Journal Club

Yasmin
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Science AAAS

Gut bacteria that prevent growth impairments transmitted by microbiota from malnourished children

Laura V. Blanton *et al.*

Science **351**, (2016);
DOI: 10.1126/science.aad3311

MICROBIOME

The right gut microbes help infants grow

Studies point the way to using microbial therapy to combat the lasting effects of poor nutrition

By **Elizabeth Pennisi**

Almost 180 million children across the globe are stunted, a severe, disabling consequence of malnutrition and repeated childhood infections that puts them at risk for cognitive impairment and disease. New studies now point to another player in stunting: the gut microbi-

of the same food typically eaten by Malawian children. Germ-free mice given the “immature” microbiomes of children with symptoms of malnourishment grew poorly, whereas mice on the same diet given “mature” microbiomes of healthy chil put on more muscle and developed s denser bones.

Francois Leulier, a biologist f

why do only some of them end up with an immature microbiome? In the *Cell* study, Gordon, graduate student Mark R. Charbonneau, and their colleagues show that breast-feeding may help the right microbes

In Malawi, studies of infant growth—and undergrowth—are revealing a key role for microbes.

Child undernutrition

- leading cause of childhood and infant mortality
- diet with low nutrient availability
- pathogenic infections
- mucosal barrier functions

- Consequences: Stunting, cognitive defects, immune dysfunction

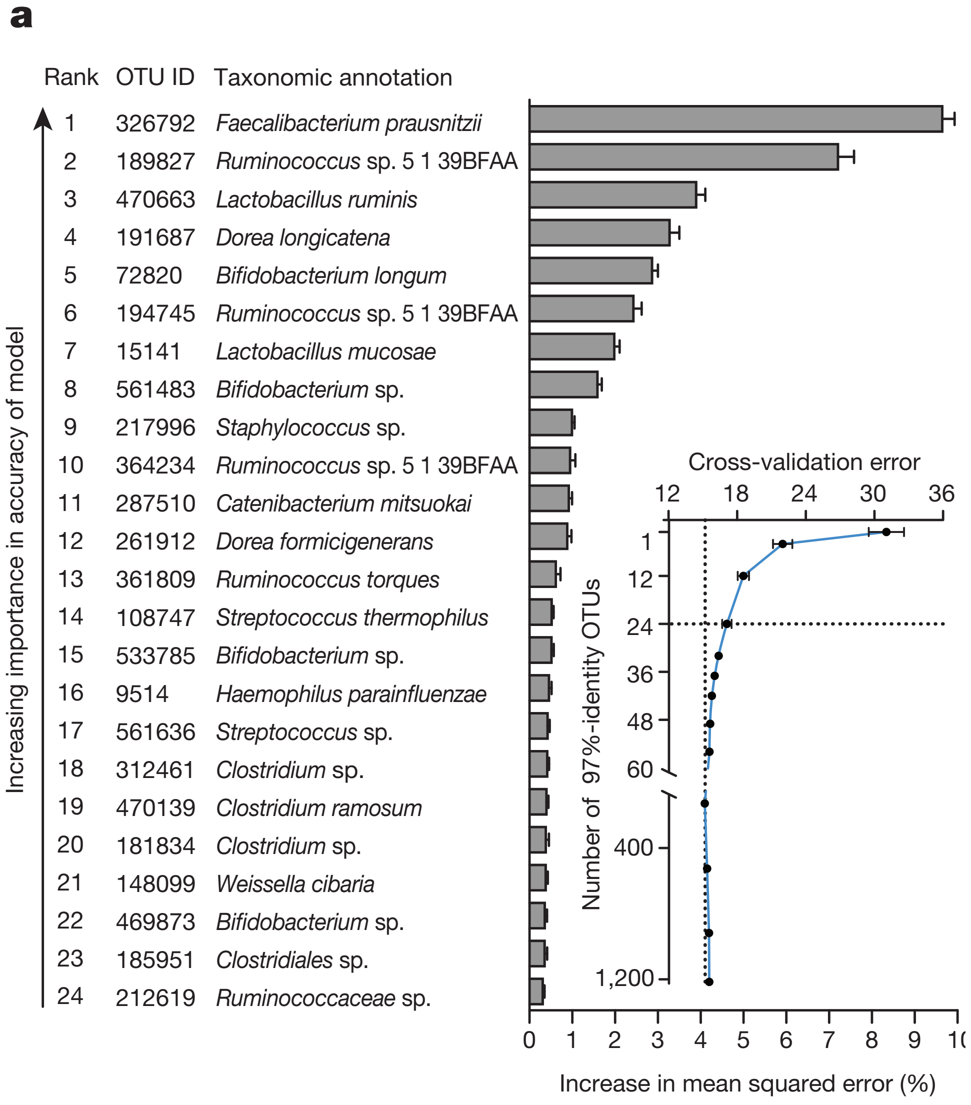
Weight-for-hight score (WHZ)
Weight-for-age score (WAZ)
Hight-for-age score (HAZ)

LETTER

doi:10.1038/nature13421

Persistent gut microbiota immaturity in malnourished Bangladeshi children

Sathish Subramanian[1], Sayeeda Huq[2], Tanya Yatsunenko[1], Rashidul Haque[2], Mustafa Mahfuz[2], Mohammed A. Alam[2], Amber Benezra[1,3], Joseph DeStefano[1], Martin F. Meier[1], Brian D. Muegge[1], Michael J. Barratt[1], Laura G. VanArendonk[1], Qunyuan Zhang[4], Michael A. Province[4], William A. Petri Jr[5], Tahmeed Ahmed[2] & Jeffrey I. Gordon[1]



Generation of a model that predicts age based on microbial composition

24 age-discriminatory taxa

Microbiota-for-age score (MAZ)

Are taxa biomarkers or mediators or healthy growth?

Protocol

Birth → 36 month

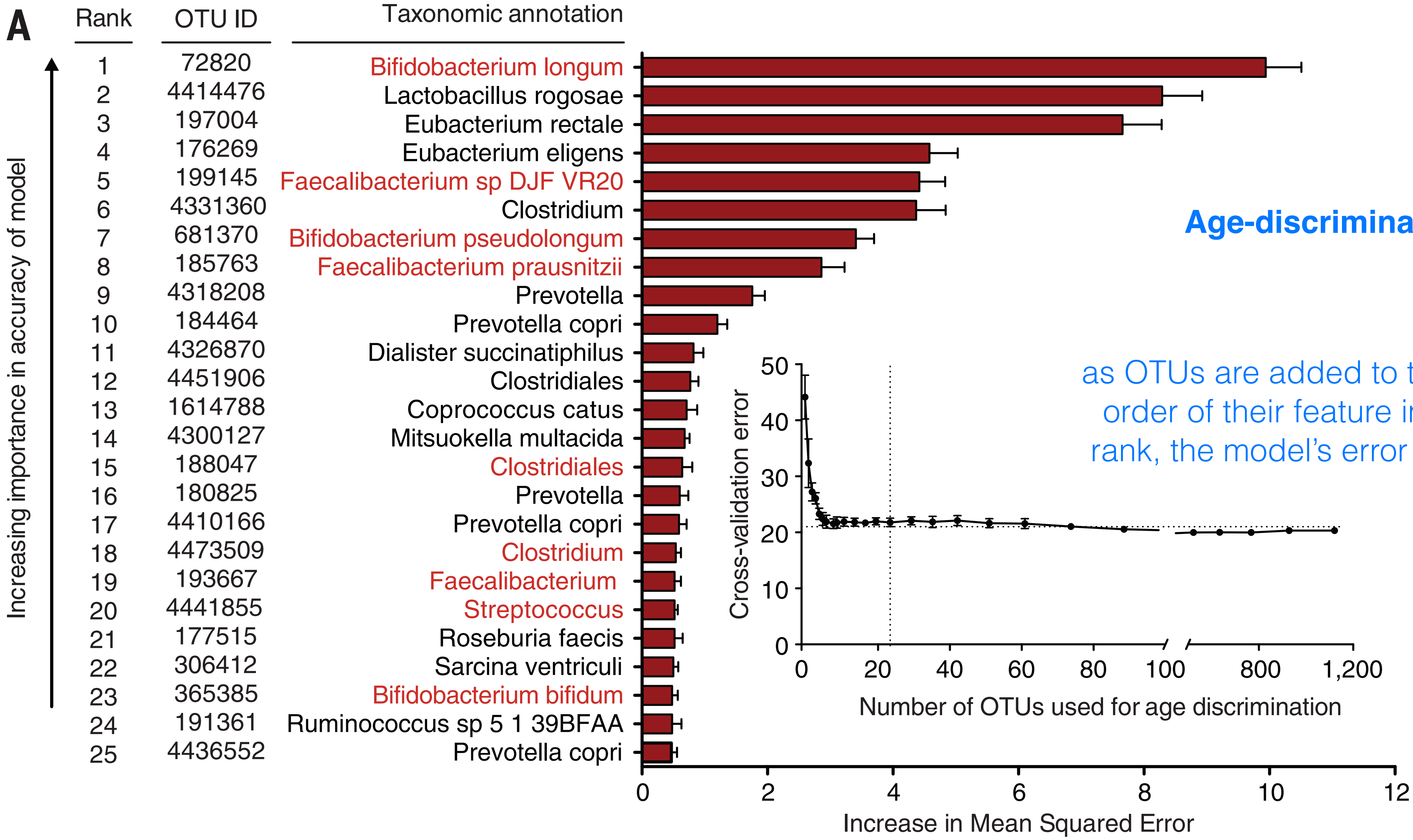
27 twins + 2 triplets

220 fecal samples → V4 16S rRNA seq and random forests

HEALTHY - TRAINING SET

Machine learning technique **(random forests - RF)** identifies species that predict age - random forests

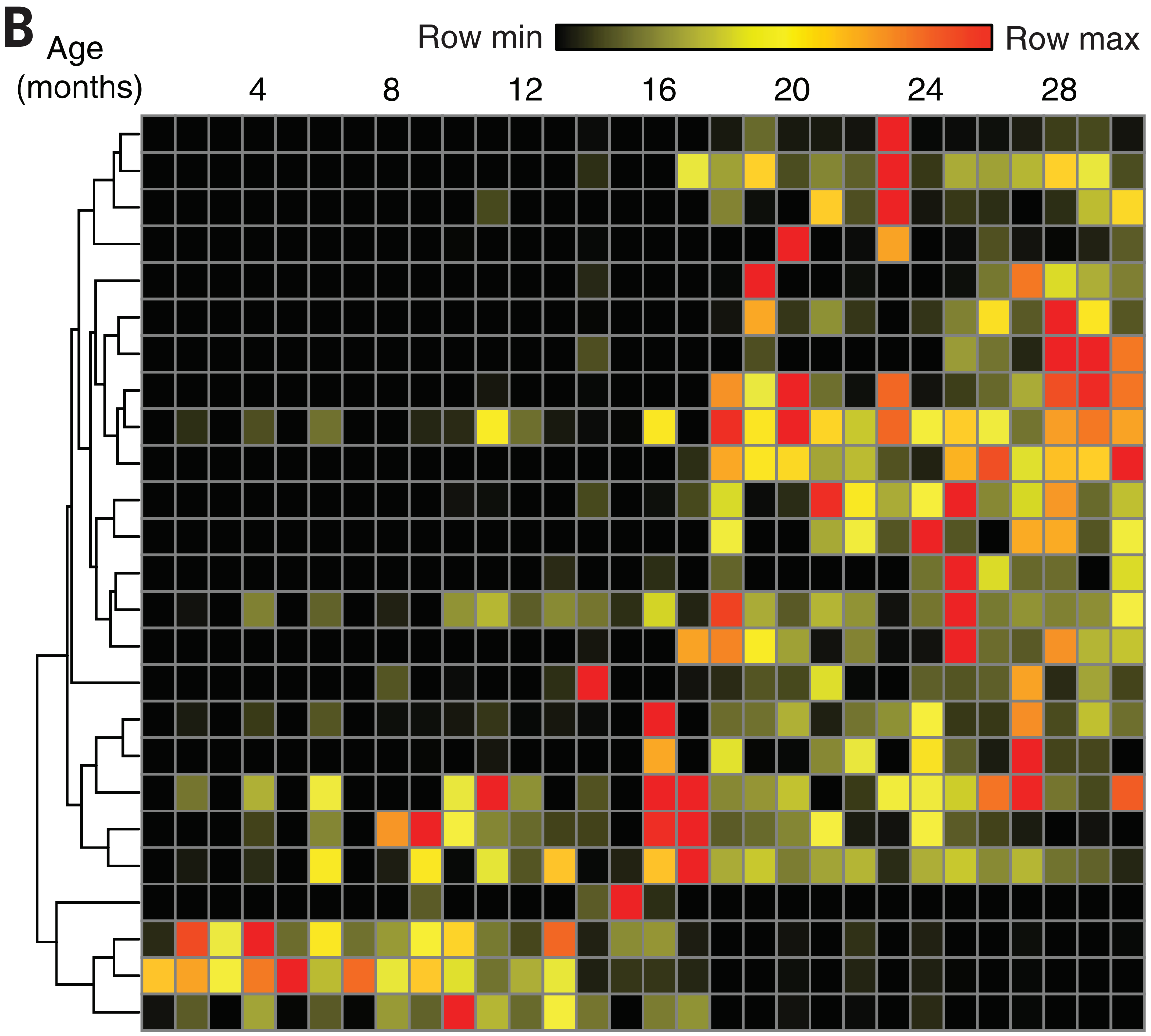
31 healthy samples



Rank	OTU ID	Taxonomic annotation
1	72820	Bifidobacterium longum
2	4414476	Lactobacillus rogosae
3	197004	Eubacterium rectale
4	176269	Eubacterium eligens
5	199145	Faecalibacterium sp DJF VR20
6	4331360	Clostridium
7	681370	Bifidobacterium pseudolongum
8	185763	Faecalibacterium prausnitzii
9	4318208	Prevotella
10	184464	Prevotella copri
11	4326870	Dialister succinatiphilus
12	4451906	Clostridiales
13	1614788	Coprococcus catus
14	4300127	Mitsuokella multacida
15	188047	Clostridiales
16	180825	Prevotella
17	4410166	Prevotella copri
18	4473509	Clostridium
19	193667	Faecalibacterium
20	4441855	Streptococcus
21	177515	Roseburia faecis
22	306412	Sarcina ventriculi
23	365385	Bifidobacterium bifidum
24	191361	Ruminococcus sp 5 1 39BFAA
25	4436552	Prevotella copri

Age-discriminatory taxa

as OTUs are added to the model in order of their feature importance rank, the model's error decreases.



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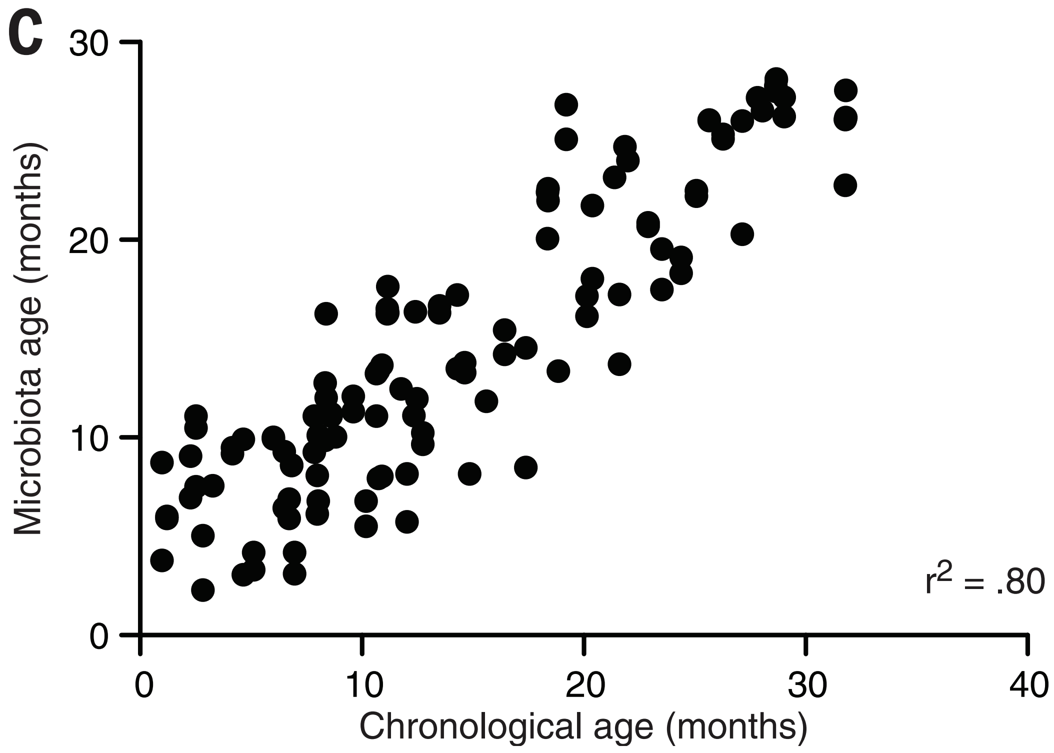
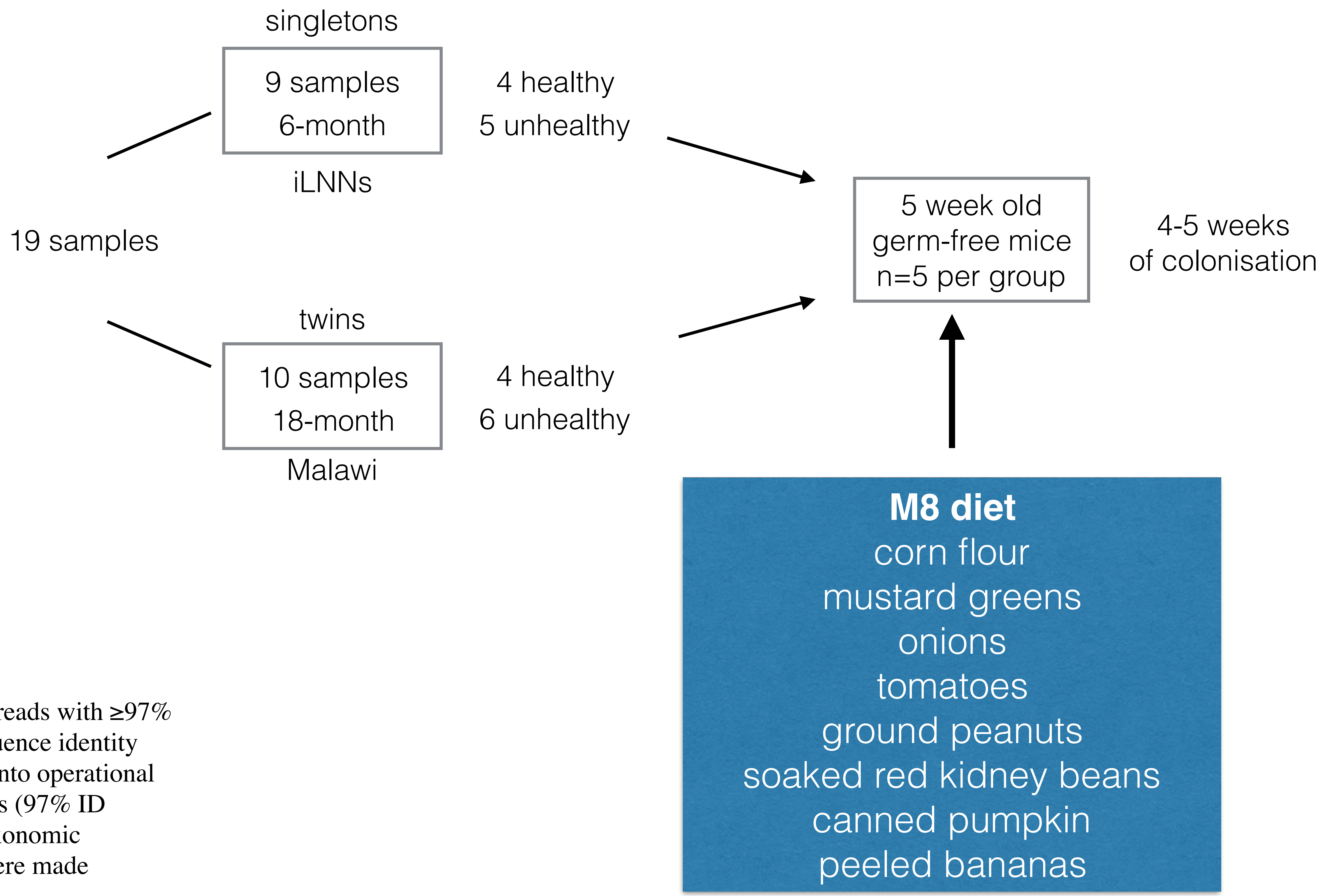
test samples (n=29) from Malawian cohort



positive MAZ with test samples from iLINS study

Protocol



19 samples

singletons

9 samples
6-month

iLNNs

4 healthy
5 unhealthy

twins

10 samples
18-month

Malawi

4 healthy
6 unhealthy

5 week old
germ-free mice
n=5 per group

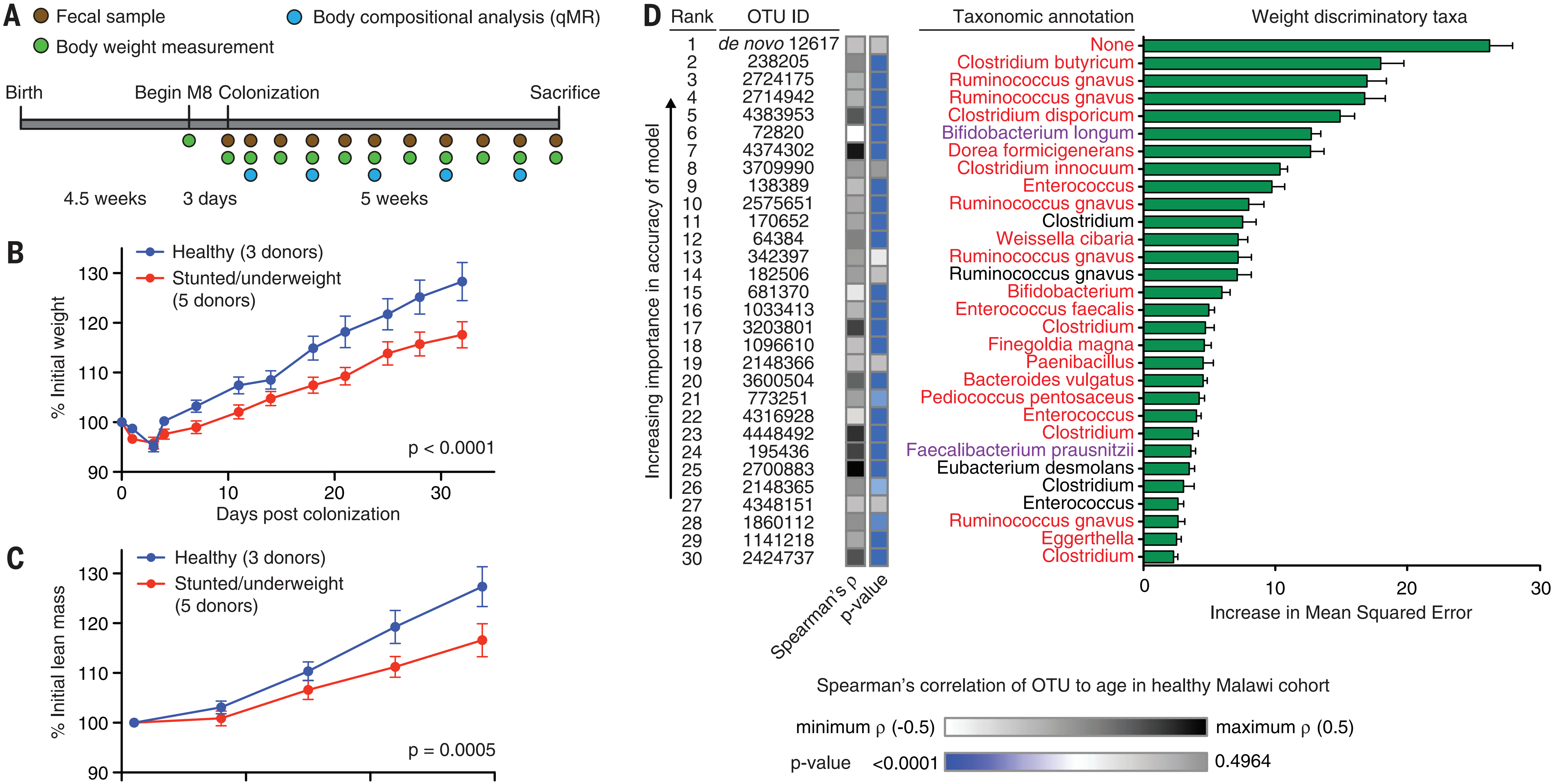
4-5 weeks
of colonisation

M8 diet
corn flour
mustard greens
onions
tomatoes
ground peanuts
soaked red kidney beans
canned pumpkin
peeled bananas

V4 16S rRNA reads with ≥97% nucleotide sequence identity were grouped into operational taxonomic units (97% ID OTUs), and taxonomic assignments were made

Causal relationship between gut microbiota and growth

Model based on weight gain

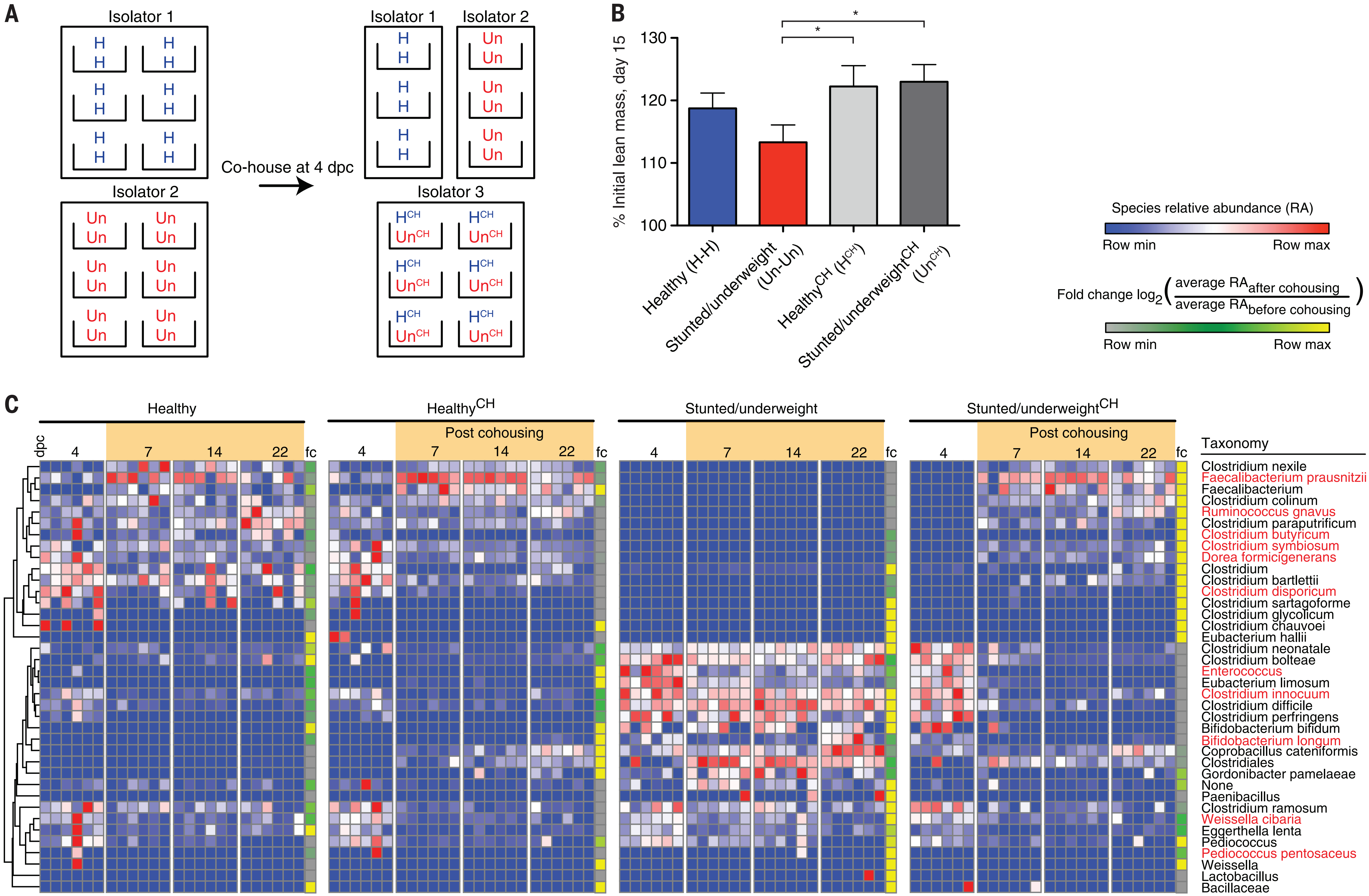


no difference in food consumption

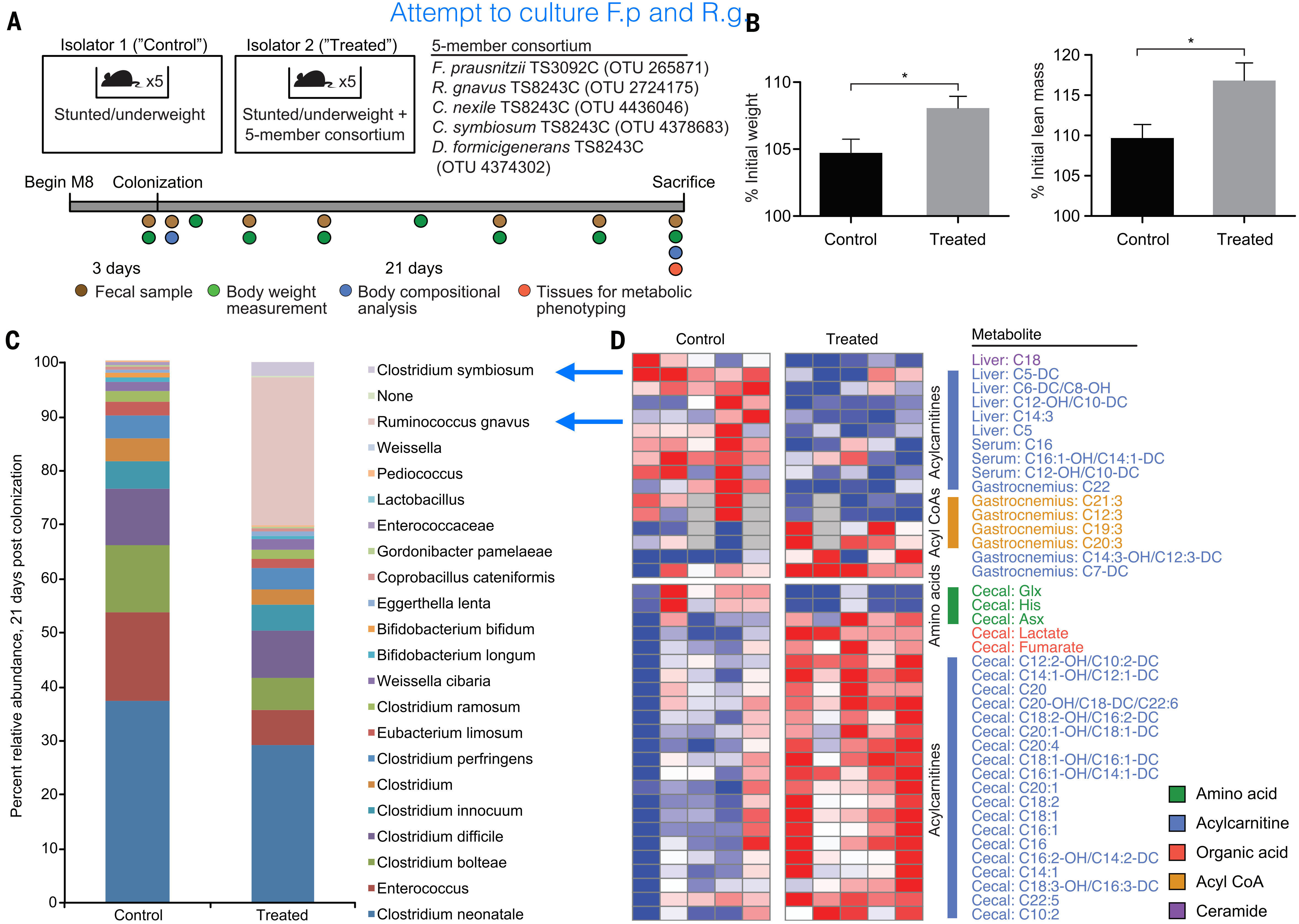
only 8 samples with transplantation efficiency >50%

Healthy microbiota is dominant over underweight microbiota

selection of 2 donor samples that transferred phenotype best

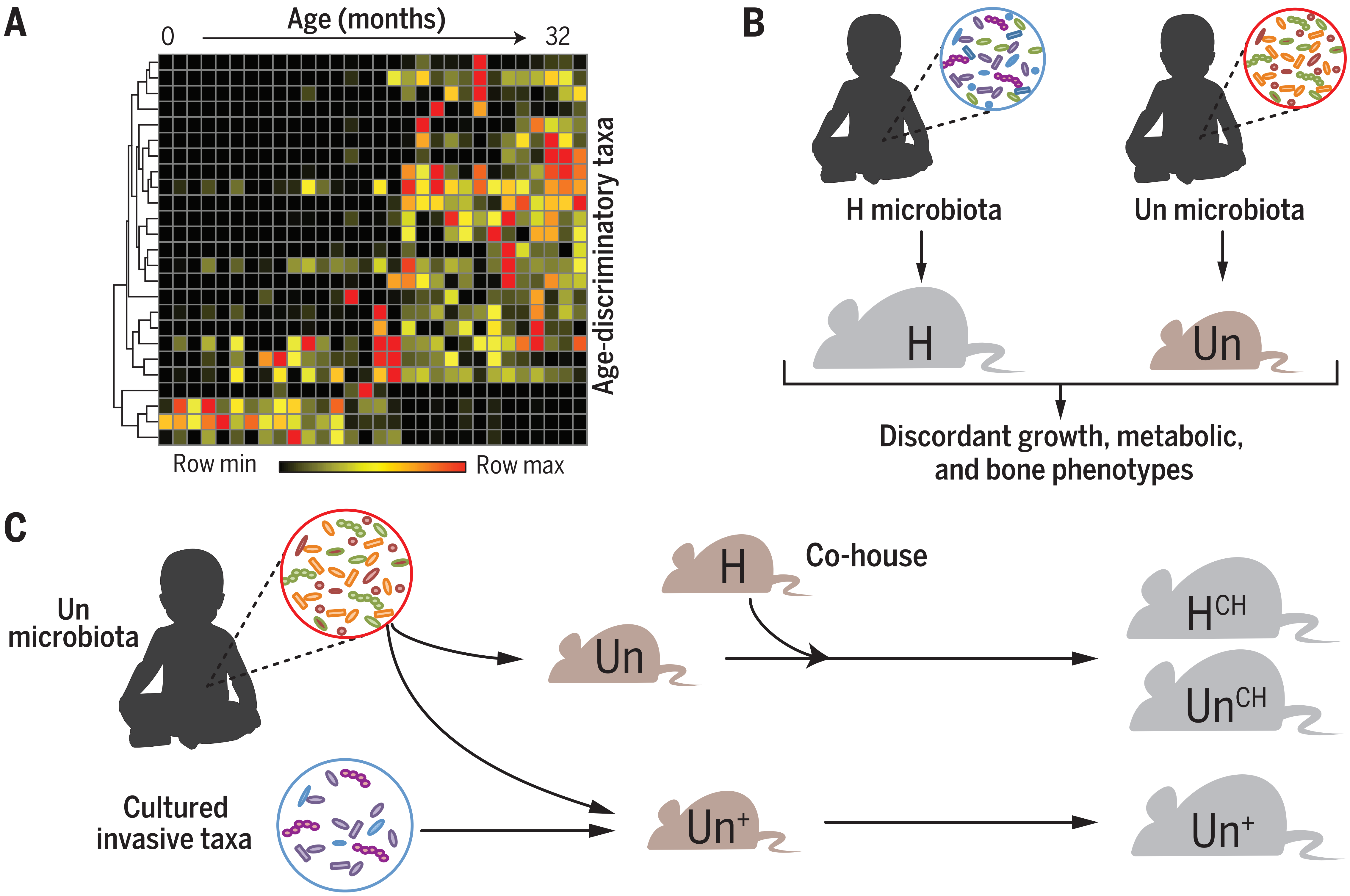


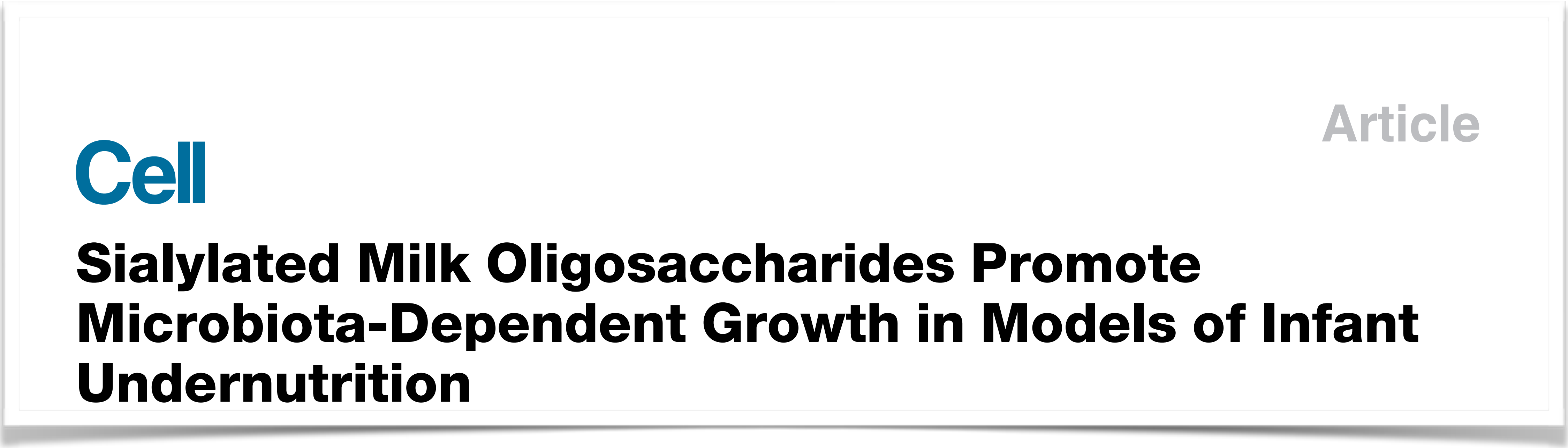
A 5-member consortium can prevent microbiota-related stunting



Attempt to culture F.p and R.g.

Summary of the study





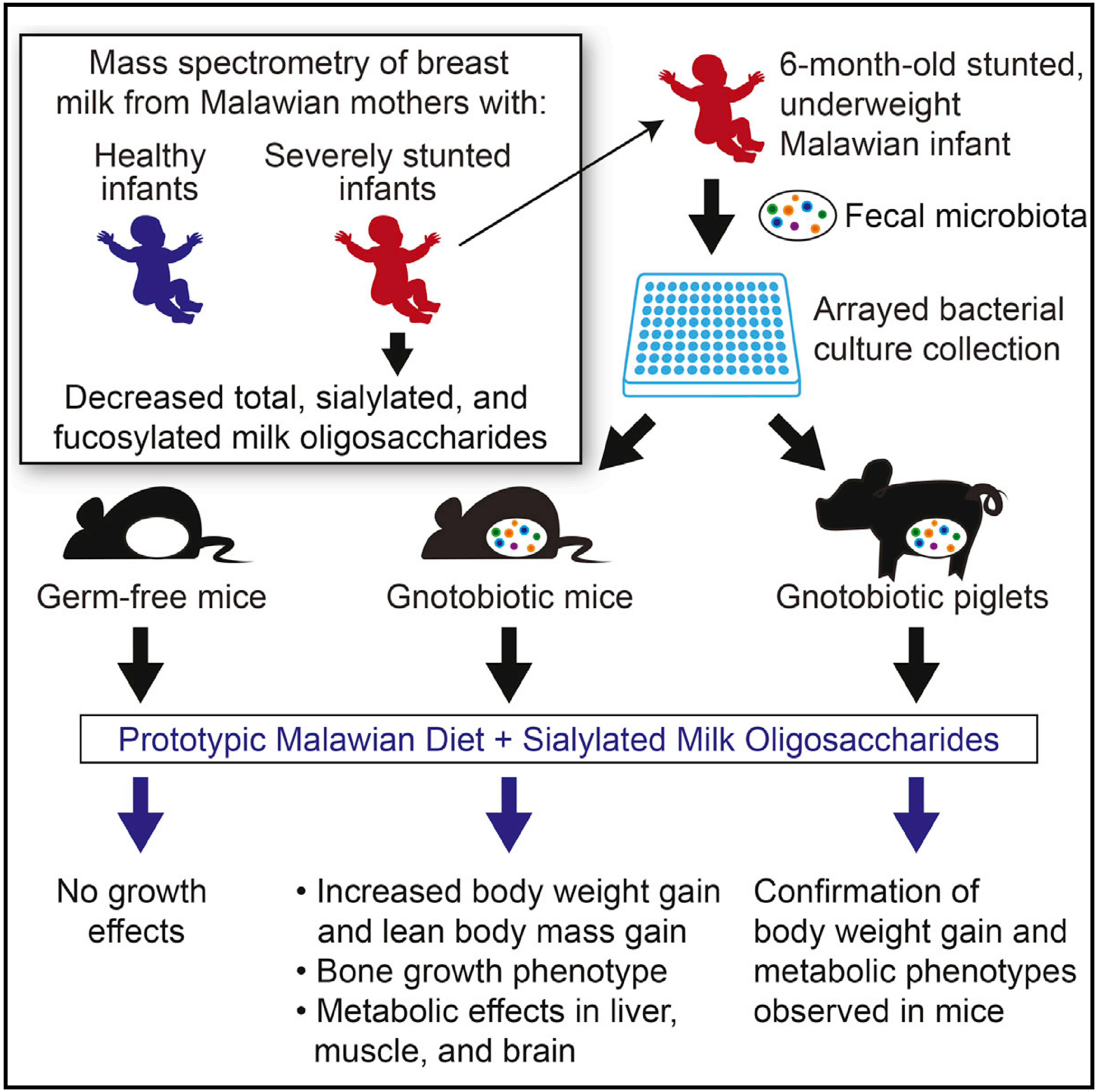
Cell

Article

Sialylated Milk Oligosaccharides Promote Microbiota-Dependent Growth in Models of Infant Undernutrition

Highlights

- Malawian mothers with undernourished infants have decreased milk oligosaccharides
- Sialylated milk sugars promote growth of animals colonized with infant microbiota
- Growth promotion does not occur with provision of inulin or in germ-free mice
- Sialylated oligosaccharides impact liver, muscle, and brain metabolism



Mass spectrometry of breast milk from Malawian mothers with:

Healthy infants

Severely stunted infants

Decreased total, sialylated, and fucosylated milk oligosaccharides

6-month-old stunted, underweight Malawian infant

Fecal microbiota

Arrayed bacterial culture collection

Germ-free mice

Gnotobiotic mice

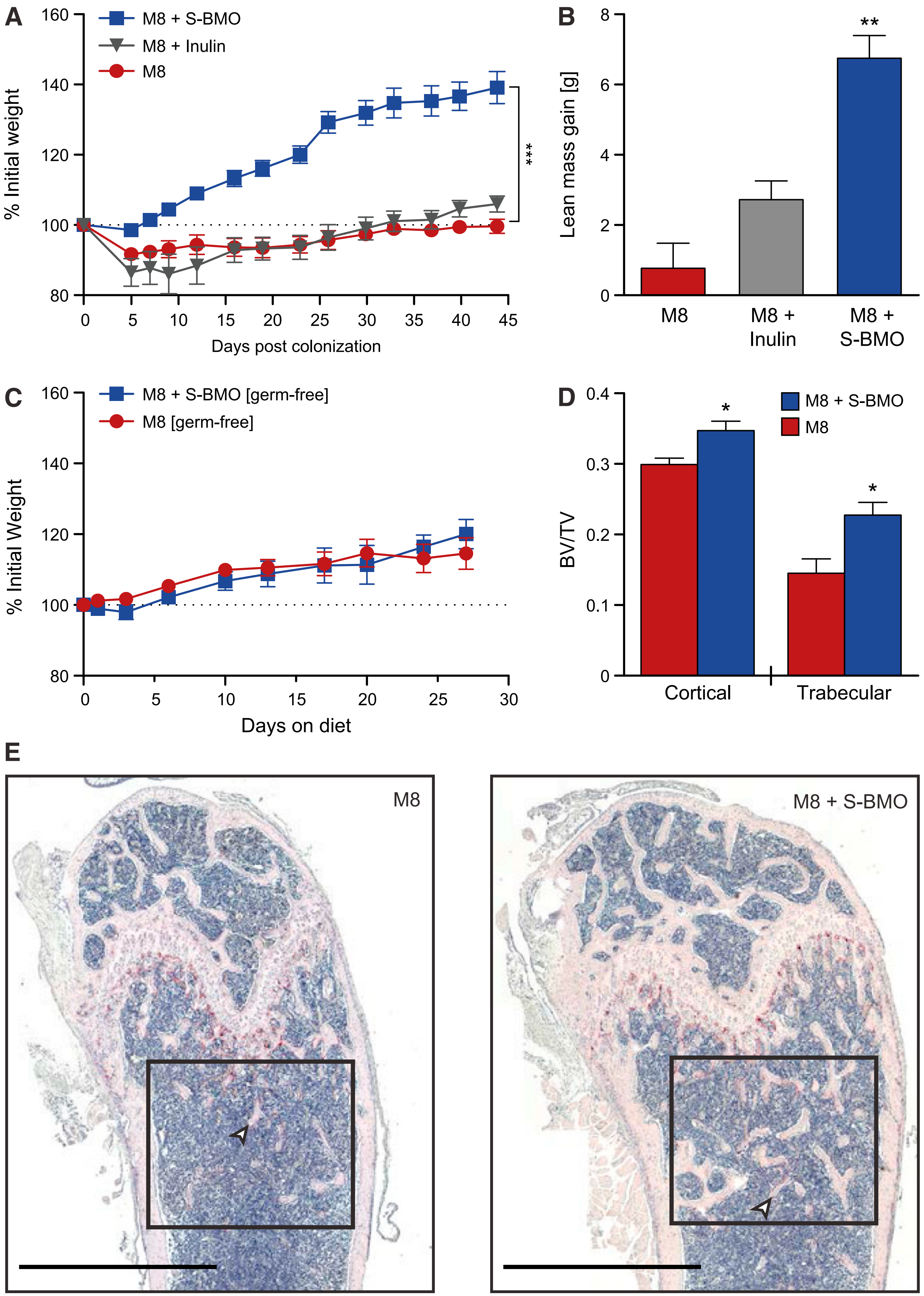
Gnotobiotic piglets

Prototypic Malawian Diet + Sialylated Milk Oligosaccharides

No growth effects

- Increased body weight gain and lean body mass gain
- Bone growth phenotype
- Metabolic effects in liver, muscle, and brain

Confirmation of body weight gain and metabolic phenotypes observed in mice


A
160
140
120
100
80
% Initial weight
M8 + S-BMO
M8 + Inulin
M8
***
0
5
10
15
20
25
30
35
40
45
Days post colonization
B
8
6
4
2
0
Lean mass gain [g]
**
M8
M8 + Inulin
M8 + S-BMO
C
160
140
120
100
80
% Initial Weight
M8 + S-BMO [germ-free]
M8 [germ-free]
0
5
10
15
20
25
30
Days on diet
D
0.4
0.3
0.2
0.1
0
BV/TV
M8 + S-BMO
M8
*
*
Cortical
Trabecular
E
M8
M8 + S-BMO

Lyon