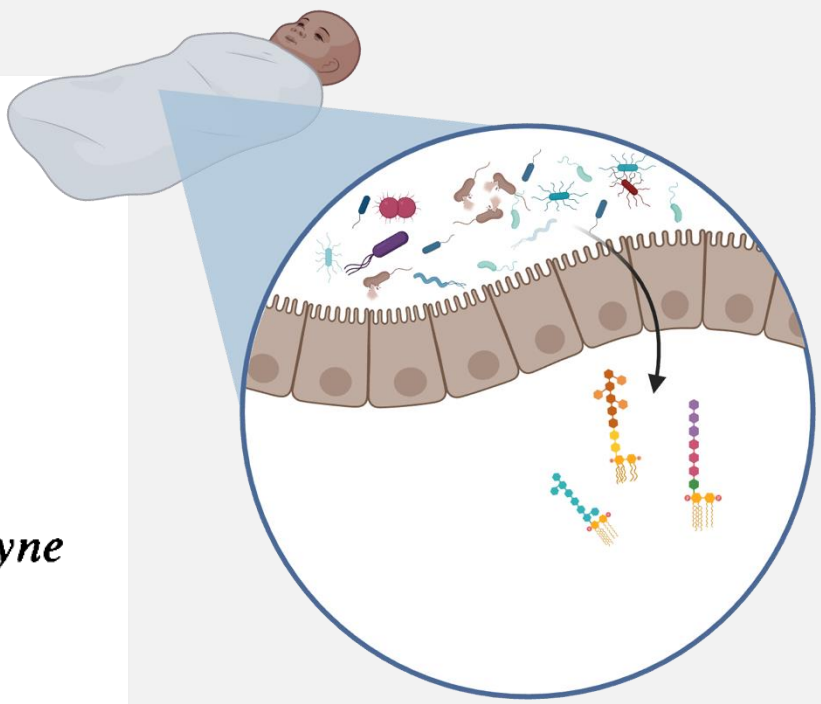
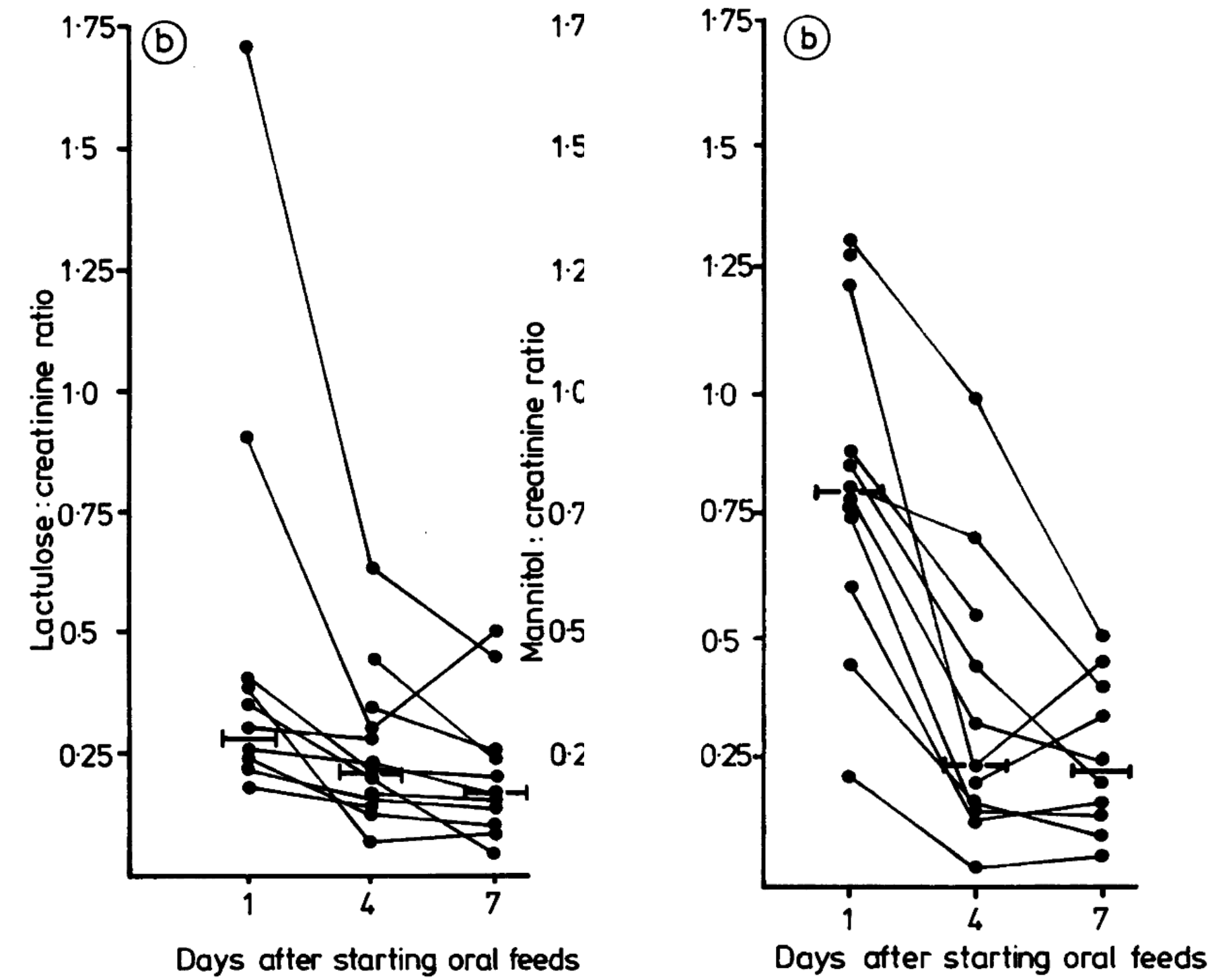
A "LEAKY GUT" AND SYSTEMIC MICROBIAL EXPOSURES 1ST WEEK OF LIFE

Archives of Disease in Childhood, 1984, **59**, 236-241

Intestinal permeability in the newborn

L T WEAVER, M F LAKER, AND R NELSON

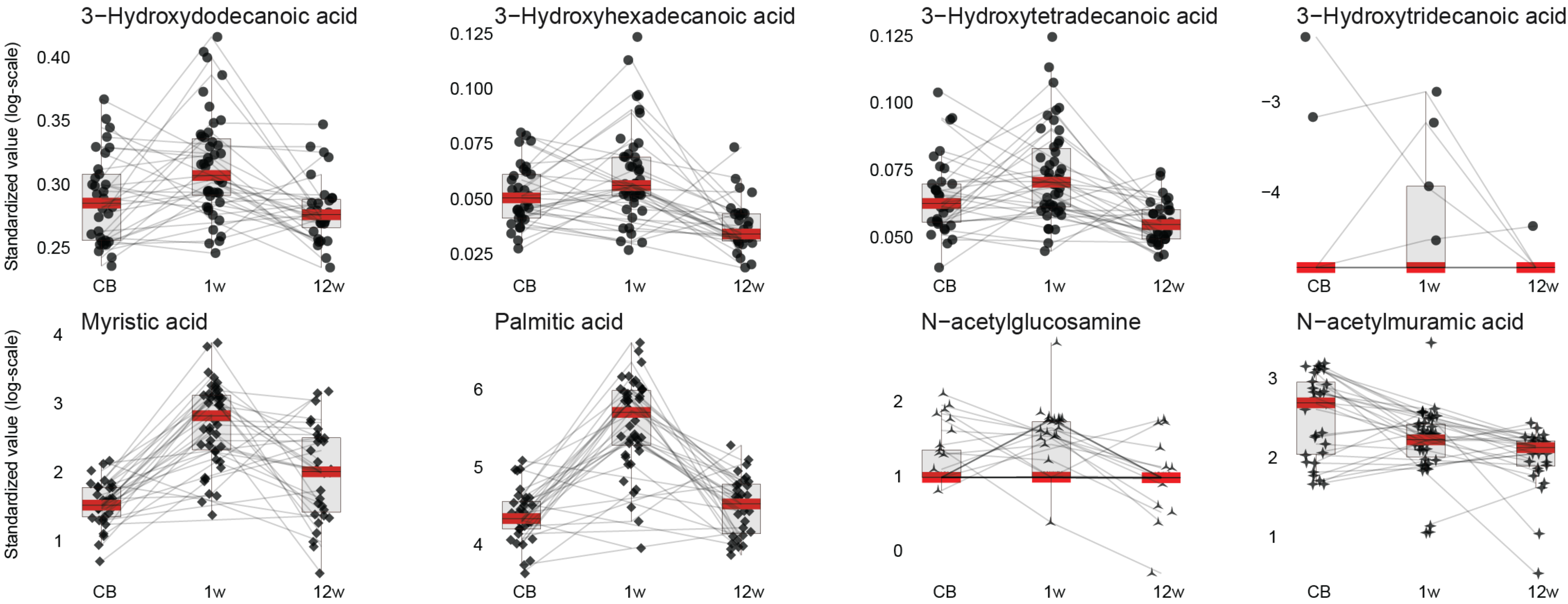
Departments of Child Health and Clinical Biochemistry, Royal Victoria Infirmary, Newcastle upon Tyne



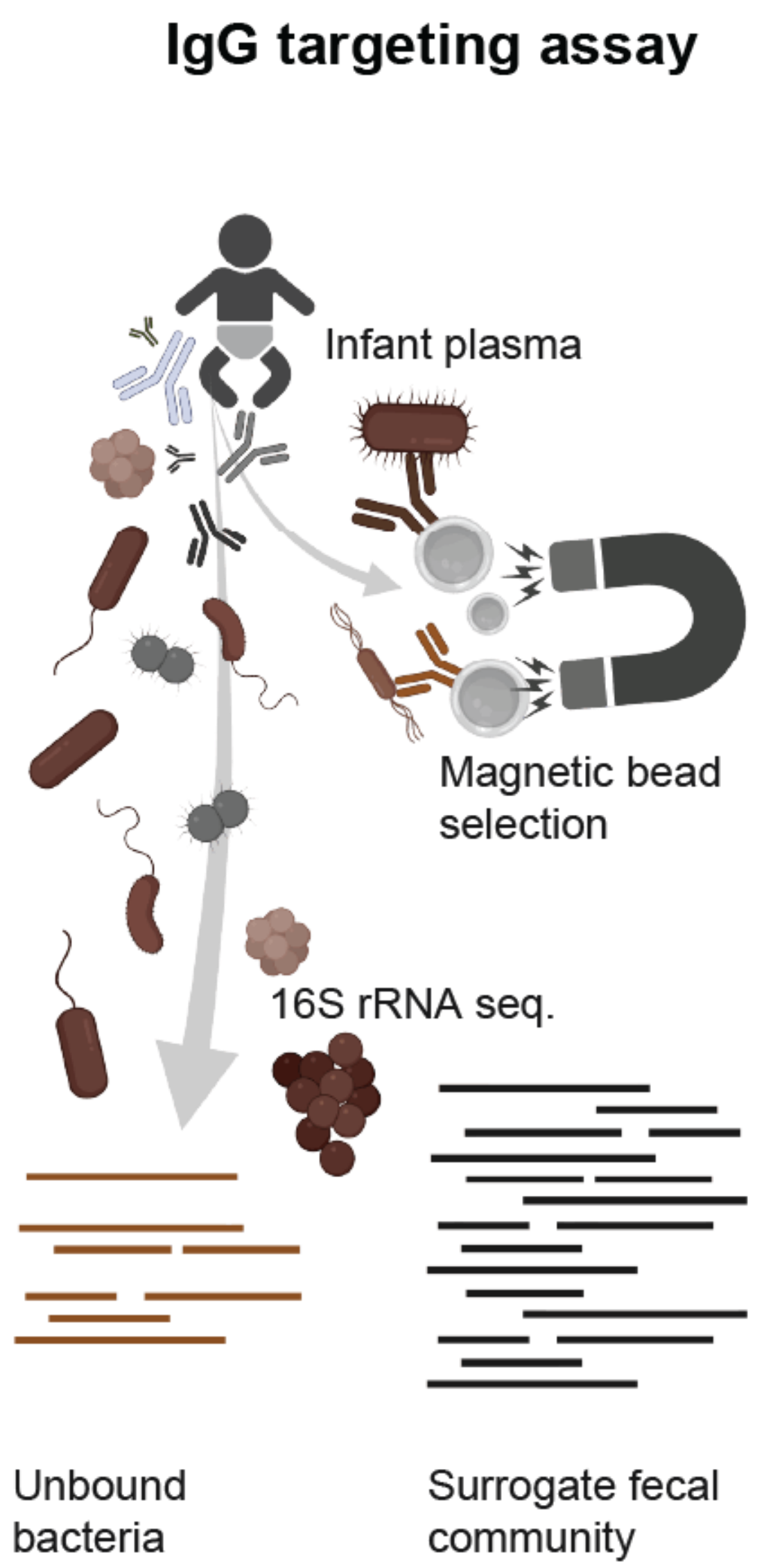
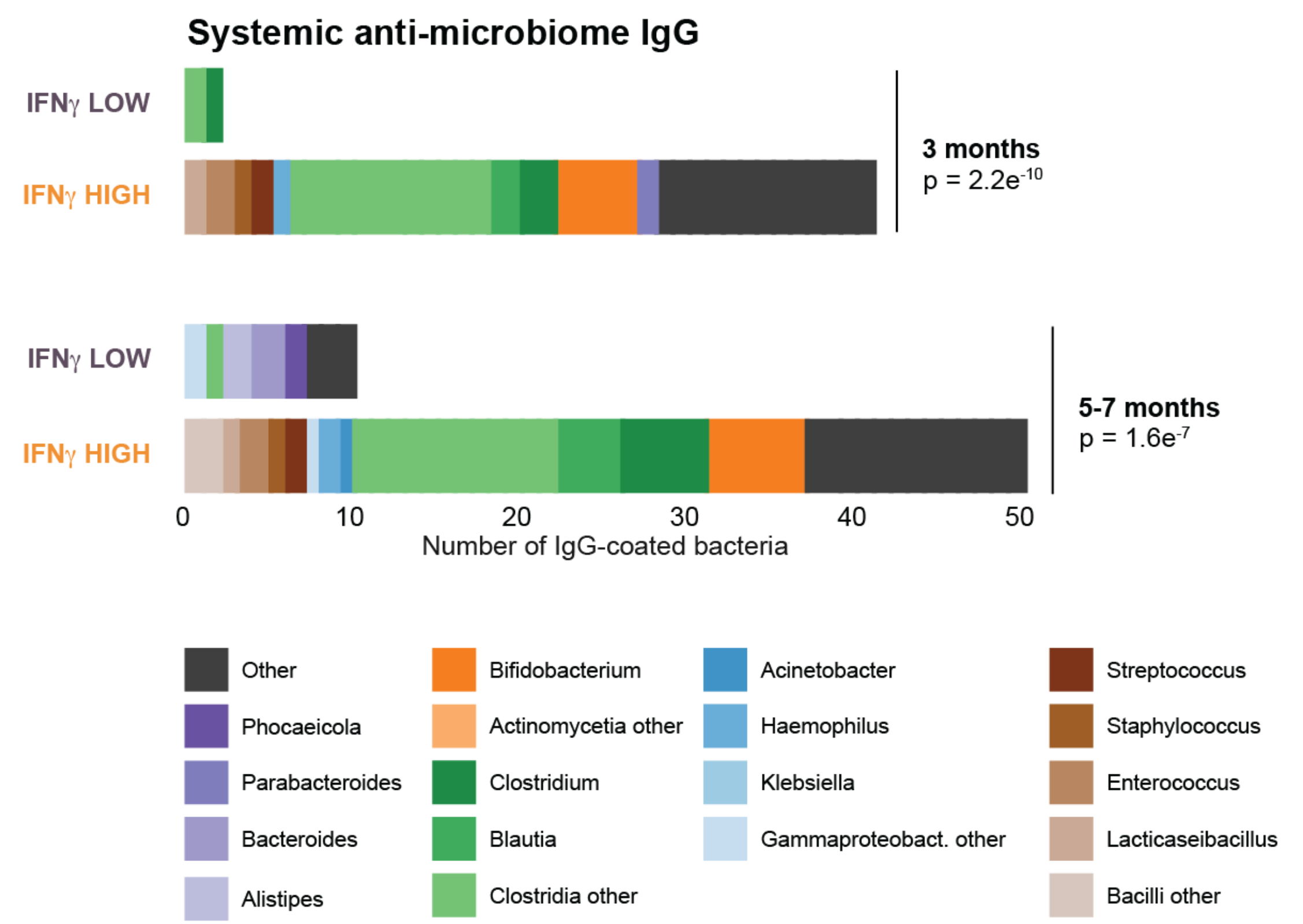
A "LEAKY GUT" AND SYSTEMIC MICROBIAL EXPOSURES 1ST WEEK OF LIFE

Microbial components detectable in plasma (Mass spectrometry)

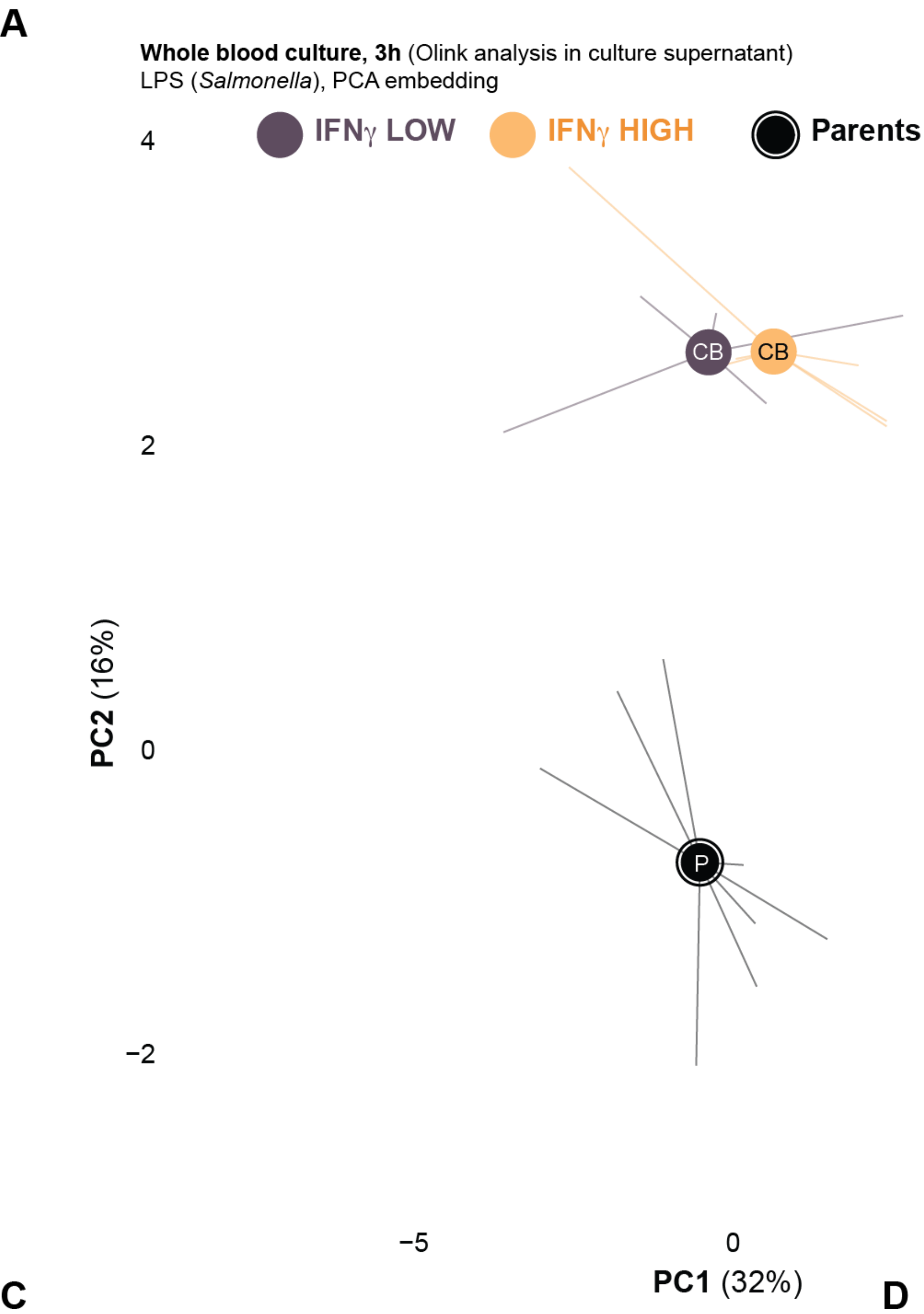
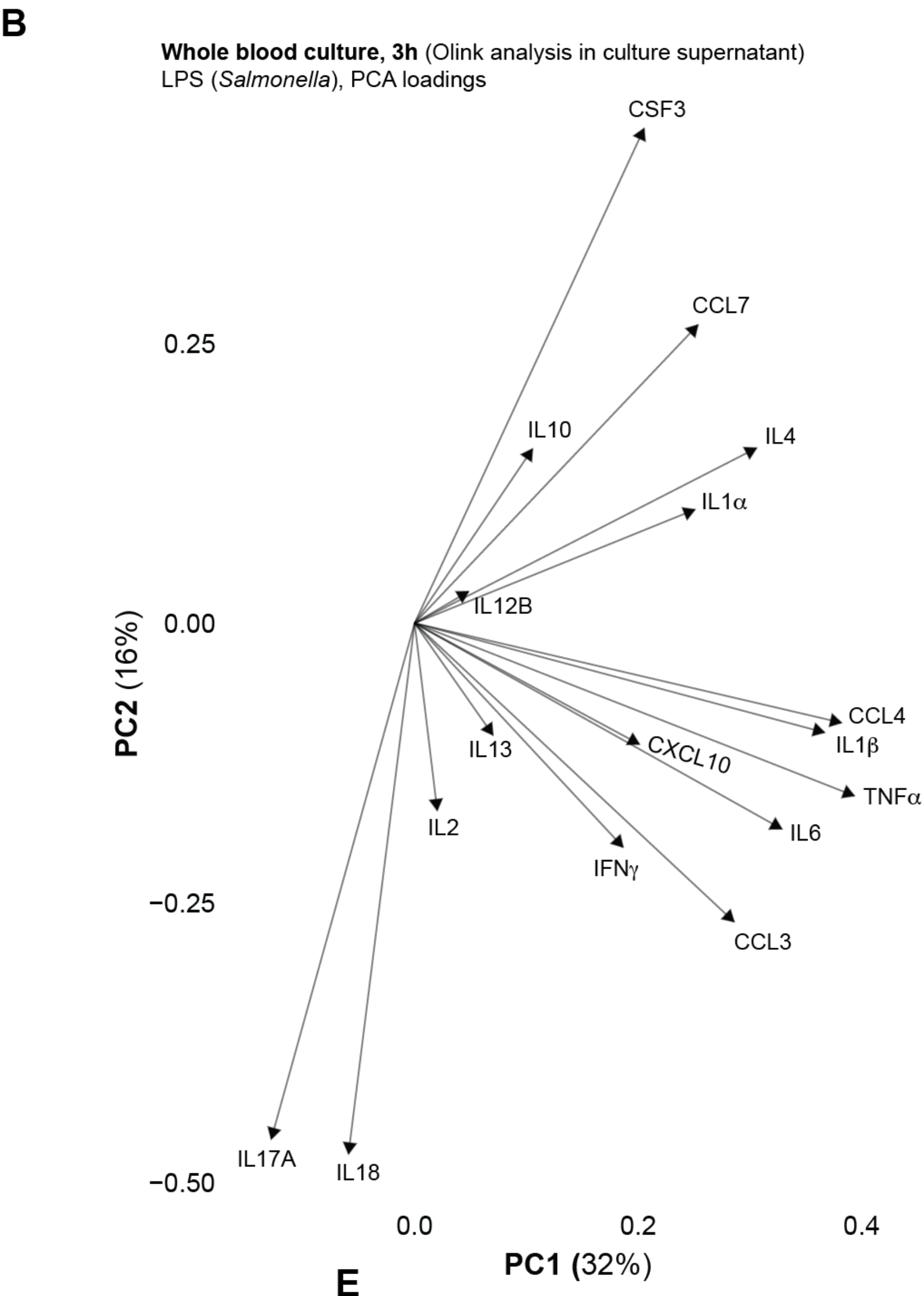
● Primarily LPS ✕ Peptidoglycan and Human ◆ LPS and Human ✦ Primarily peptidoglycan



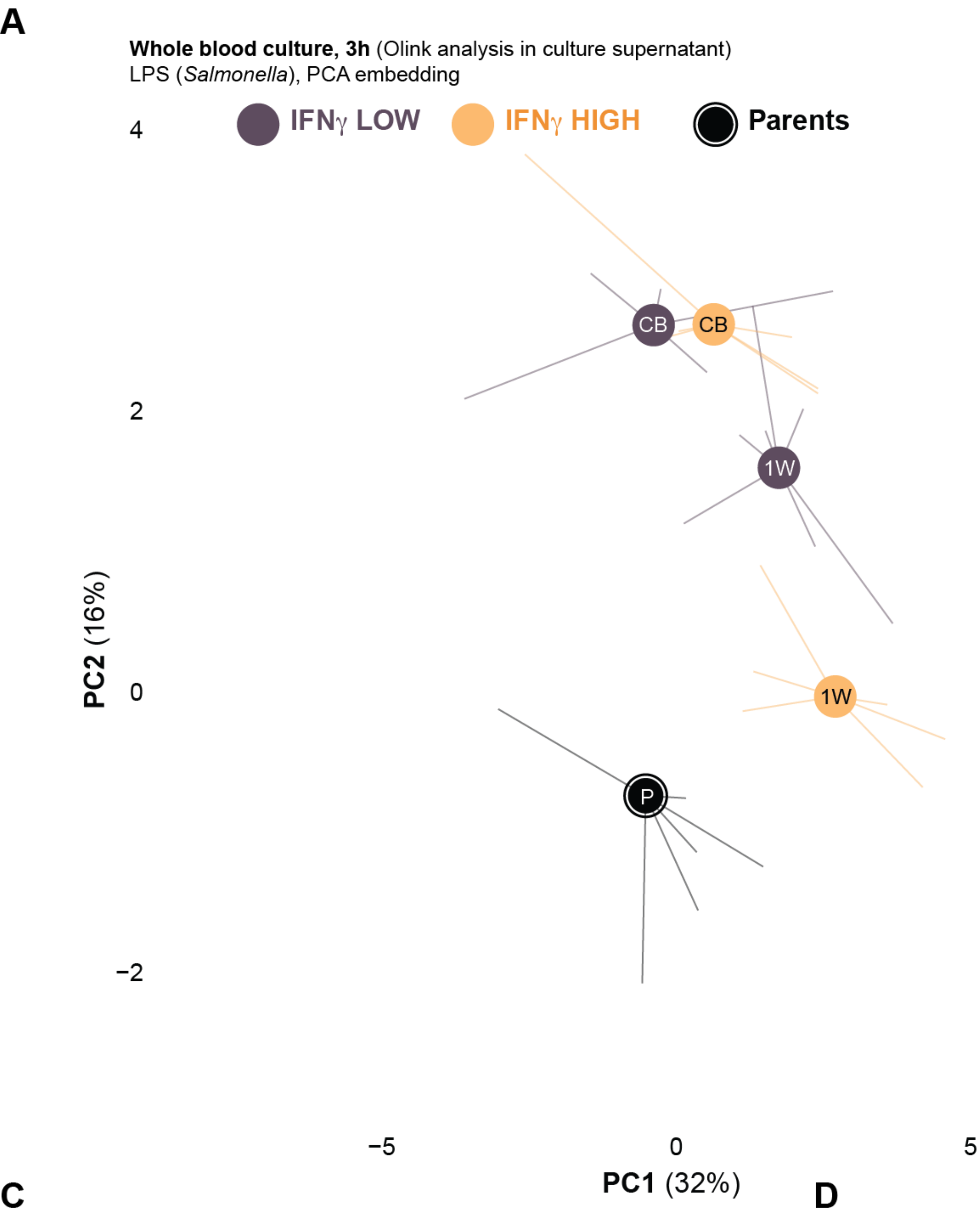
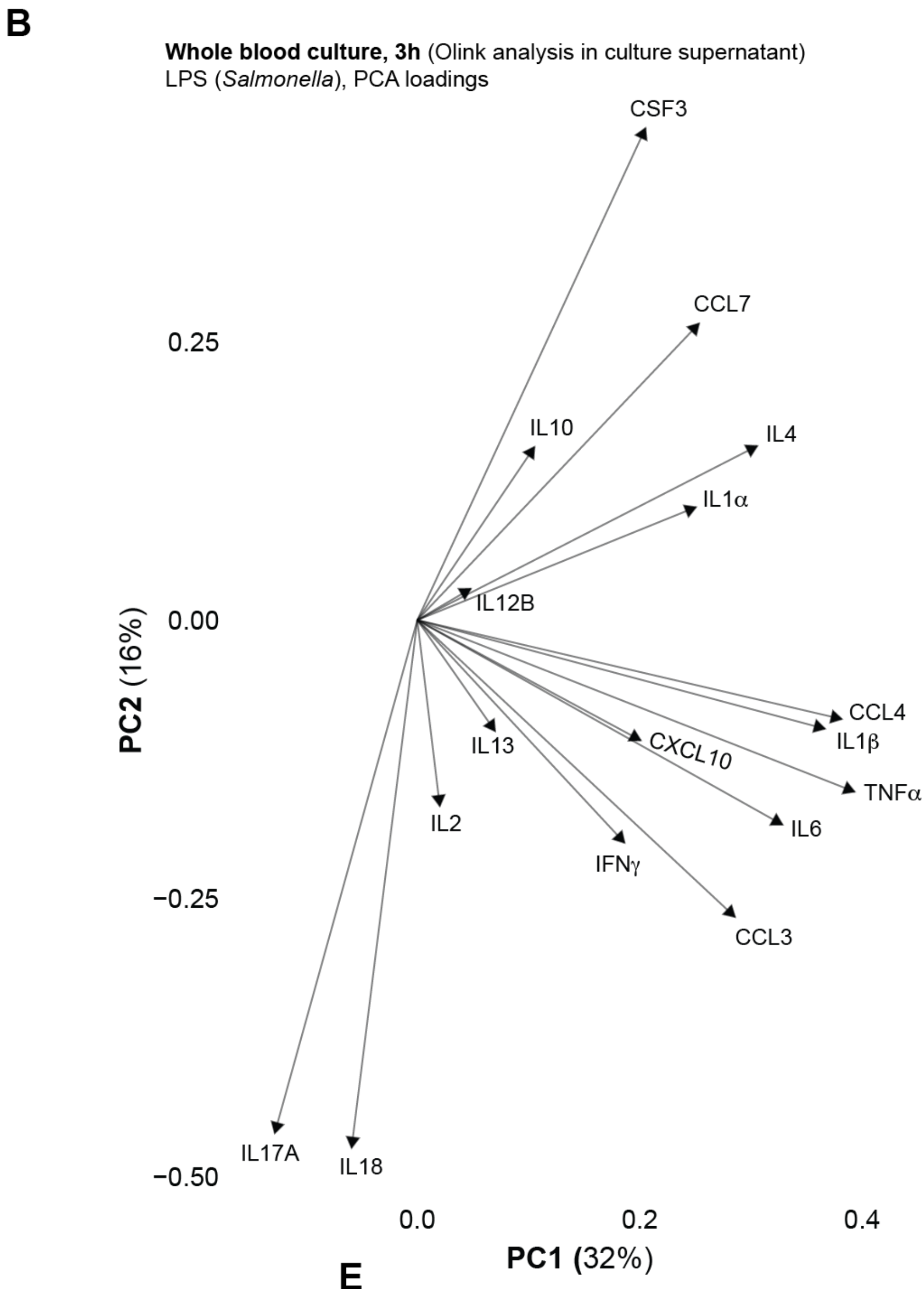
ADAPTIVE IMMUNE RESPONSES FOLLOWING VARIABLE SEEDING REACTIONS



IMMUNE CELL FUNCTIONAL DEVELOPMENT – MINIATURIZED WHOLE BLOOD CULTURES

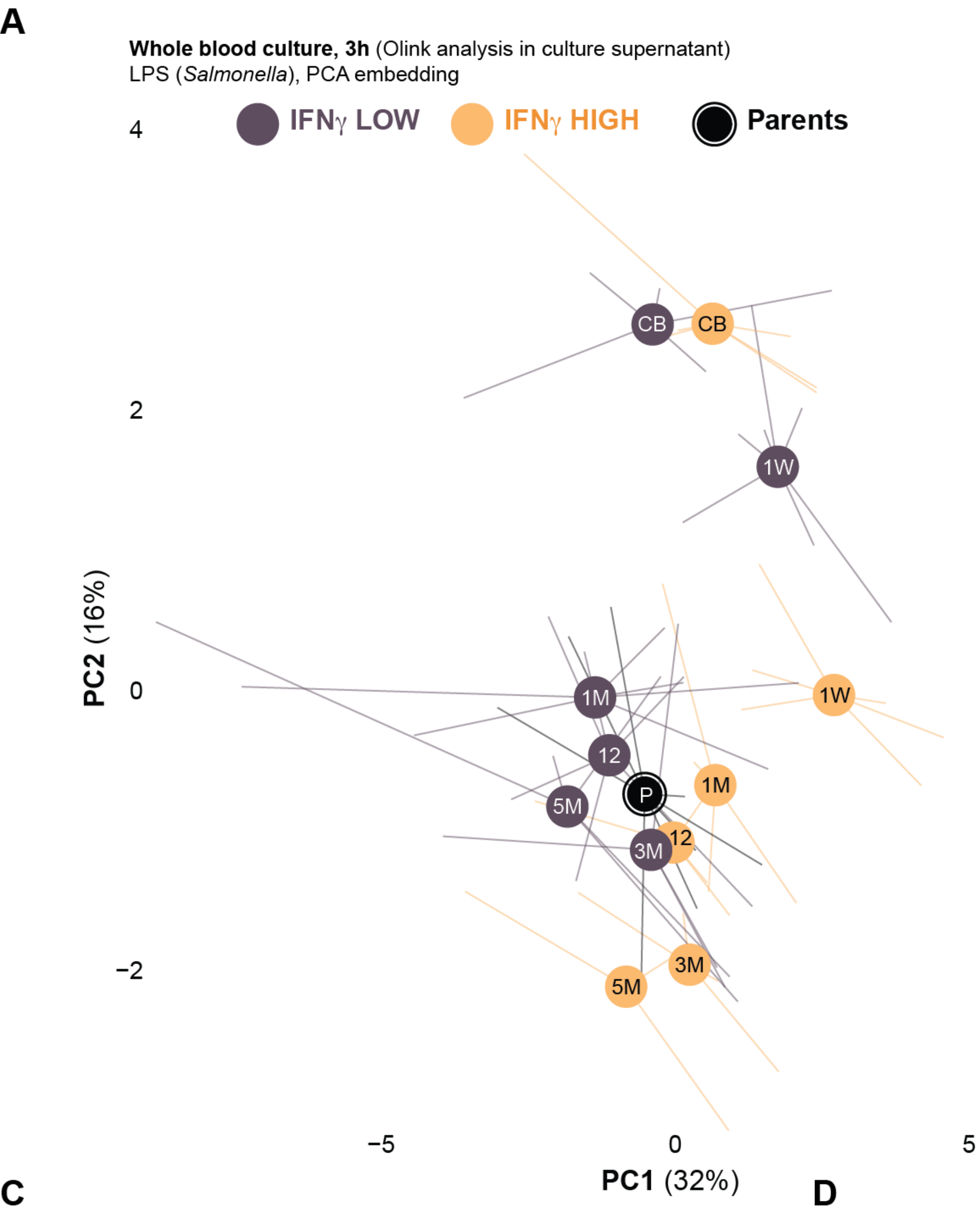
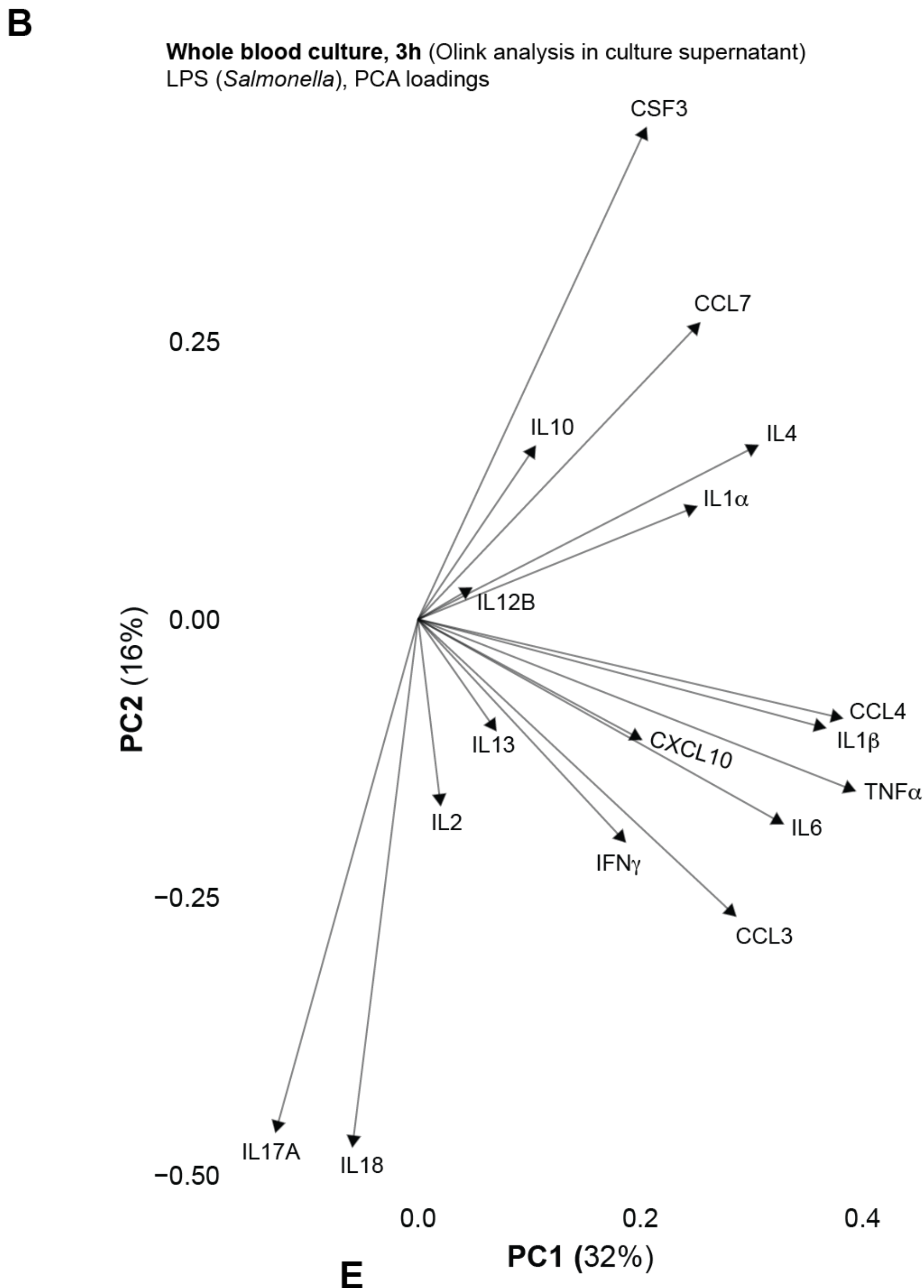


IMMUNE CELL FUNCTIONAL DEVELOPMENT – MINIATURIZED WHOLE BLOOD CULTURES

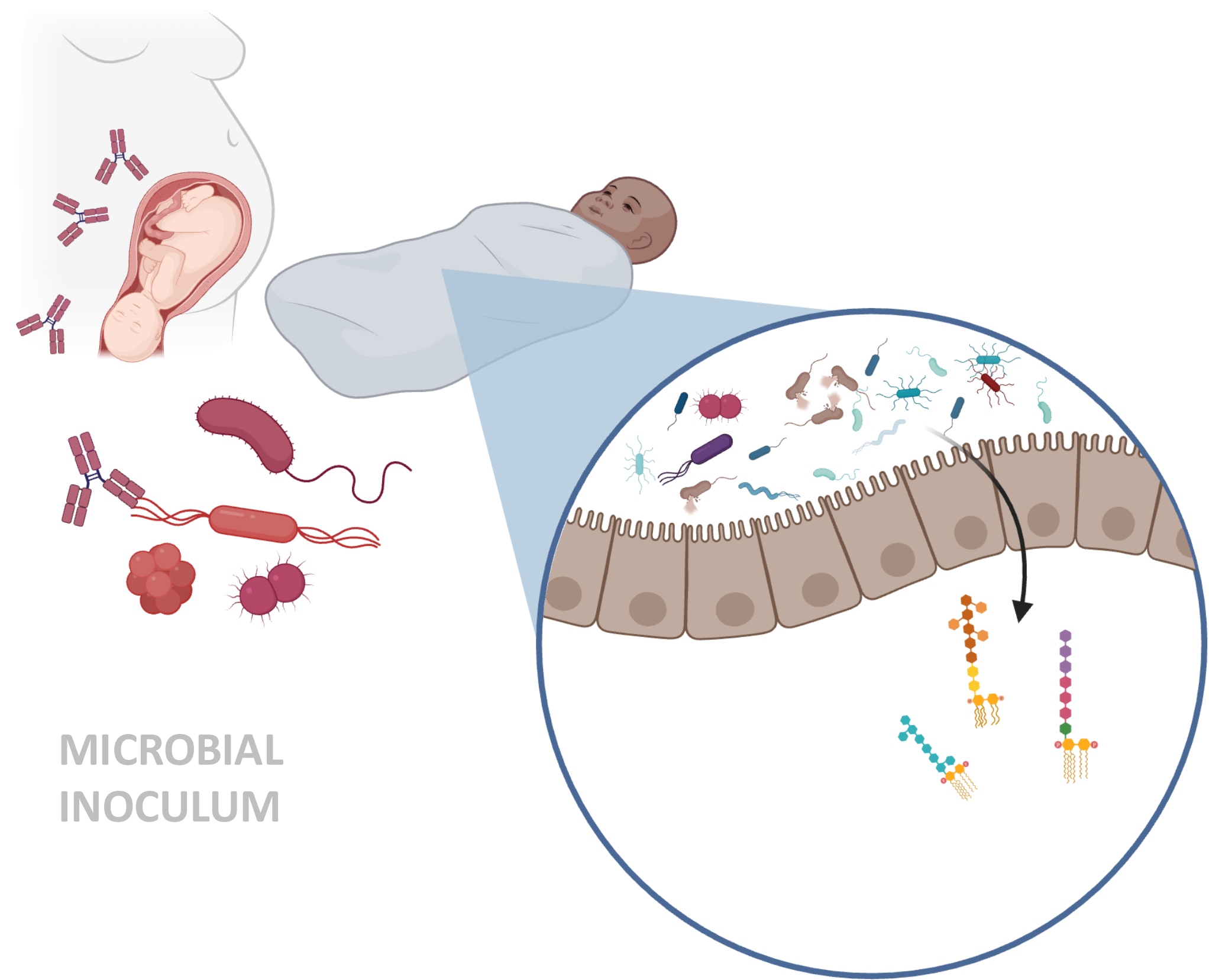


C

IMMUNE CELL FUNCTIONAL DEVELOPMENT – MINIATURIZED WHOLE BLOOD CULTURES



"THE SEEDING REACTION"



MICROBIAL
INOCULUM

ADAPTIVE IMMUNE RESPONSES

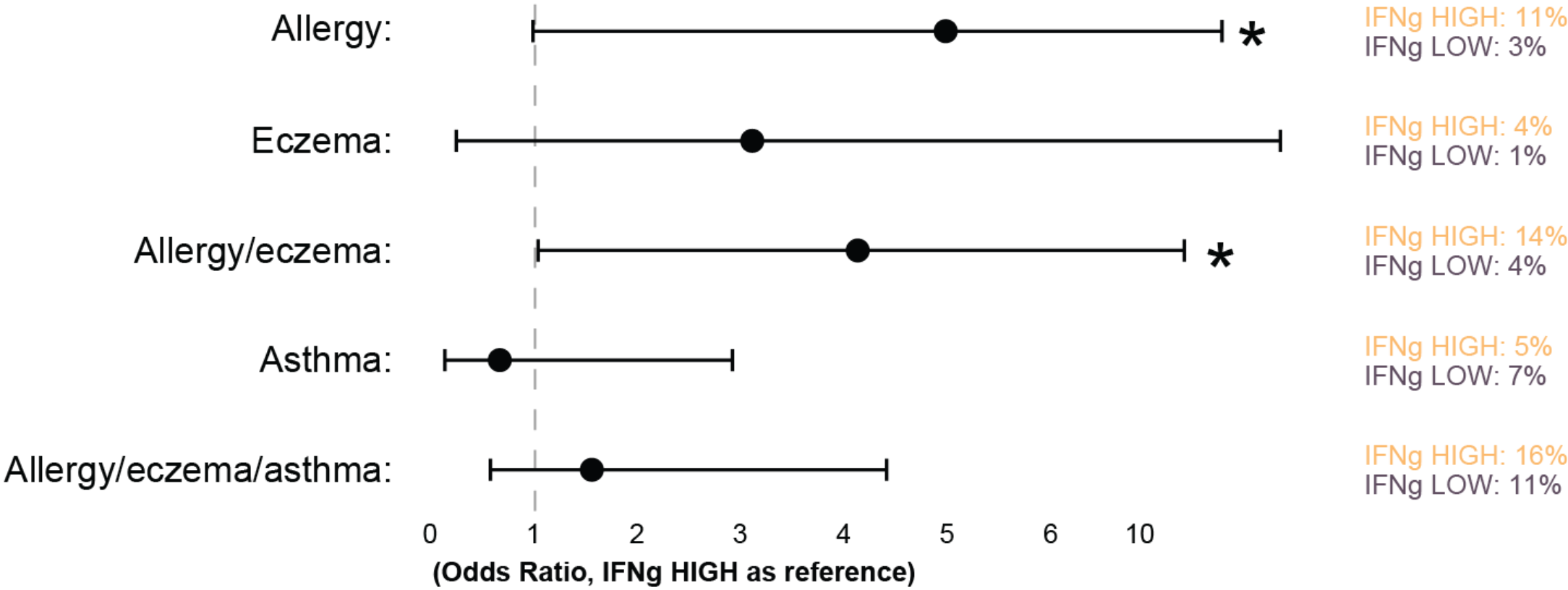
INNATE CELL MATURATION

RISK OF FUTURE IMMUNE-MEDIATED DISEASE?

A

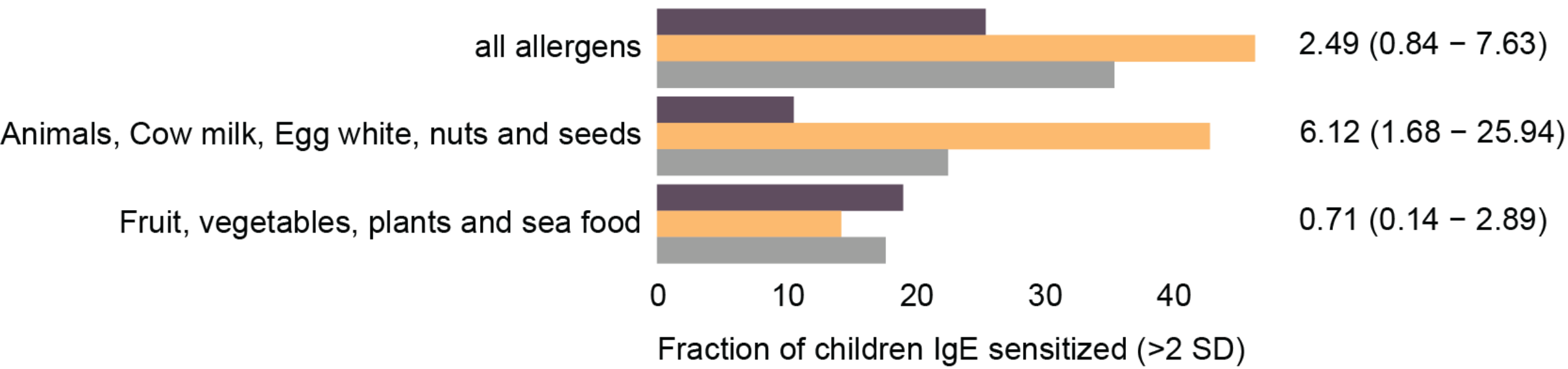
Disease incidences in relation to seeding reactions

(N_{IFNg^{HIGH}}=79; N_{IFNg^{LOW}}=80)

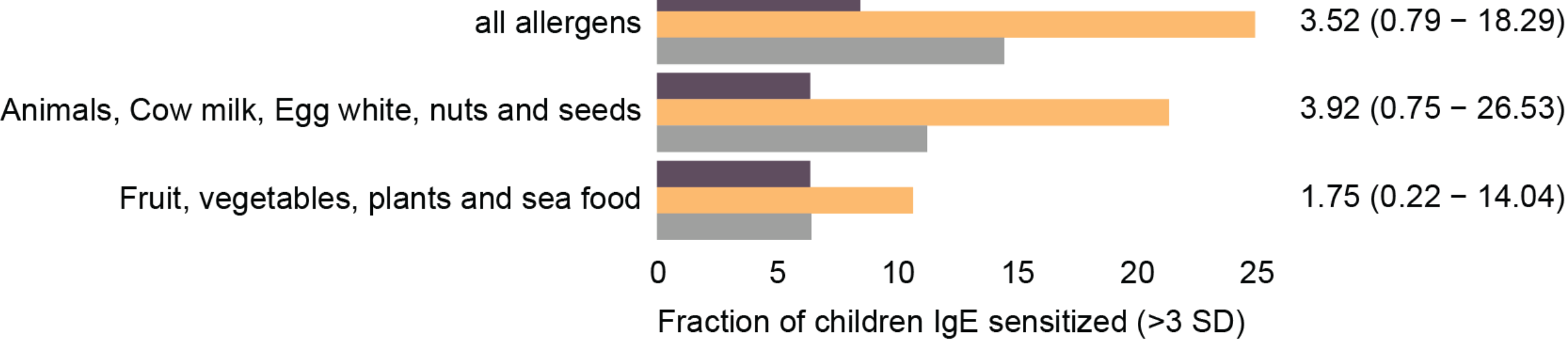


B

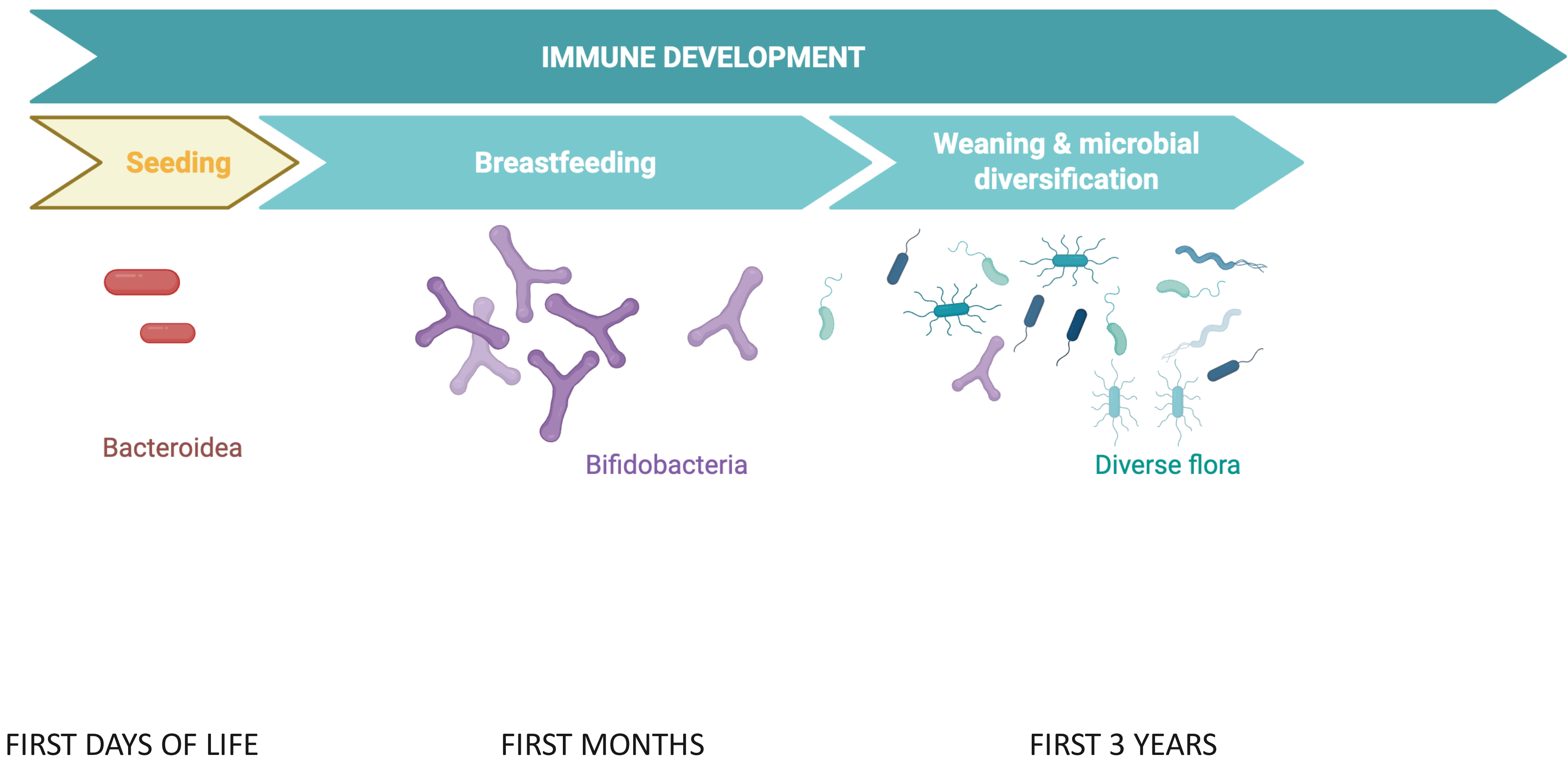
IgE sensitization in relation to seeding reactions



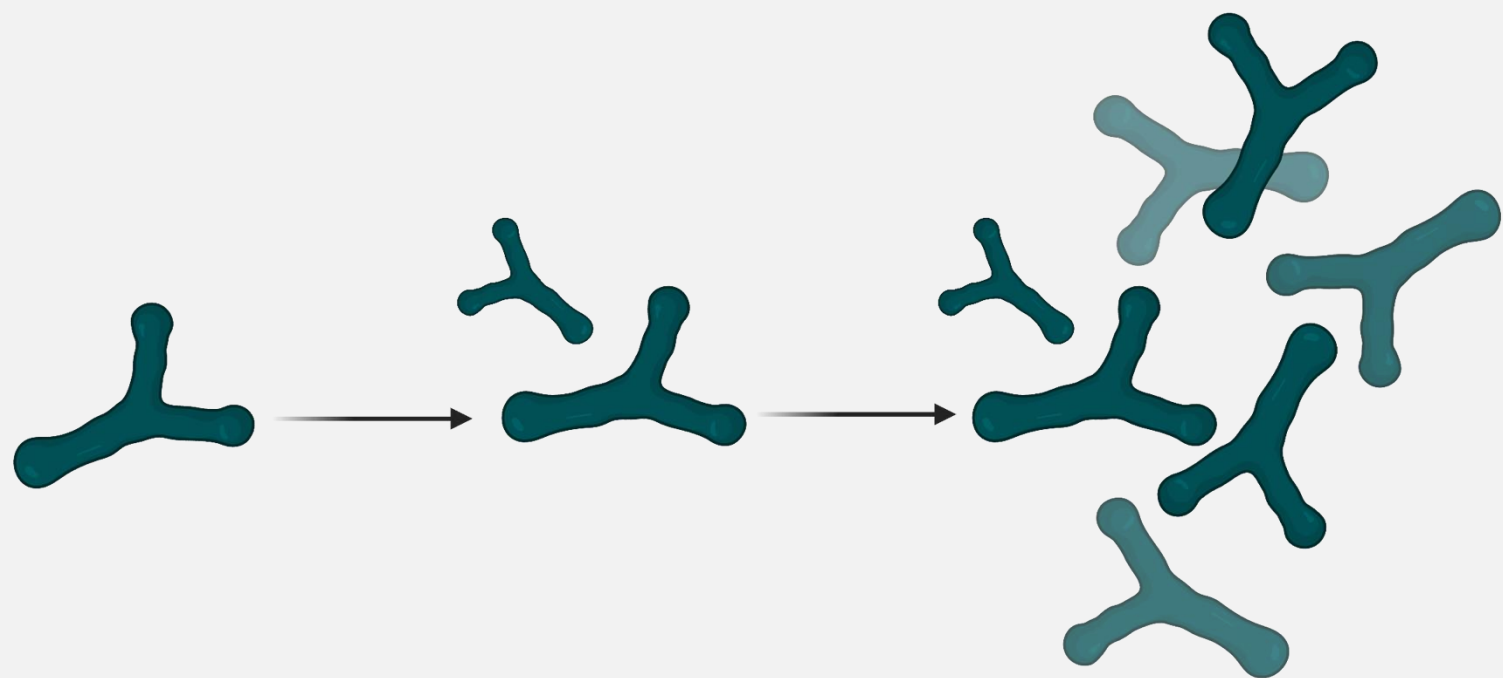
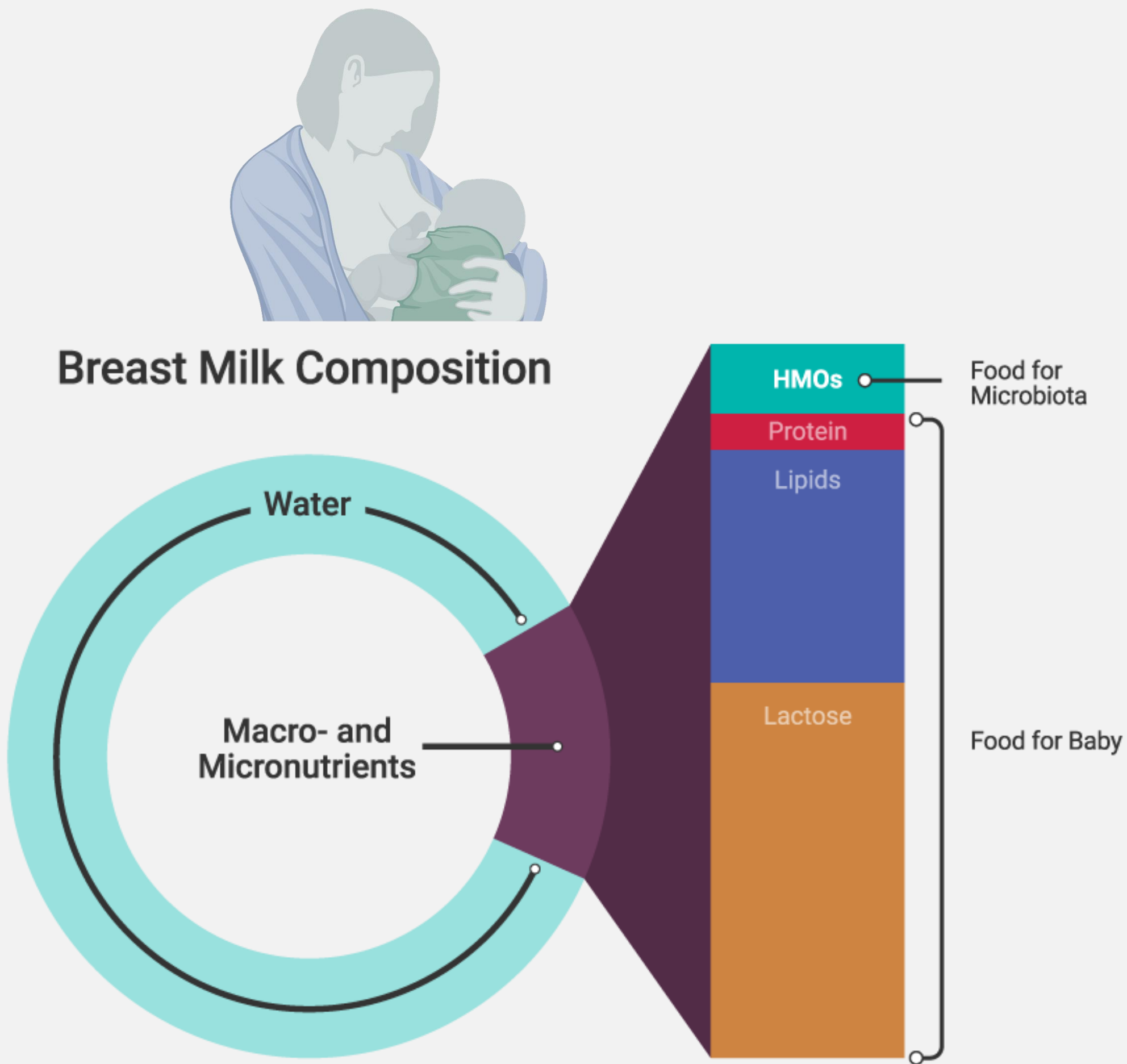
C



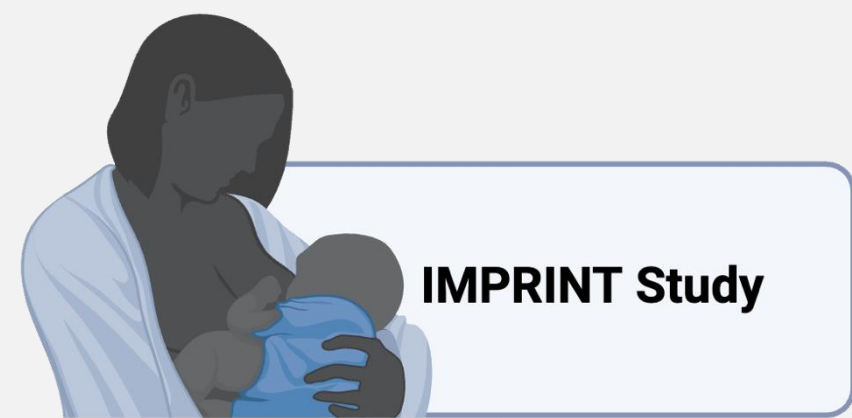
IMMUNE DEVELOPMENT - A CHAIN OF EVENTS



BENEFICIAL MICROBES - BIFIDOBACTERIA



PROMOTING HEALTHY IMMUNE-MICROBE INTERACTIONS



Control
(n=20)

EVC001
(n=20)

Day 6

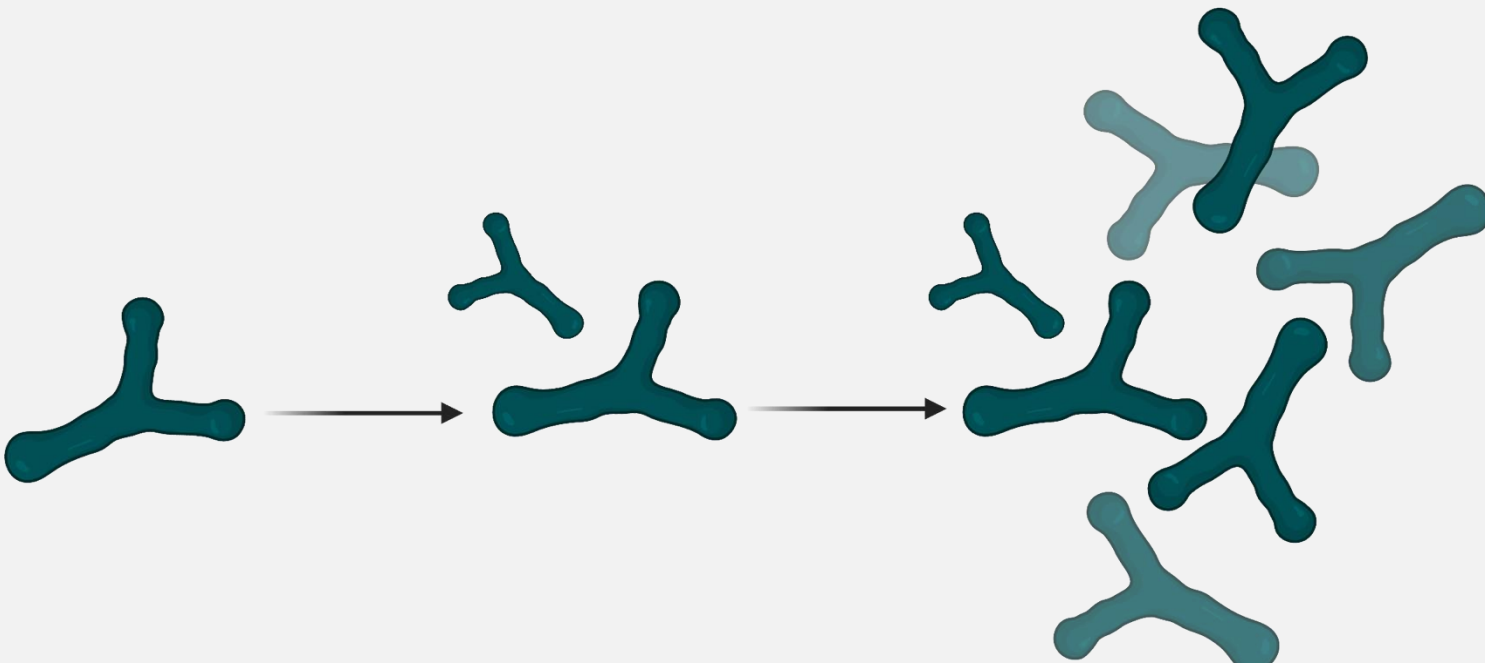
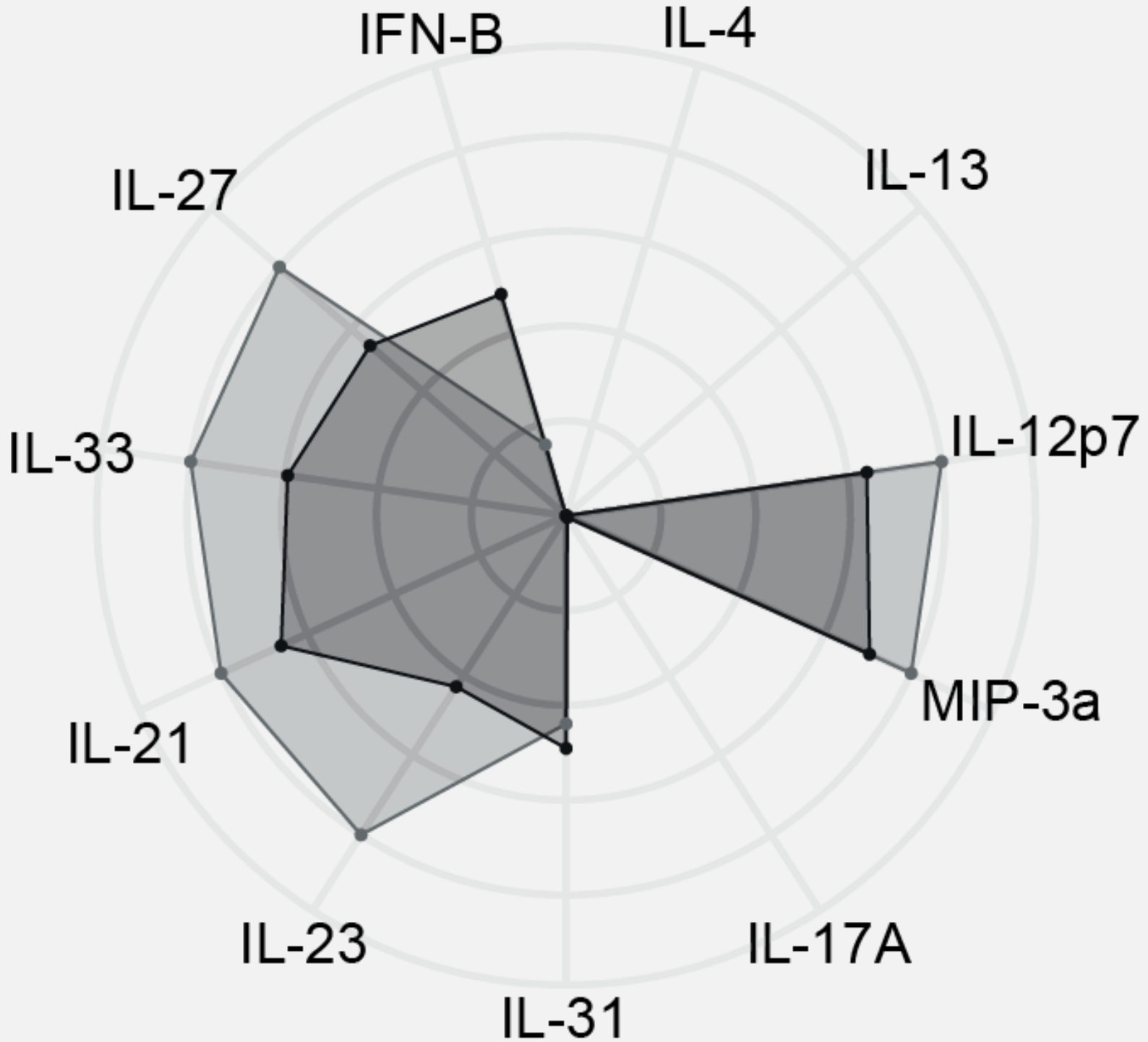
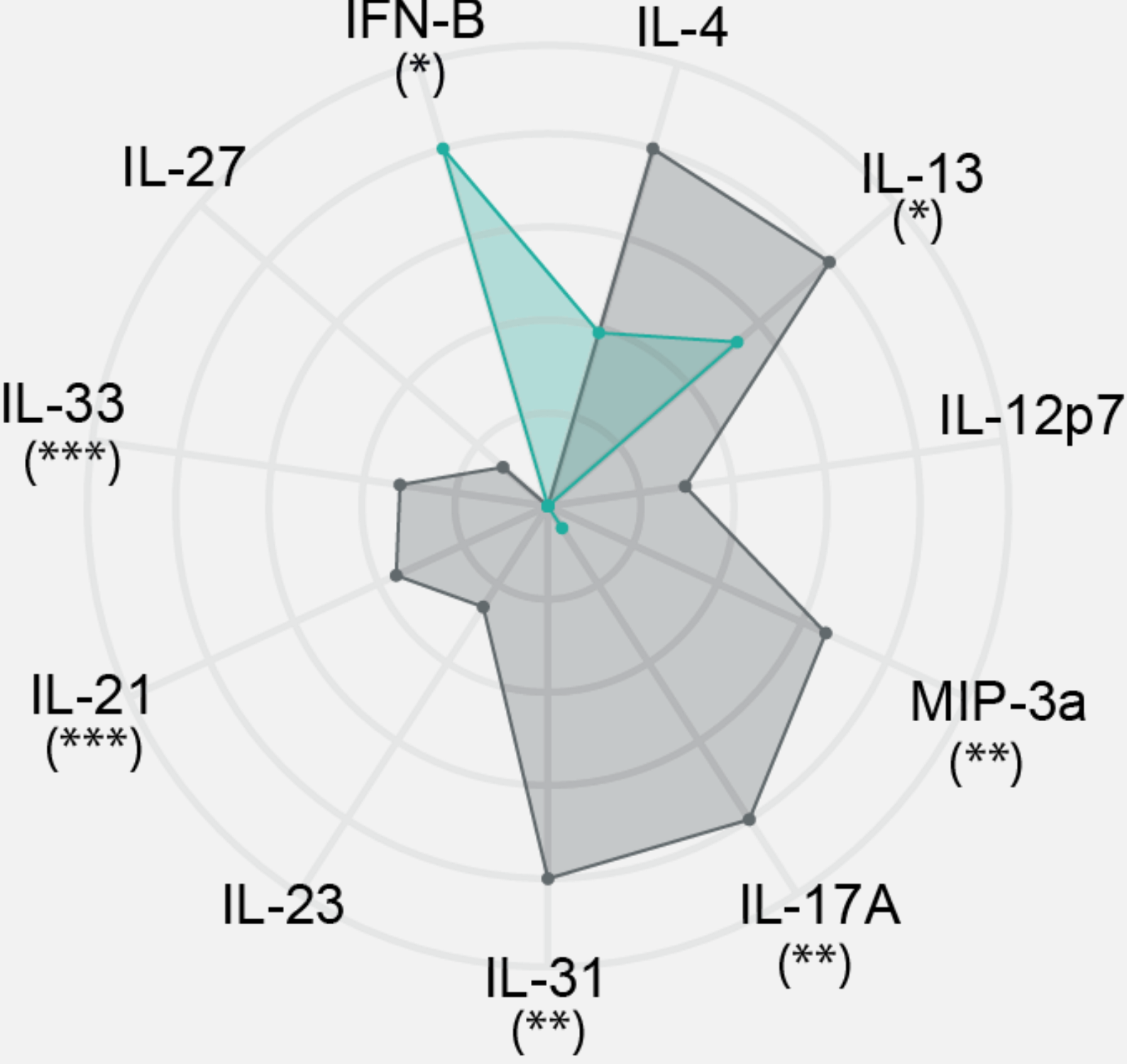


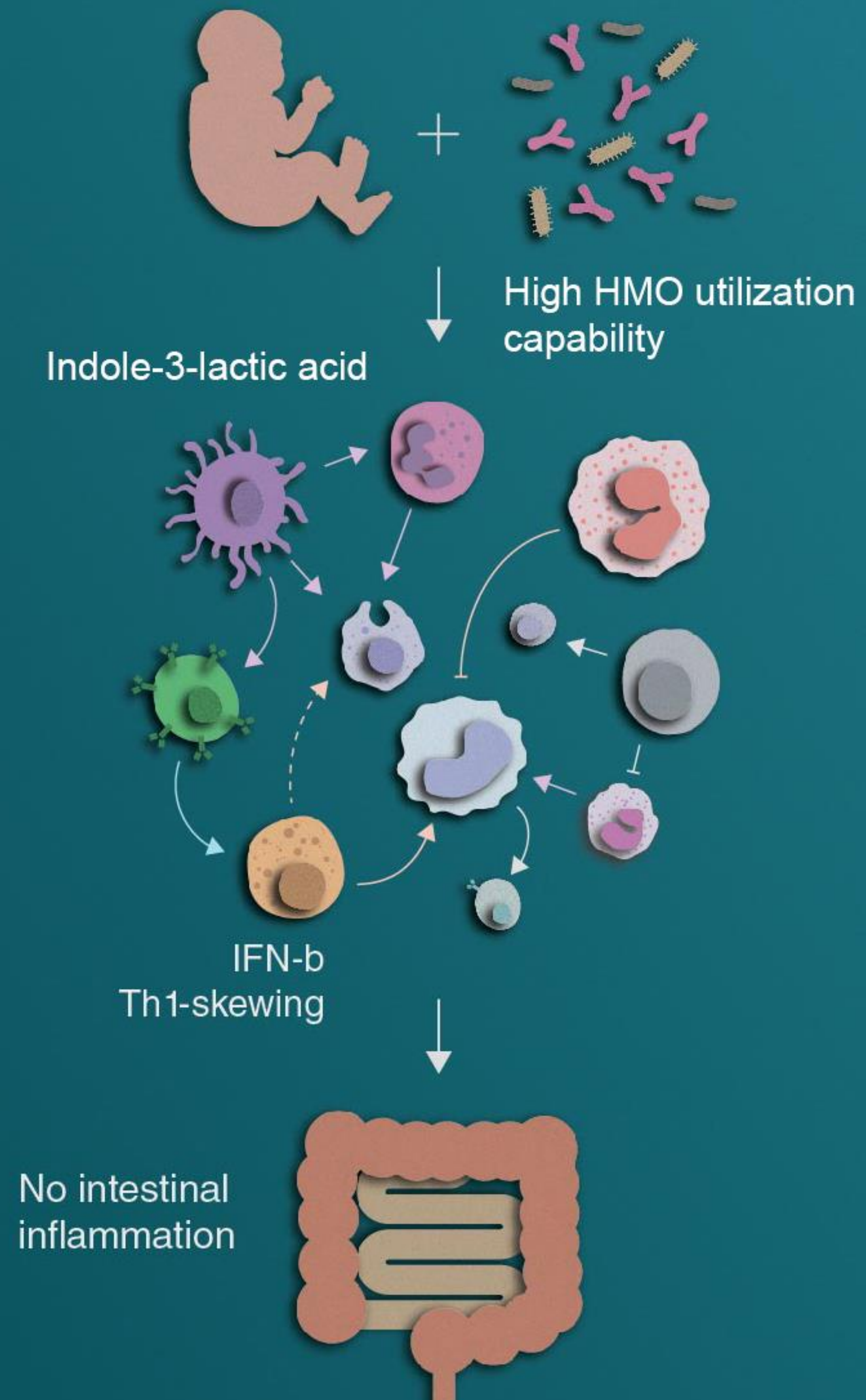
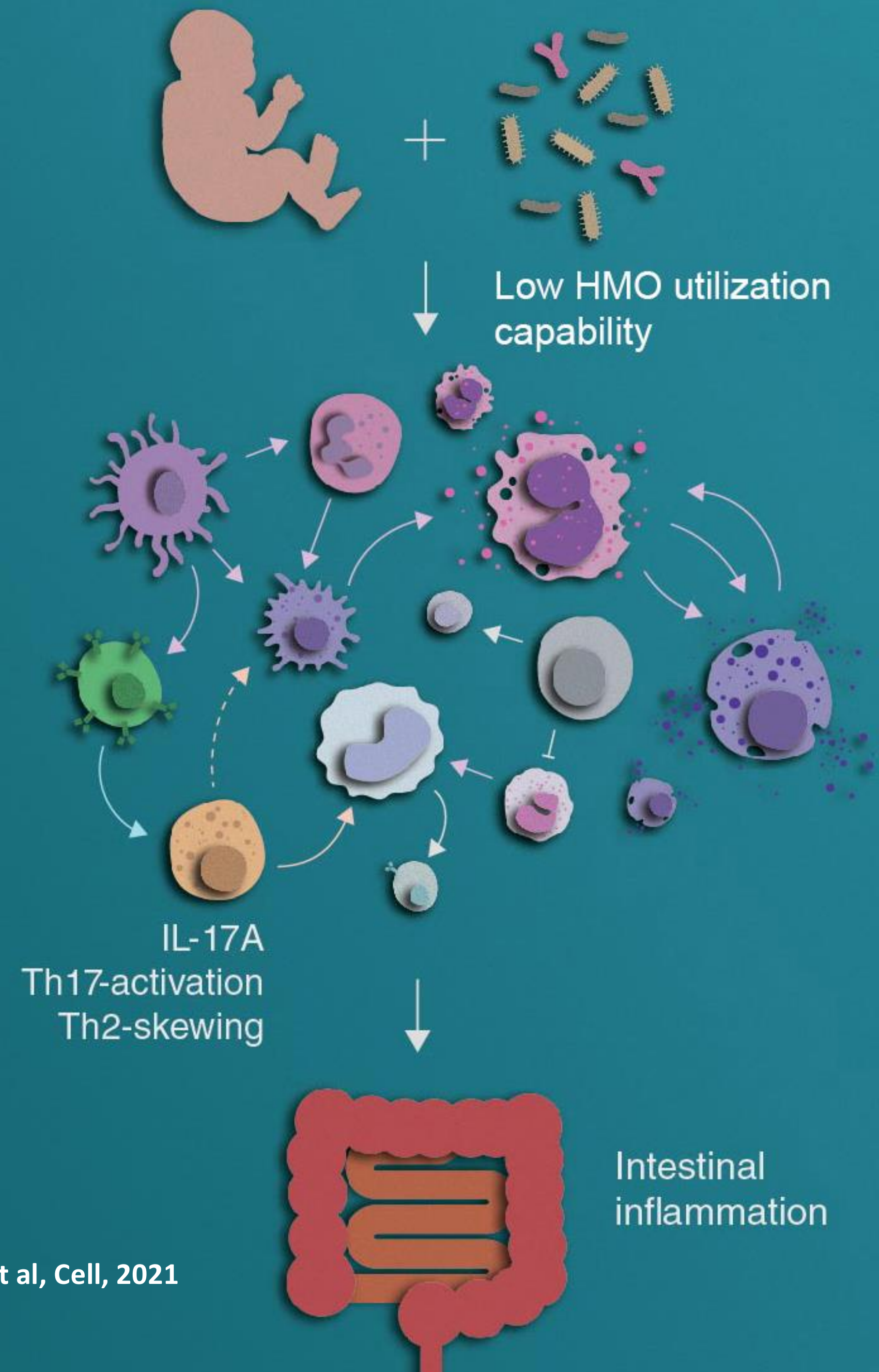
Control



B. Infantis

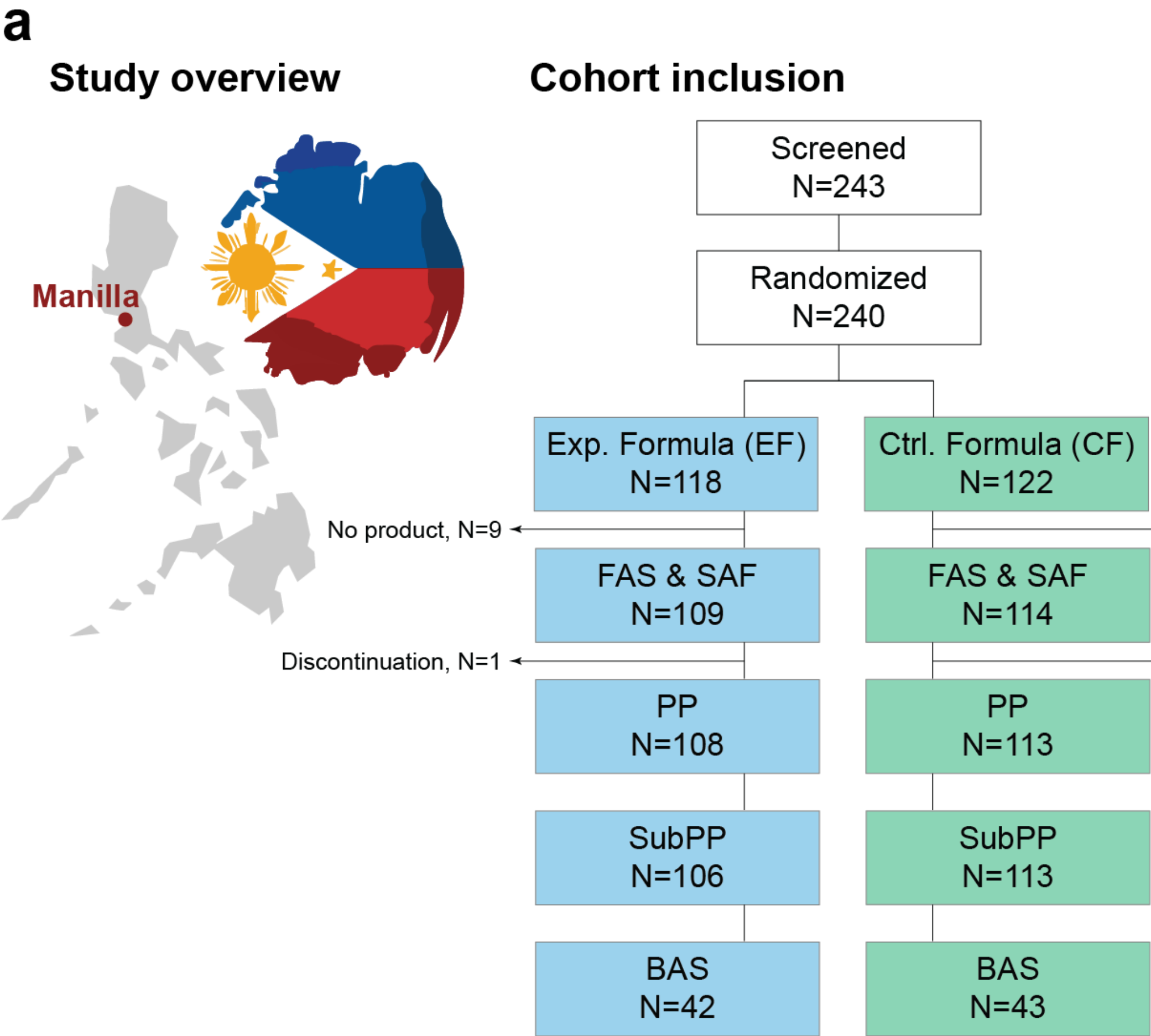
Day 60





Henrick et al, Cell, 2021

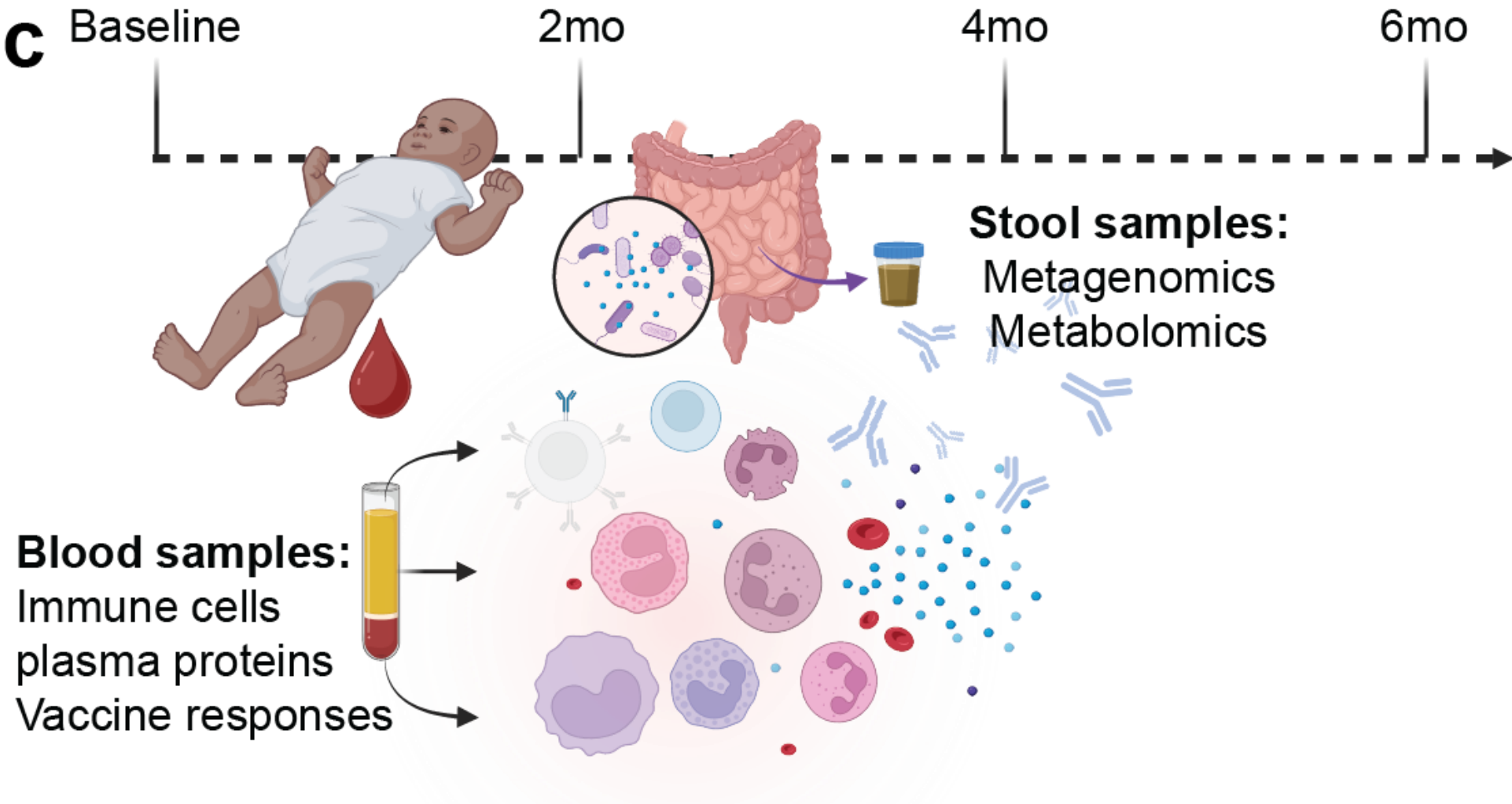
IMMUNE DEVELOPMENT – OPTIMIZING FORMULA FEEDING



b

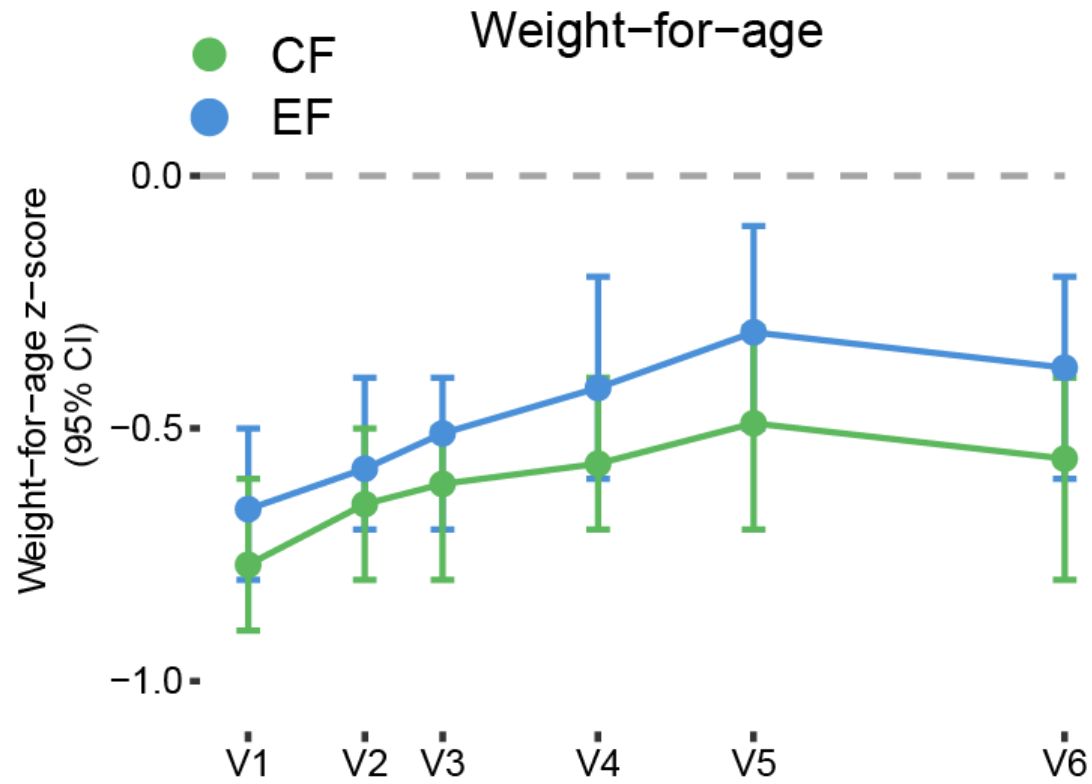
Demographics

	EF, N=118	CF, N=122
Sex, % Female	48%	47%
Gestational age at birth in wks. Mean (SD)	38.6 (1.1)	38.5 (1.0)
Age at enrollment in days. Mean (SD)	27.4 (4.9)	28.0 (4.9)
Vaginal birth, %	86%	88%
Infants with siblings, %	78%	83%
Tagalog ethnicity, %	98%	90%
Weight at birth in kg. Mean (SD)	3.04 (0.36)	2.99 (0.30)

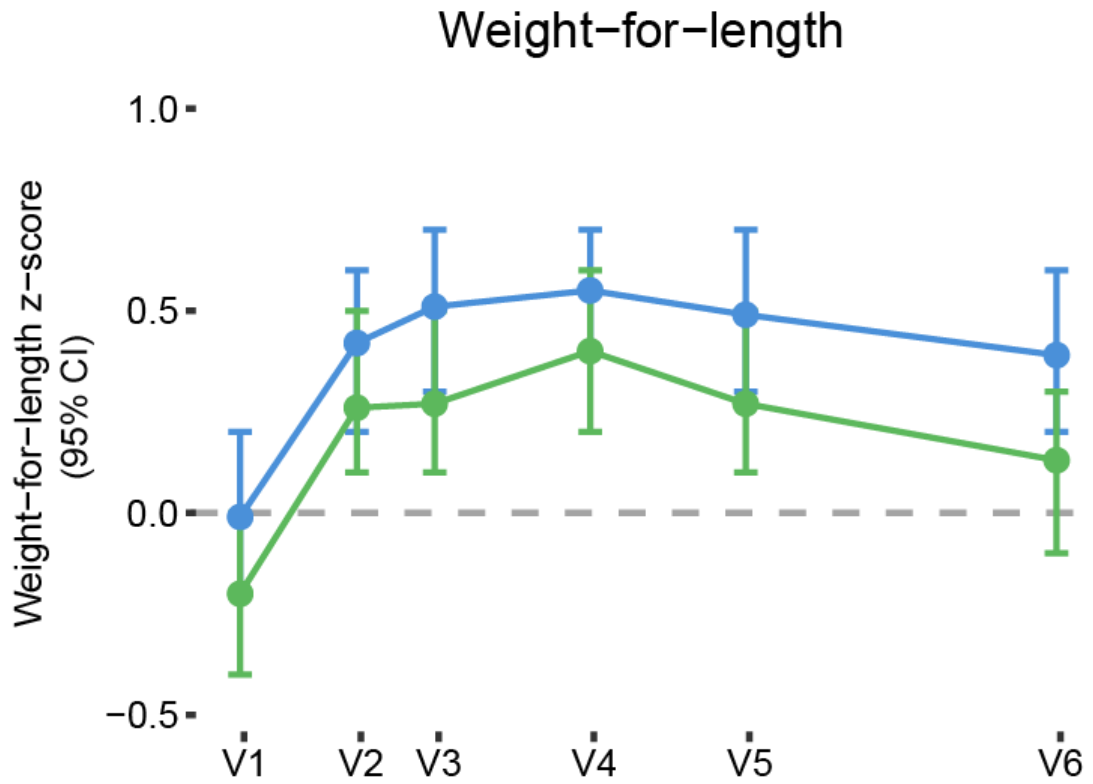


IMMUNE DEVELOPMENT – OPTIMIZING FORMULA FEEDING

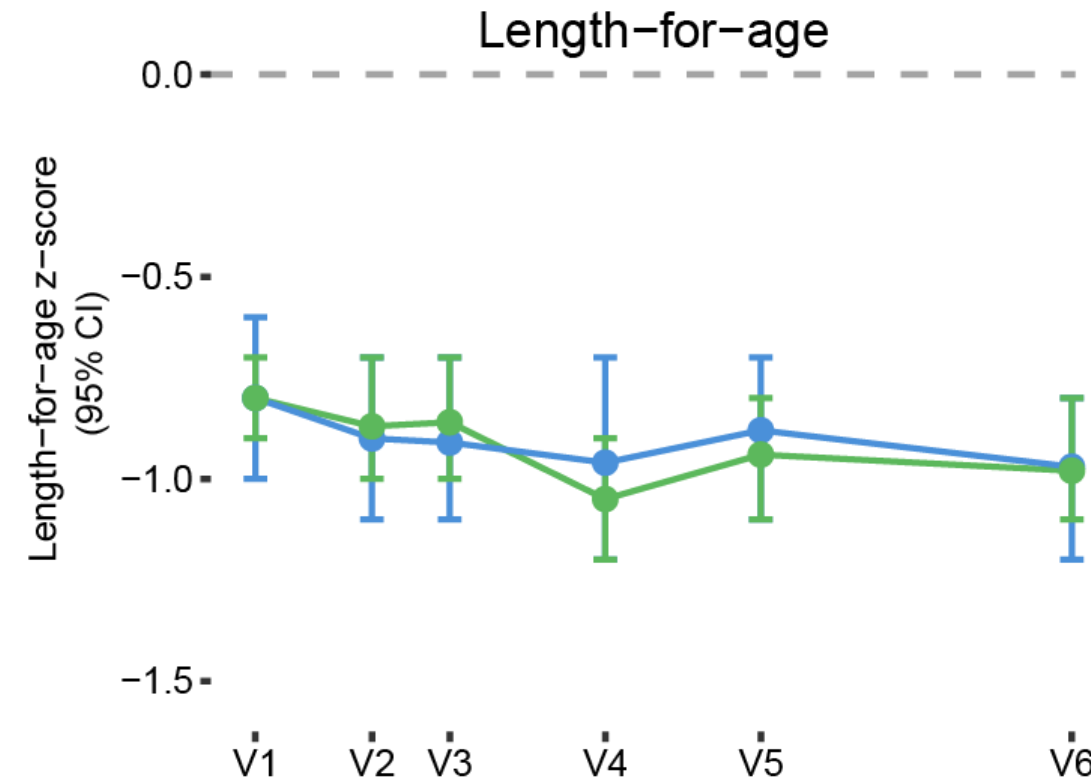
a Anthropometrics



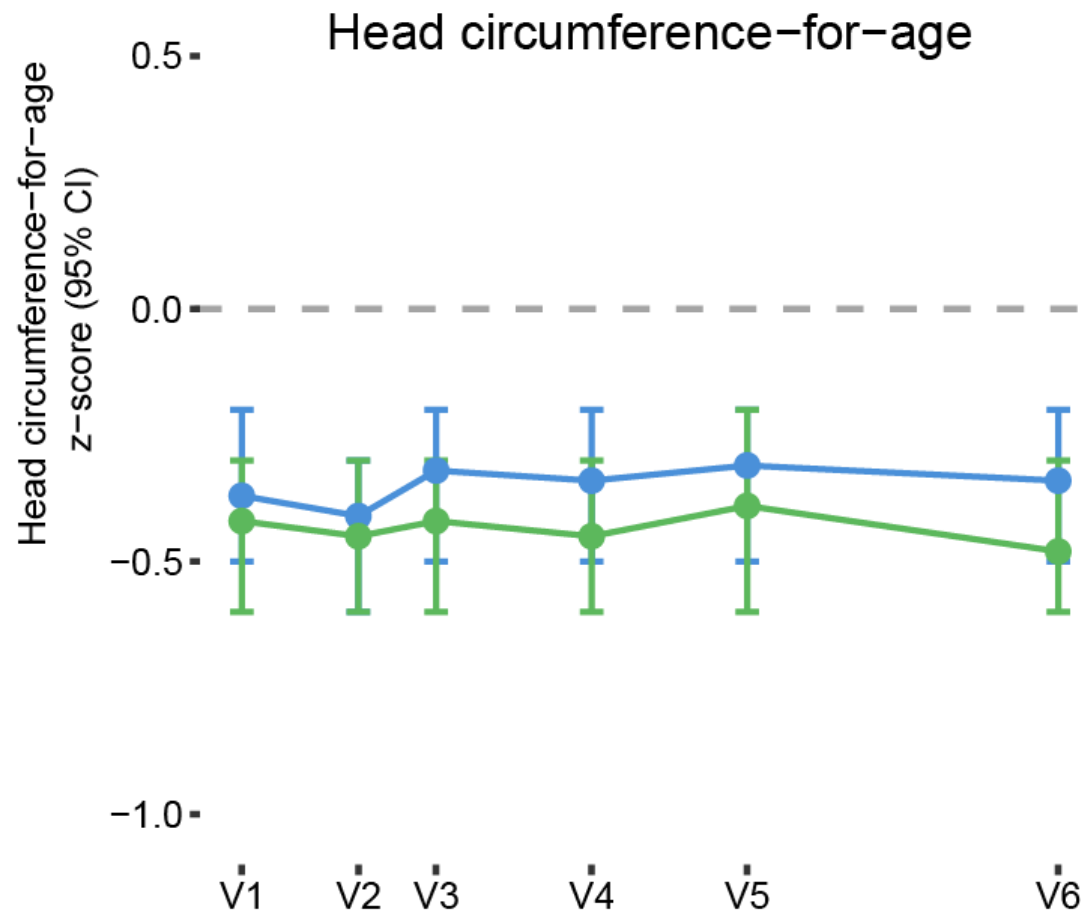
b



c

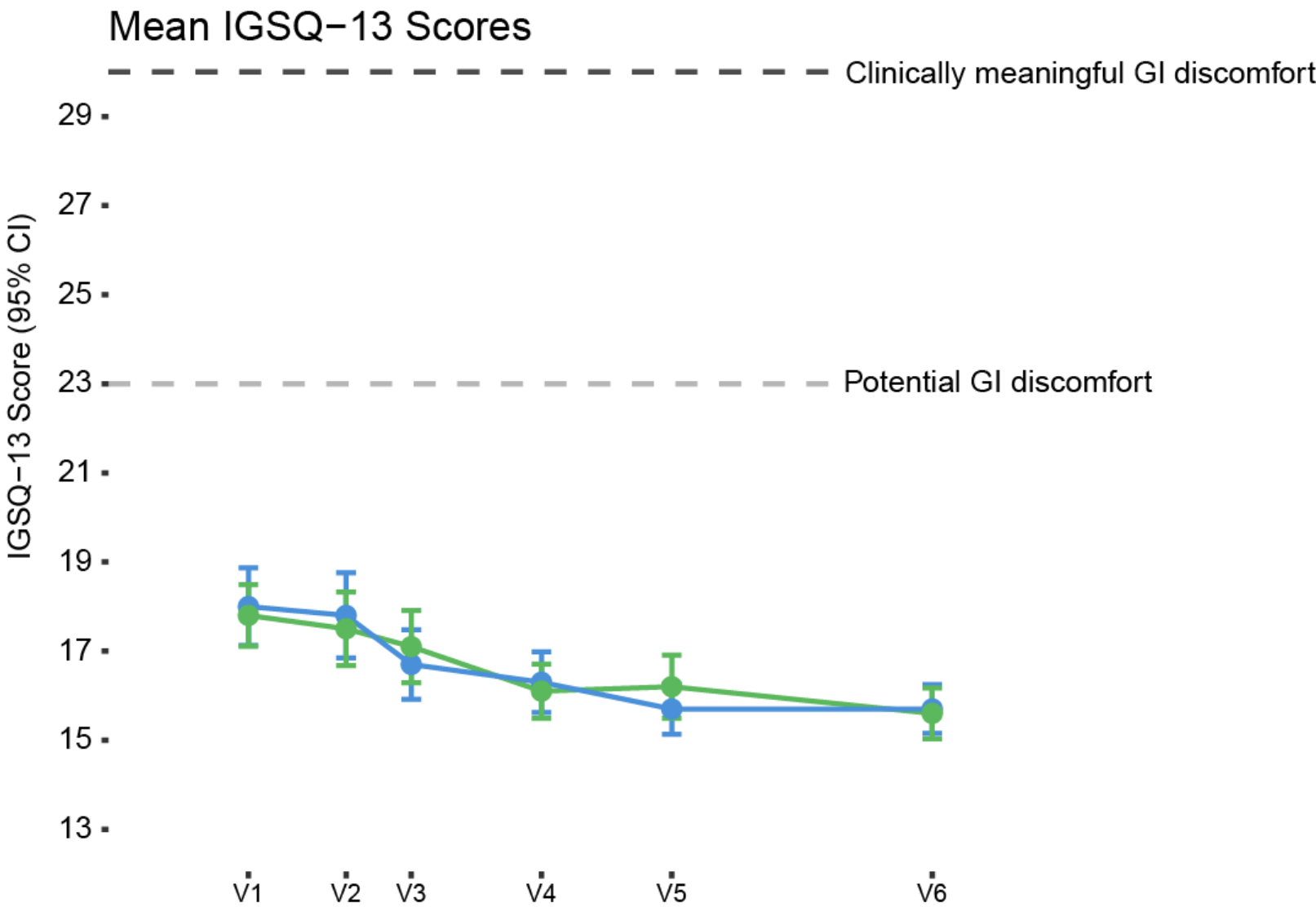


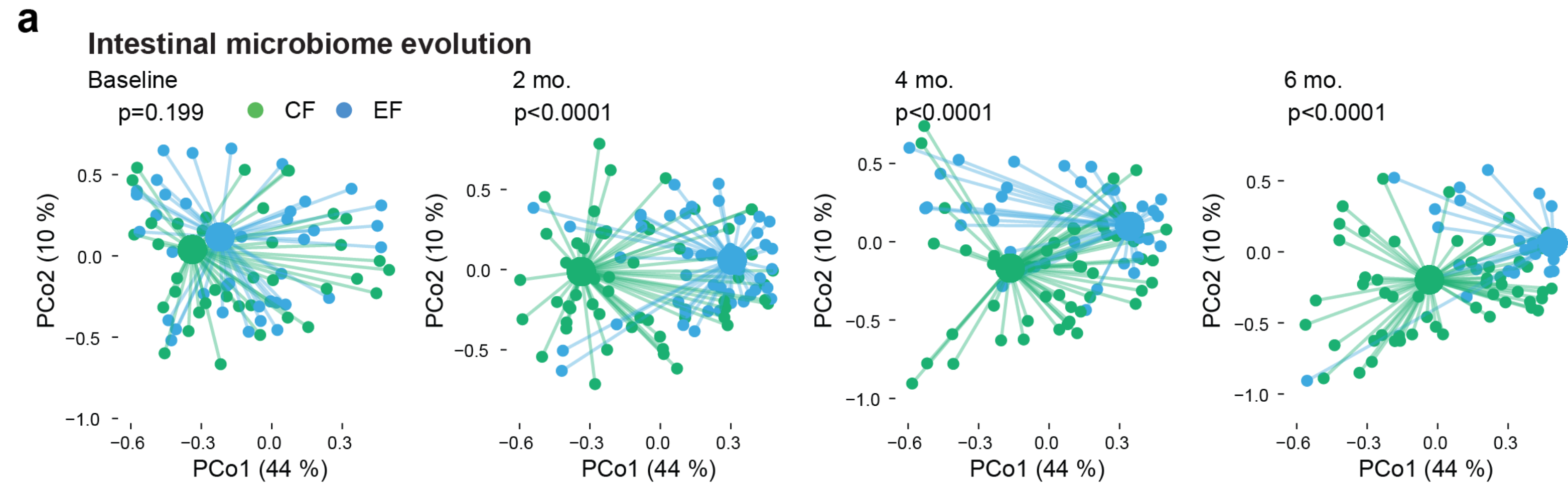
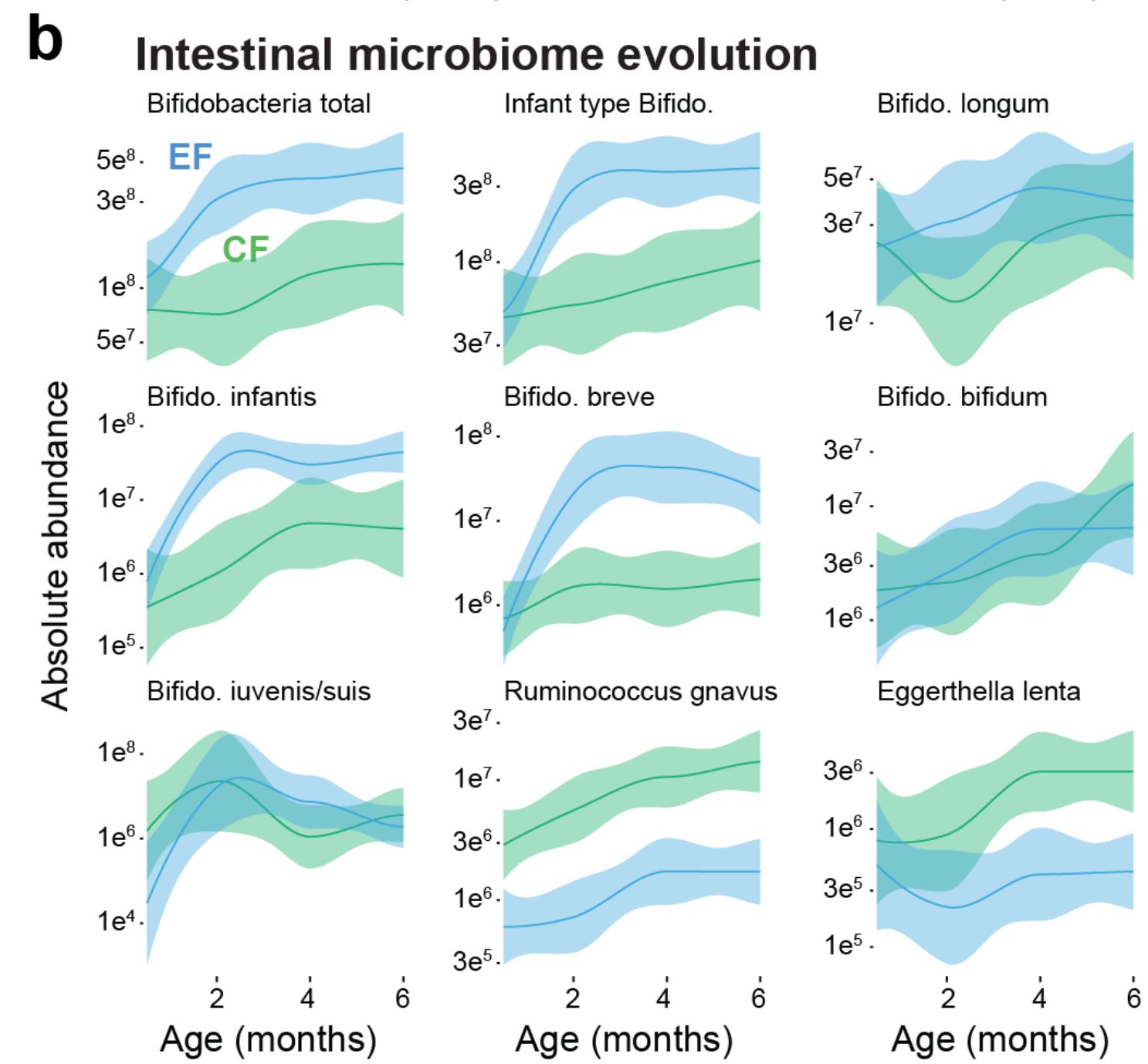
d



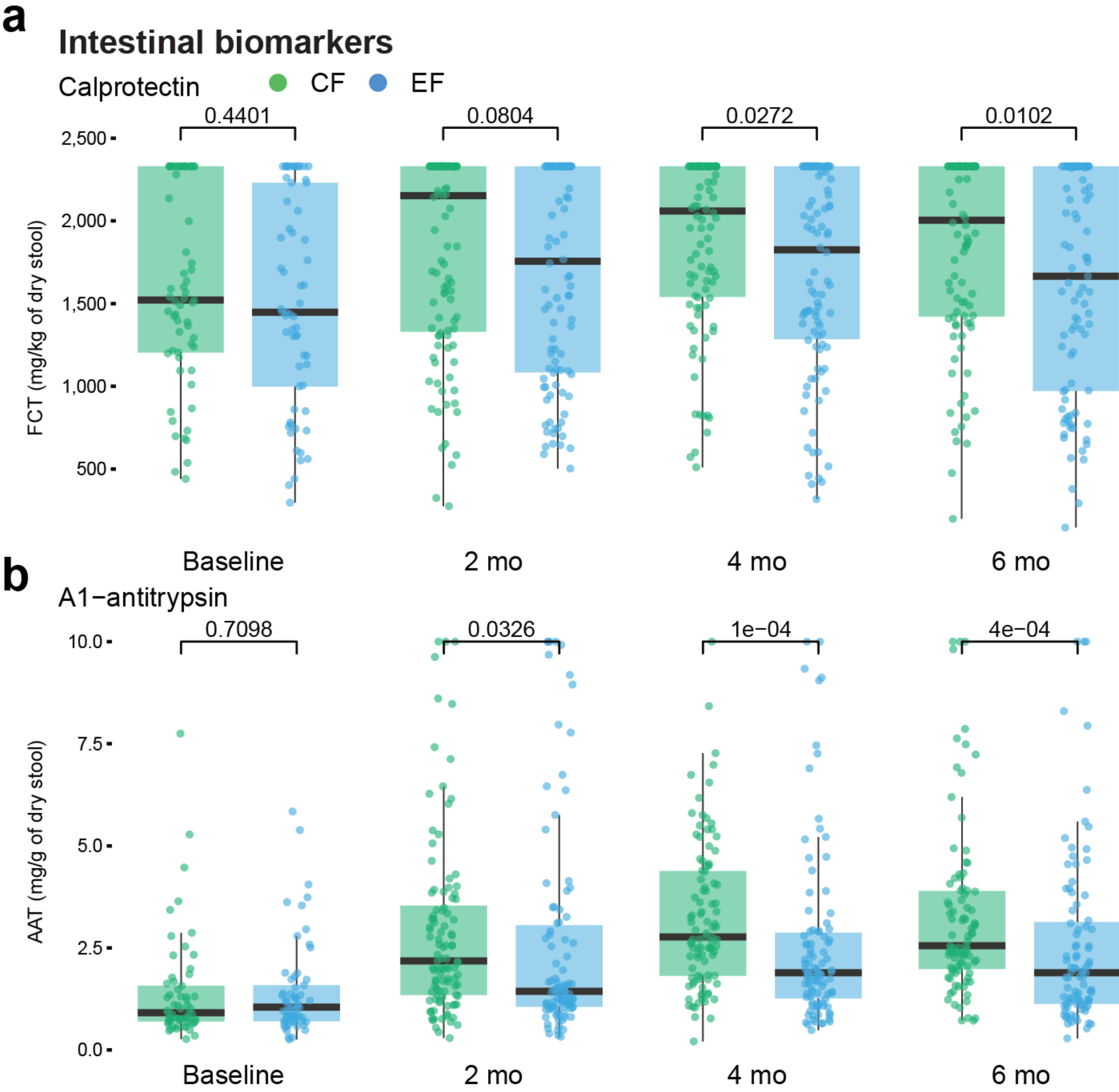
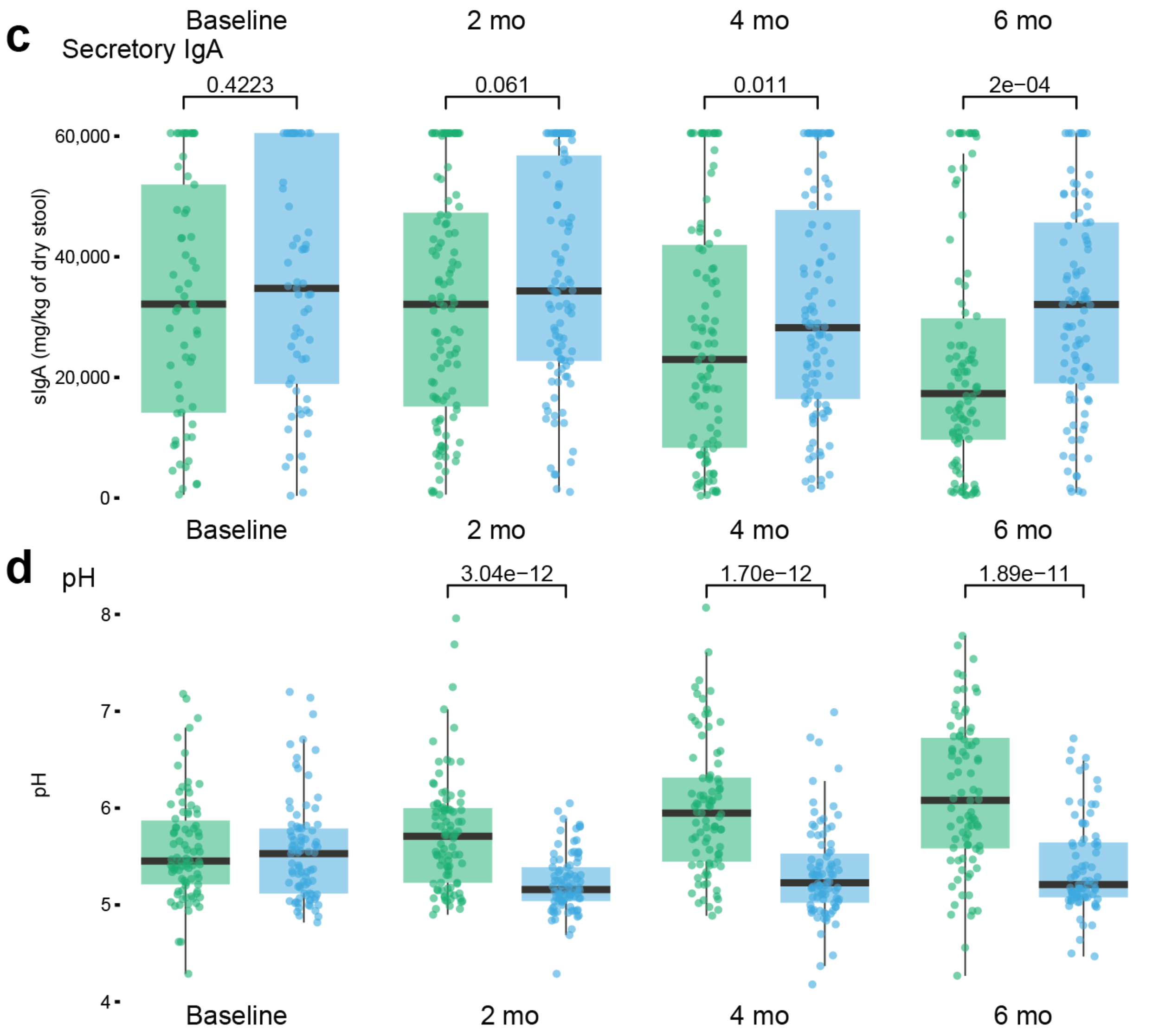
e

GI tolerance

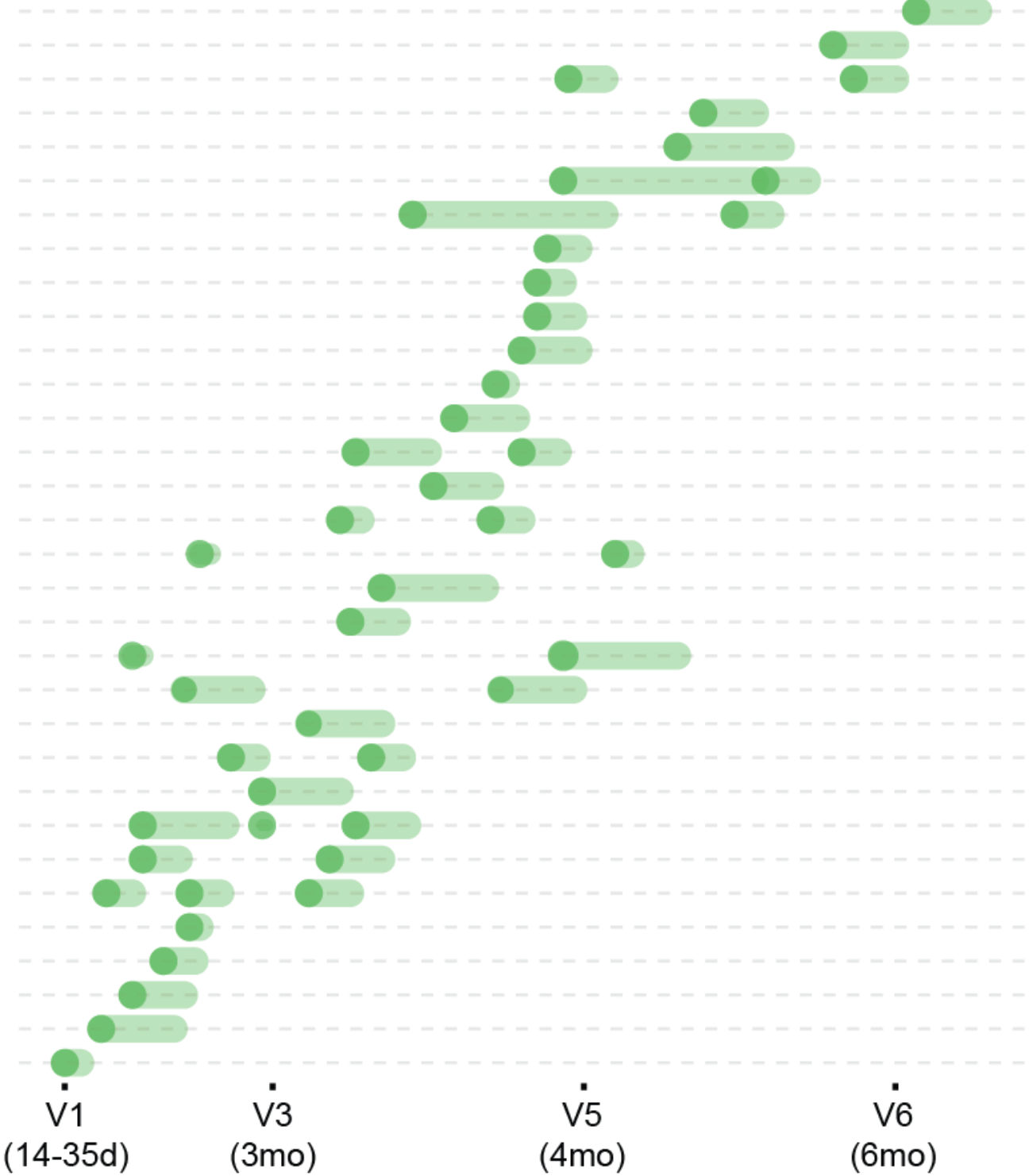




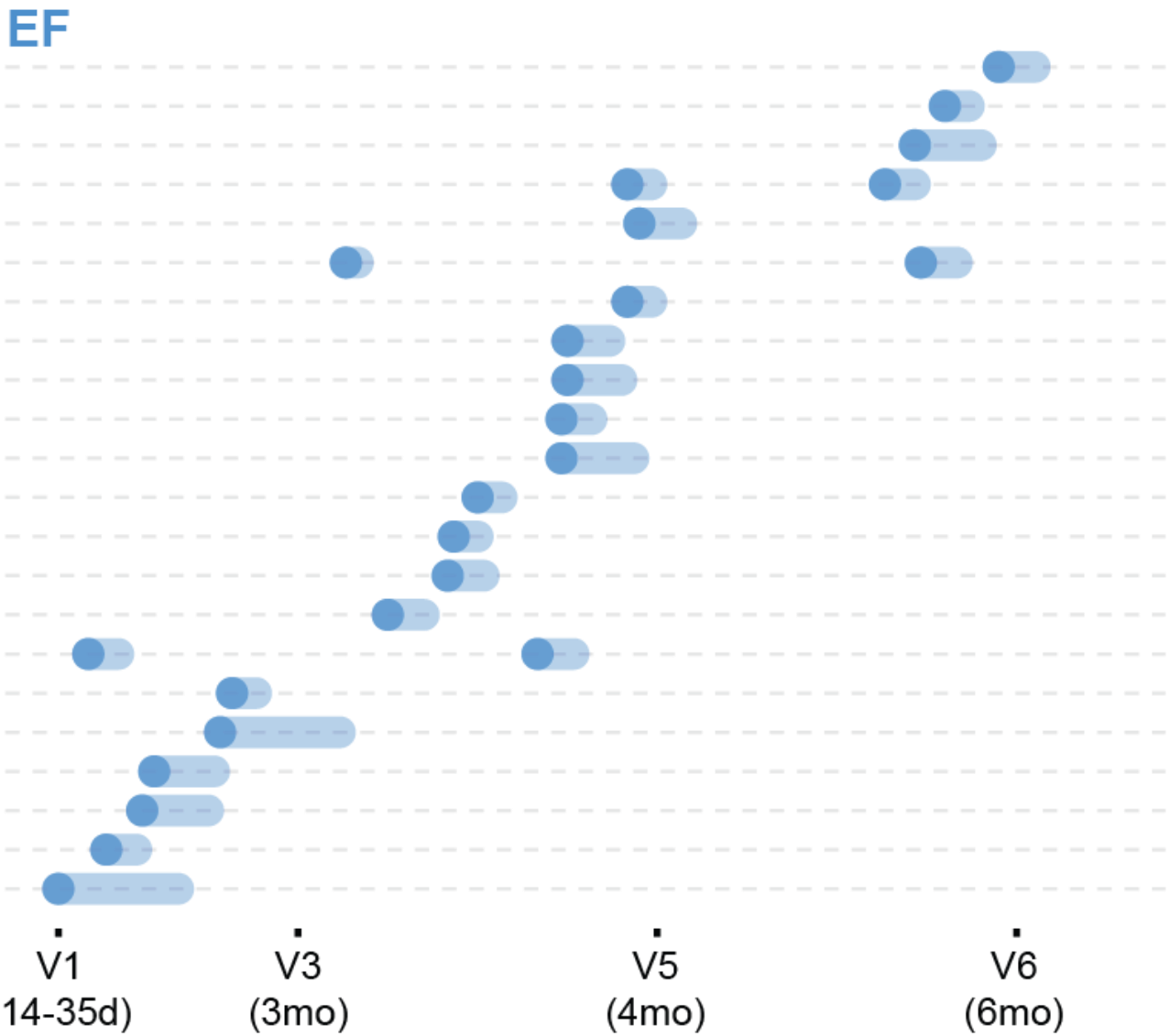
IMMUNE DEVELOPMENT – OPTIMIZING FORMULA FEEDING



a Upper respiratory tract infections
CF



b



c

Duration of URTI episodes

