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INTERNATIONAL UNION OF NUTRITIONAL SCIENCES

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Human Microbiome, Sharing our diet: an Asian Perspective

(Disclosure: There is no conflict of interest)

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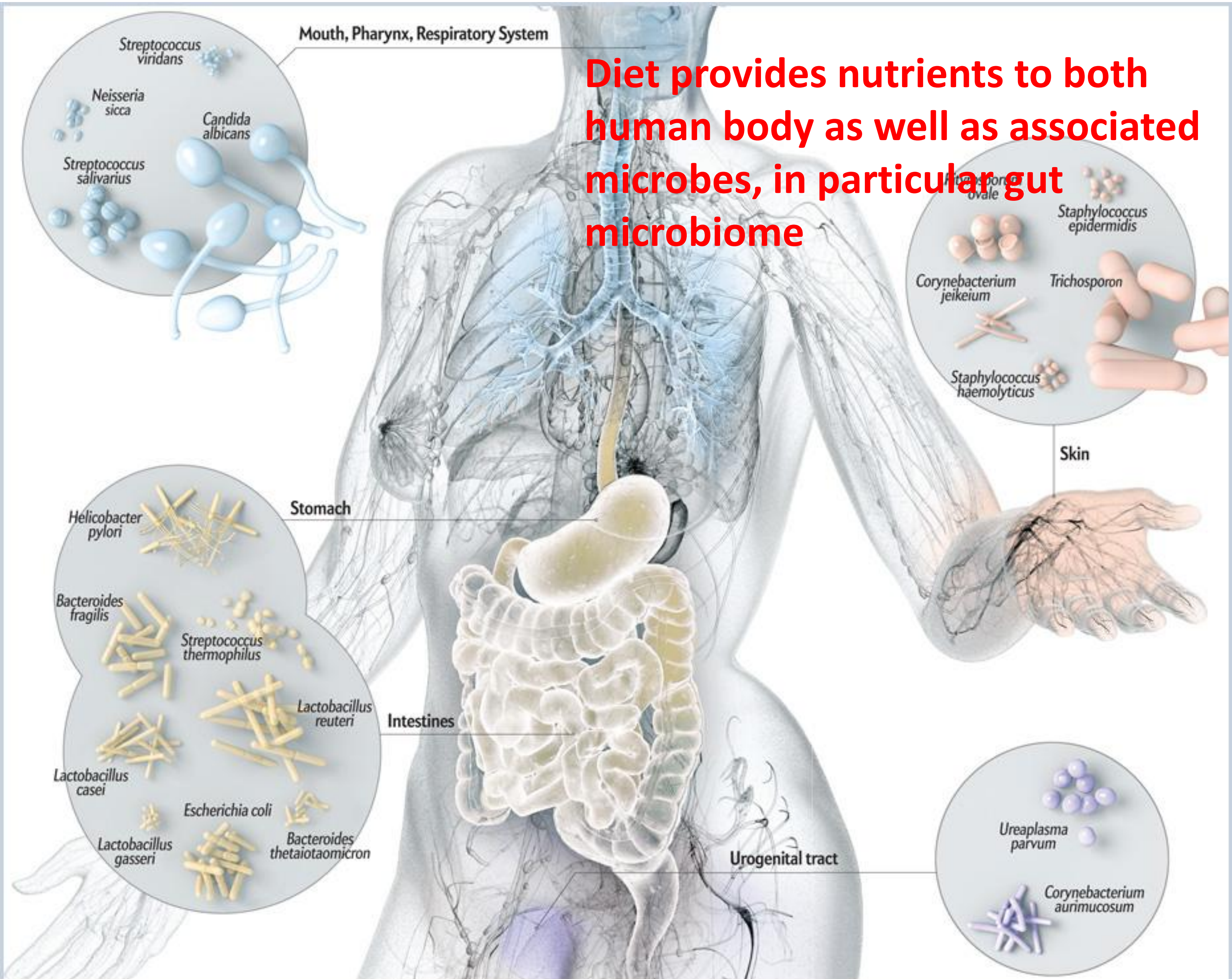
Gut microbiota deviations associated with diseases or disease risk

Subject group	Microbiota at 0 -12 months	Microbiota at 24 months
Autistic children	Higher numbers of clostridia	Higher numbers of clostridia
Wheezing infants	High clostridia	Less diverse microbiota
Infants at risk of diarrhoeal	Low bifidobacteria, high clostridia, less diverse microbiota	Less diverse microbiota
Allergic infants	At 6 months lower bifidobacteria and higher clostridia	Less lactobacilli, high numbers of aerobic bacteria, high coliforms, higher *Staphylococcus aureus* counts
Infants later developing allergic disease	Early microbiota (already at 2-3 weeks or 1 month) less bifidobacteria, and different species composition, often higher numbers of *Bifidobacterium adolescentis*, higher clostridia	Differences similar but not so pronounced, but still present even at 5 years of age (including the higher numbers of *B. adolescentis* in allergic infants
Normal infants	At 6 months high bifidobacteria, low clostridia (especially in breastfed infants)	High numbers of aerobic bacteria, high diversity, number of unculturable bacteria increase

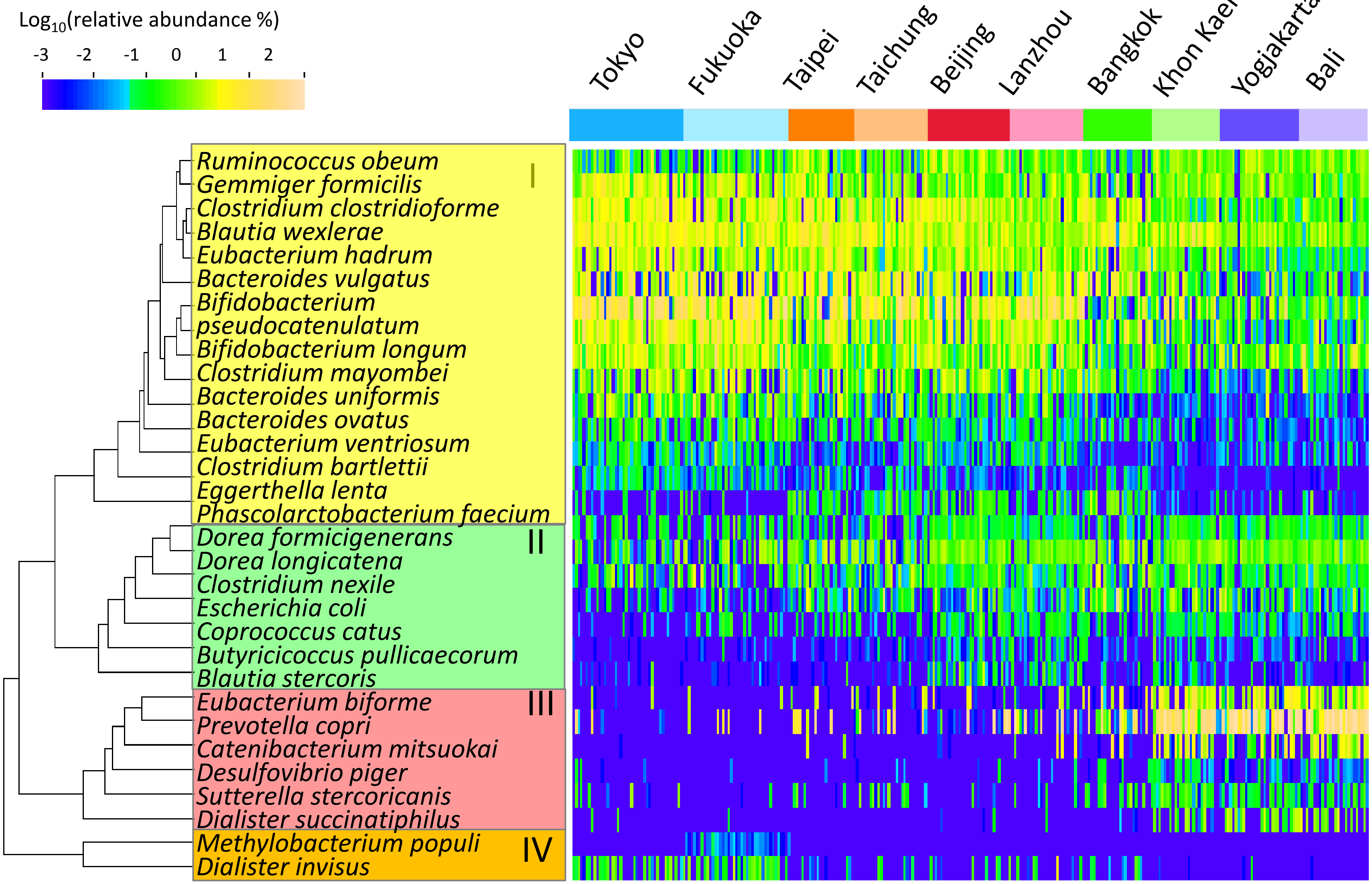
Diet provides nutrients to both human body as well as associated microbes, in particular gut microbiome



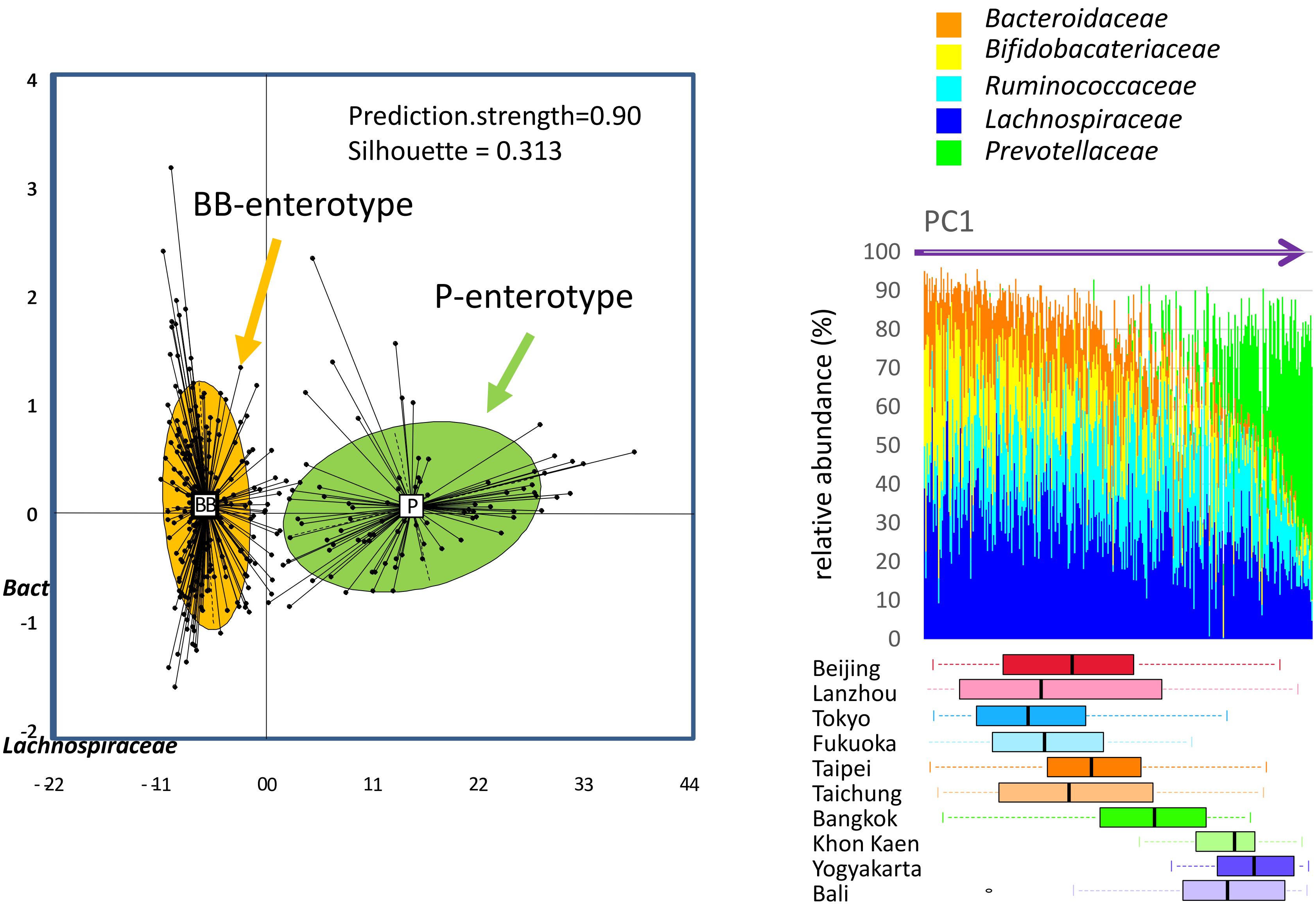
Asian Microbiome Project (AMP) Phase I initiated in 2009

Species abundance in 303 Asian children / 5 countries in Asia

"Signature of country in gut microbiota" (MiSeq sequencing)



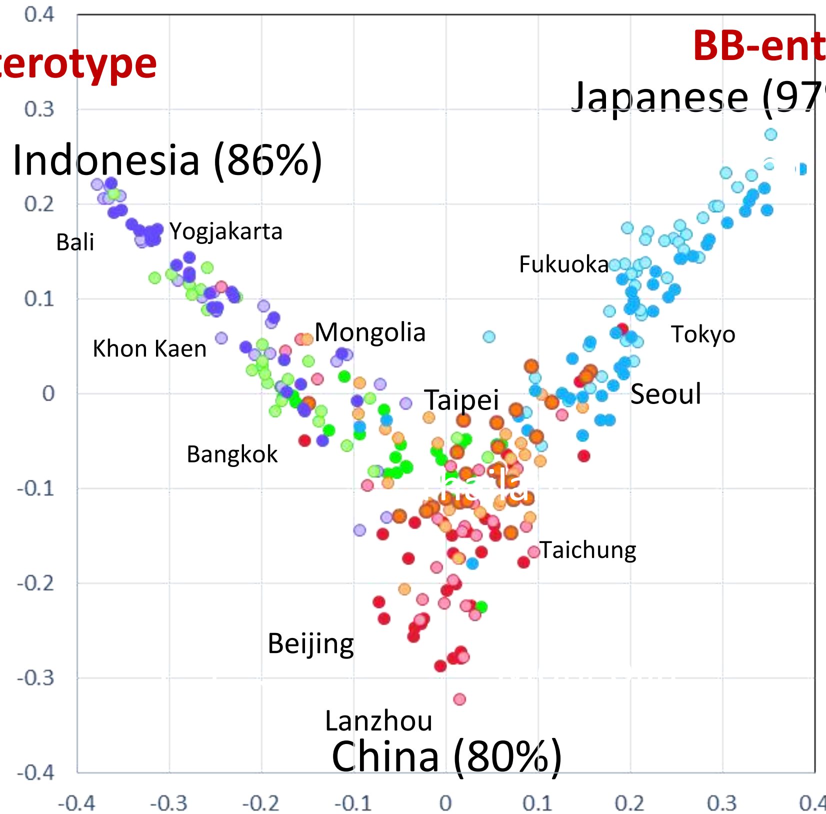
PCA and clustering of fecal microbiota of 303 Asian children, 7-11 yr (at family level)



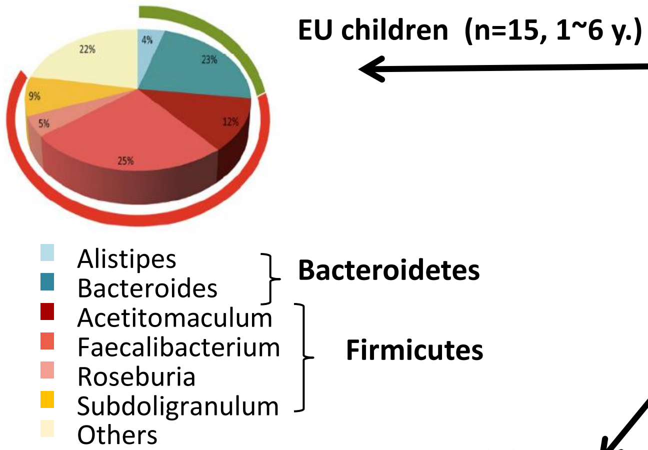
Gut microbiome of Asian children across geographical region

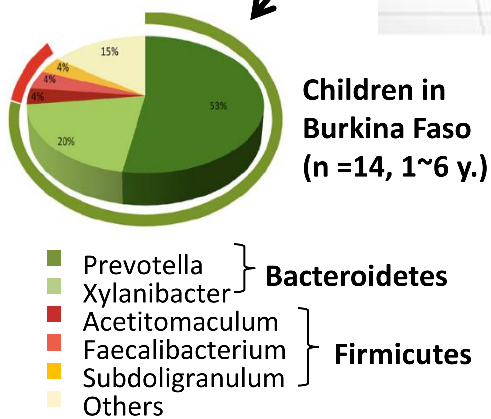
Random forest clustering of 303 Asian children

Percentage = accuracy
in random forest clustering



J Nakayama, K Watanabe, JH Jiang, K Matsuda, SH Chao, P Haryono, O La-ongkham, MA Sarwoko, IN Sujaya, L Zhao, KT Chen, YP Chen, HH Chiu, T Hidaka, NX Huang, C Kiyohara, T Kurakawa, N Sakamoto, K Sonomoto, K Tashiro, H Tsuji, MJ Chen, V Leelavatcharamas, CC Liao, S Nitisinprasert, ES Rahayu, FZ Ren, YC Tsai, YK Lee (2015) Diversity in gut bacterial community of school-age children in Asia. Scientific Reports, 5:8397/DOI 10.1038/srep08397.





Filippo, C. D. *et al.* PNAS (2010) 107, 14691-14696

Enteropes:

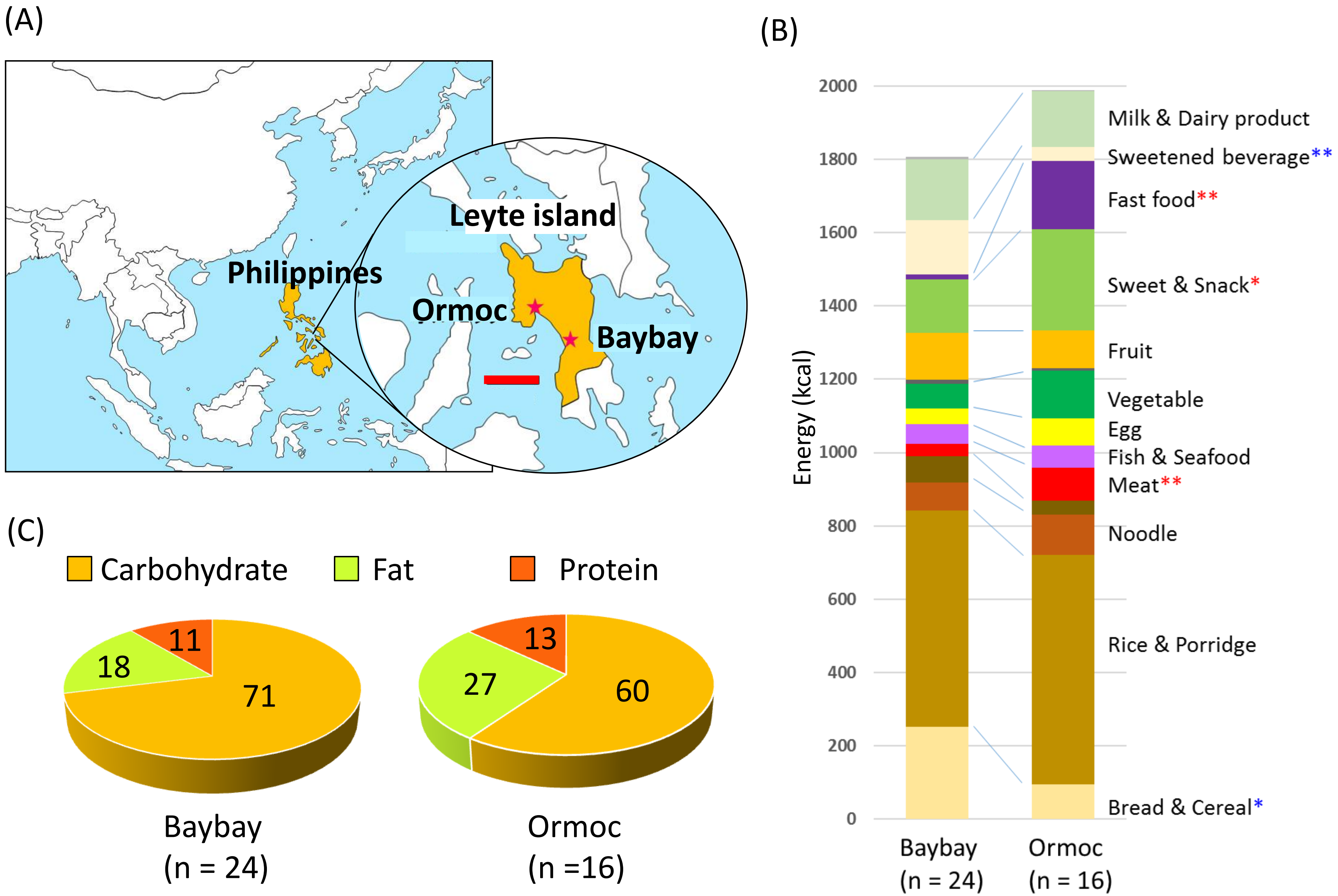
Type 1: Consumed lots of meat & saturated fat- more *Bacteroides*

Type 2: People who consumed lots of alcohol & polyunsaturated fats- *Ruminicoccus* prevailed

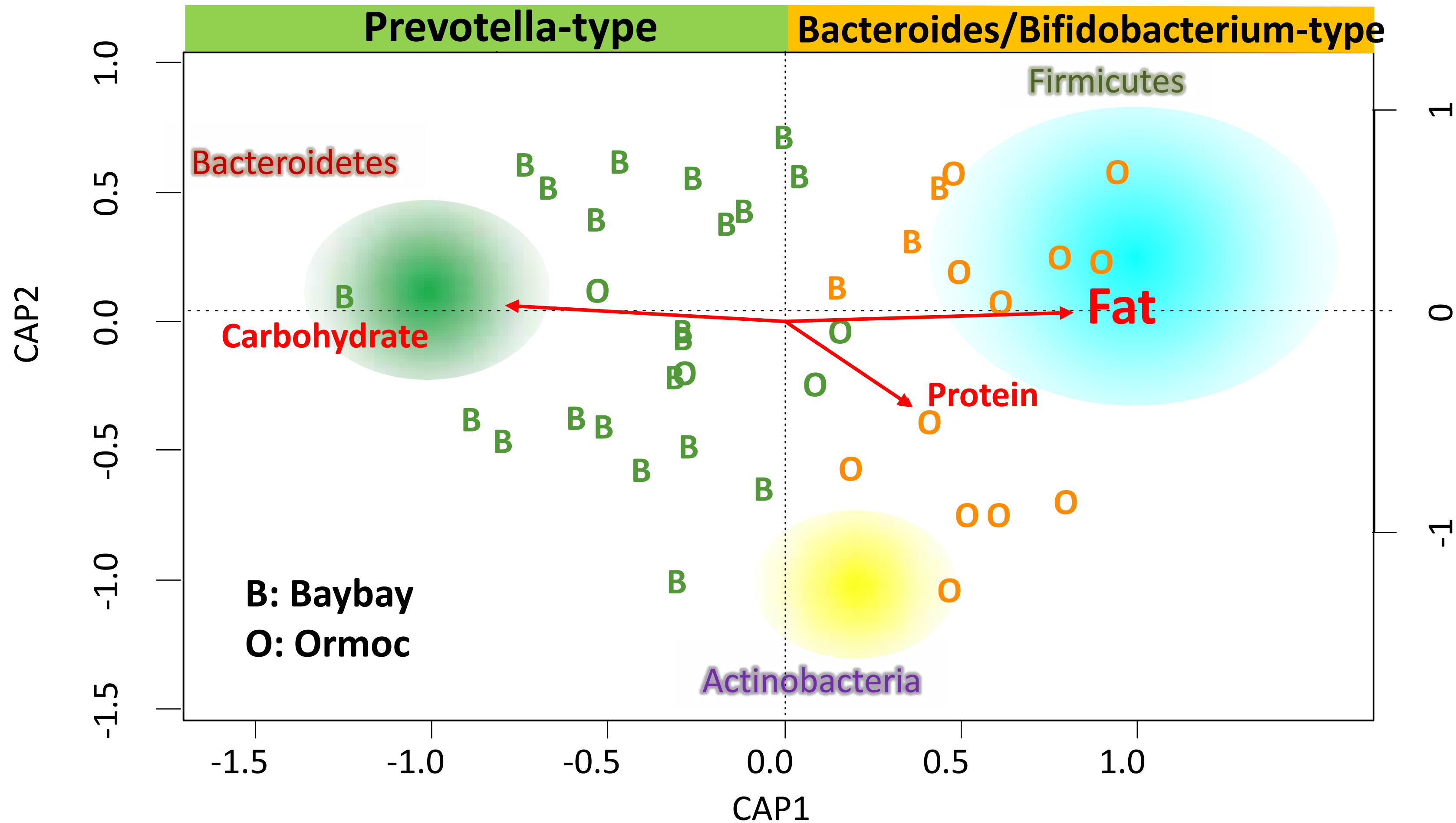
Type 3: Diet rich in carbohydrates- favored *Prevotella*

Linking long-term dietary patterns with gut microbial enterotypes
Wu GD, Chen J, Hoffman C, et al. Science 2011, DOI: 10.1126/Science 1208344

Impact of modern high-meat/-fat diet on gut microbiota in children on Leyte island Philippines

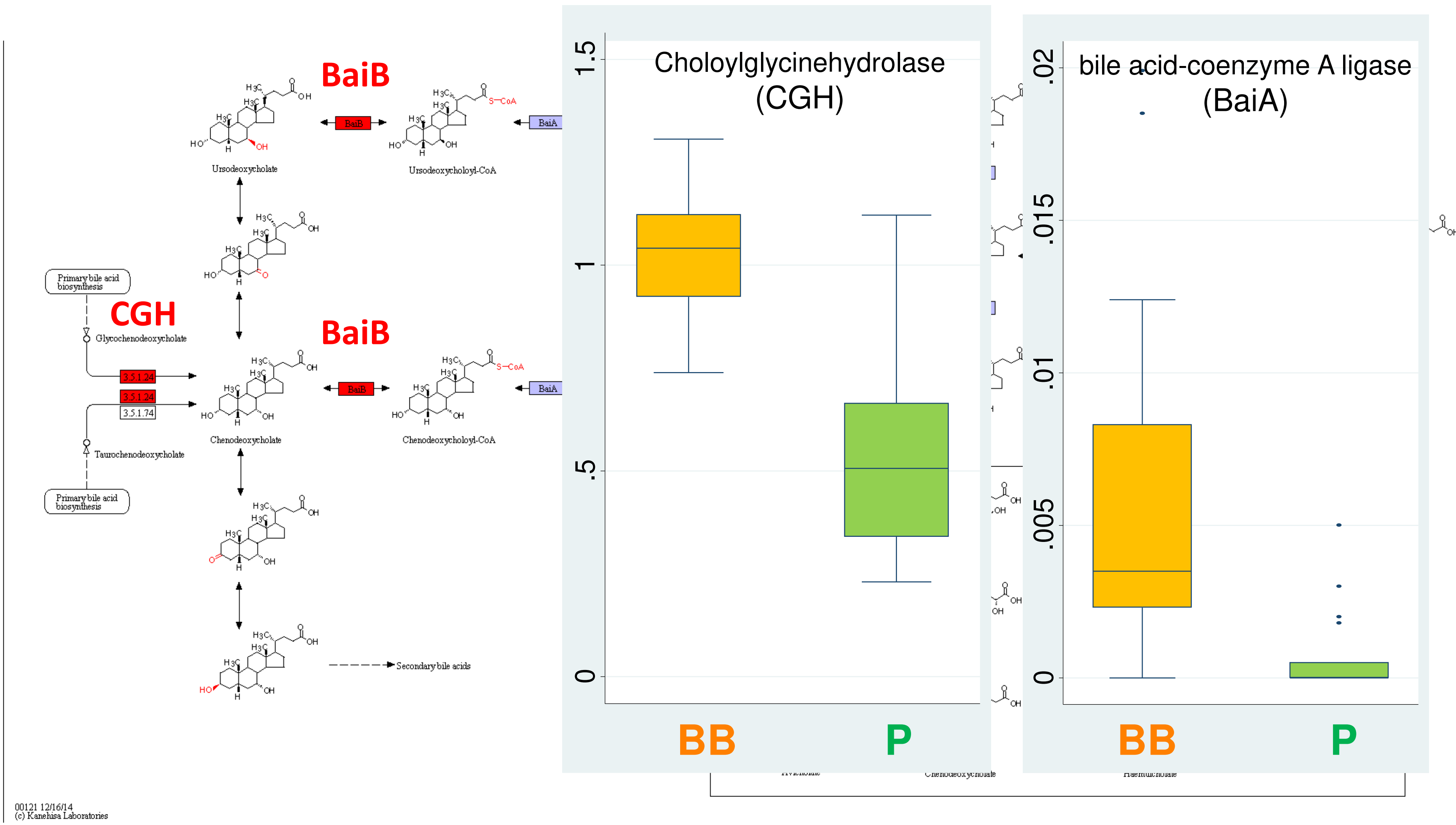


Redundancy analysis to correlate macronutrient intake with gut microbiota



Jiro Nakayama, Azusa Yamamoto, Ladie A. Palermo-Conde, Kanako Higashi, Kenji Sonomoto, Julie Tan, Yuan Kun Lee* (2017) Impact of high-fat diet on gut microbiota in children on Leyte island. Frontiers in Microbiology, doi: 10.3389/fmicb.2017.00197

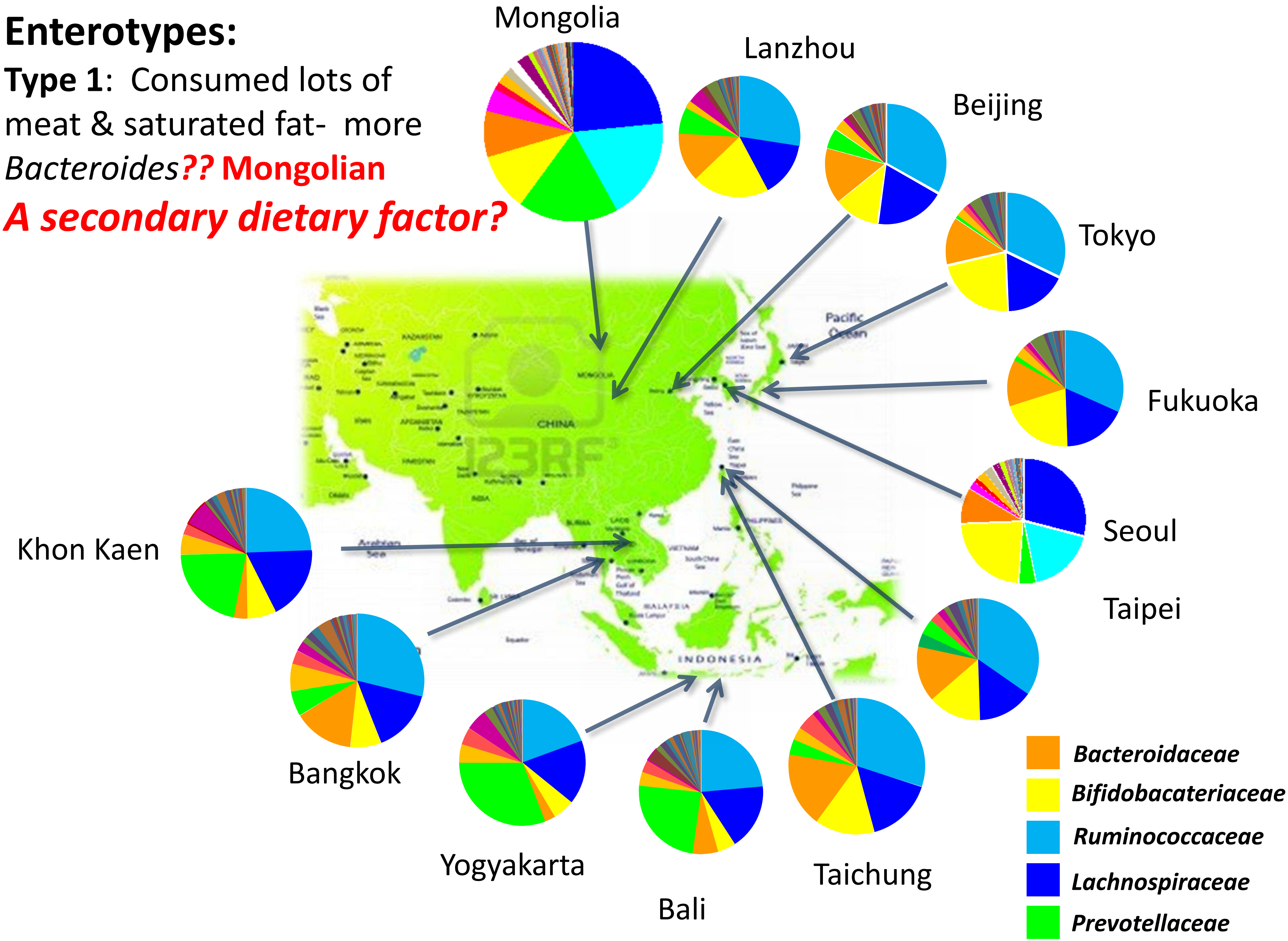
Enrichment of genes involved in bile acid metabolism in BB-enterotype



Enterotypes:

Type 1: Consumed lots of meat & saturated fat- more *Bacteroides*?? **Mongolian**

A secondary dietary factor?



	Staple carbohydrate	Insoluble fibre (g/100 g)	Amylose (% total starch)	Starch fraction (% dry matter)		
			Amylose	Rapidly digestible	Slow digestible	Resistant
Mongolia	Barley	12.0	29	24.9	12.1	18.2
	wheat	14.7	26	38.1	29.0	1.7
	Oat	33.9	26	35.8	0.3	7.2
	Buckwheat	7.0	25			37
	Millets	3.1	21	35.9	37.7	12.6
Burkina Faso	Millet	3.1	21	35.9	37.7	12.6
	Sorghum	4.2	24	29.2	13.9	36.1
	Black-eyed peas	32.4	38	18.5	18.5	17.7
Indonesia Thailand	Indica rice	1.2	33	32.0	48.9	14.1
Japan Korea China	Japonica rice		20			0.2
	Wheat flour	8.5	26	38.1	29.0	1.7
Italy USA	Wheat flour	8.5	26	38.1	29.0	1.7
	Potato	1.1	20	75.5	3.8	1.7

Resistant starch: RS1- starch in seeds or legumes and unprocessed whole grains; RS2- natural granular form, e.g. high amylose corn; RS3- retrograded cooked starch. Drives *Prevotella*!

Badnar et al., 2001. Starch and fiber fractions in selected food and feed ingredients affect their small intestinal digestibility and fermentation and their large bowel fermentability in vitro in a canine model. J Nutr. 131:276-286.

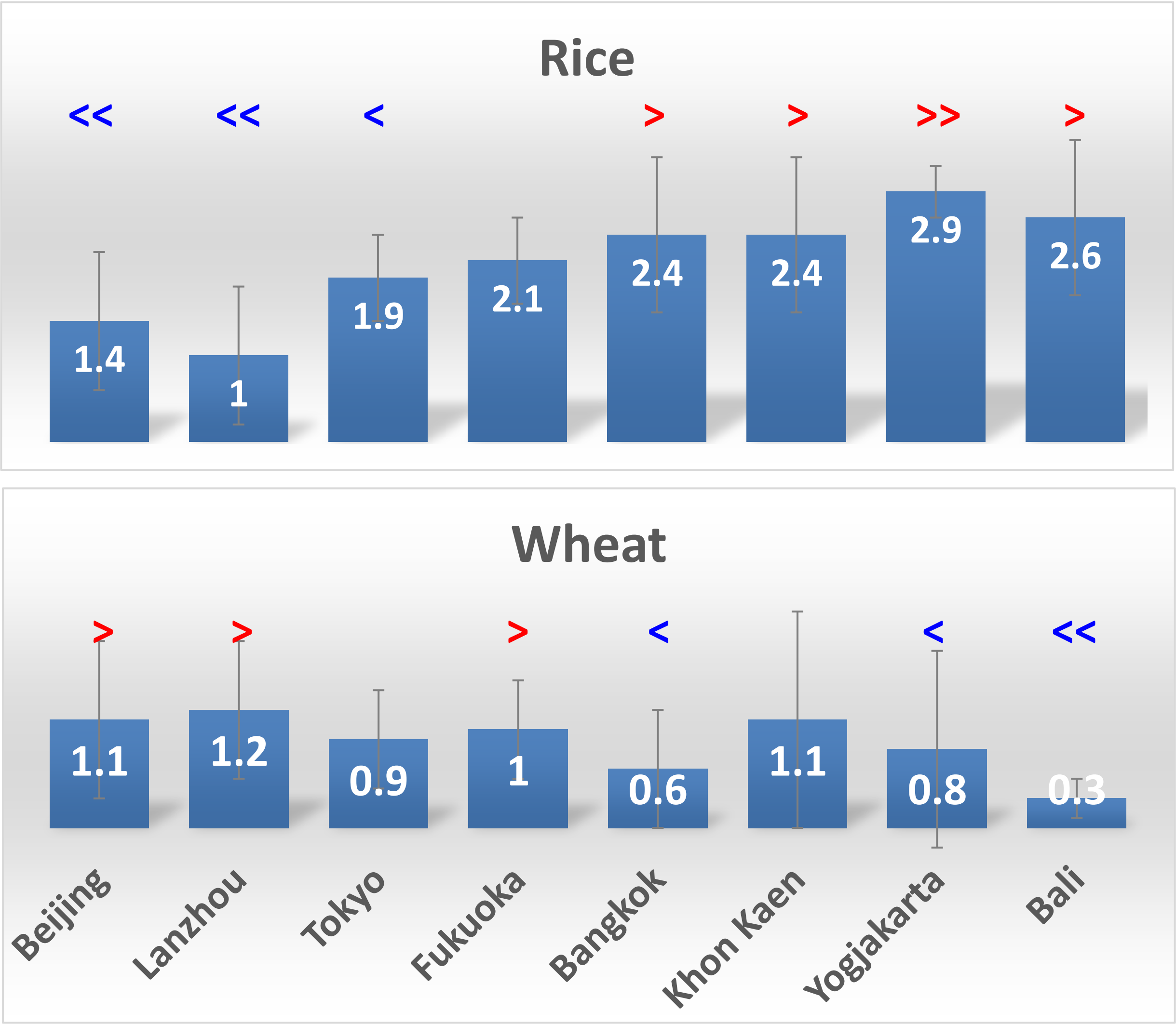
Behall et al. 1995. Effect of long term consumption of amylose vs amylopectin starch on metaboloic variables in human subject. Am J Clin Nutr 61:334-340.

Lbaneiah et al. 1981. Changes of starch, crude fiber, and oligosaccharides in germinating dry beans. Cereal Chem. 58: 135-138.

Food intake (Carbohydrate) frequency (per day)

Japonica

Resistant Starch
(0.6%)

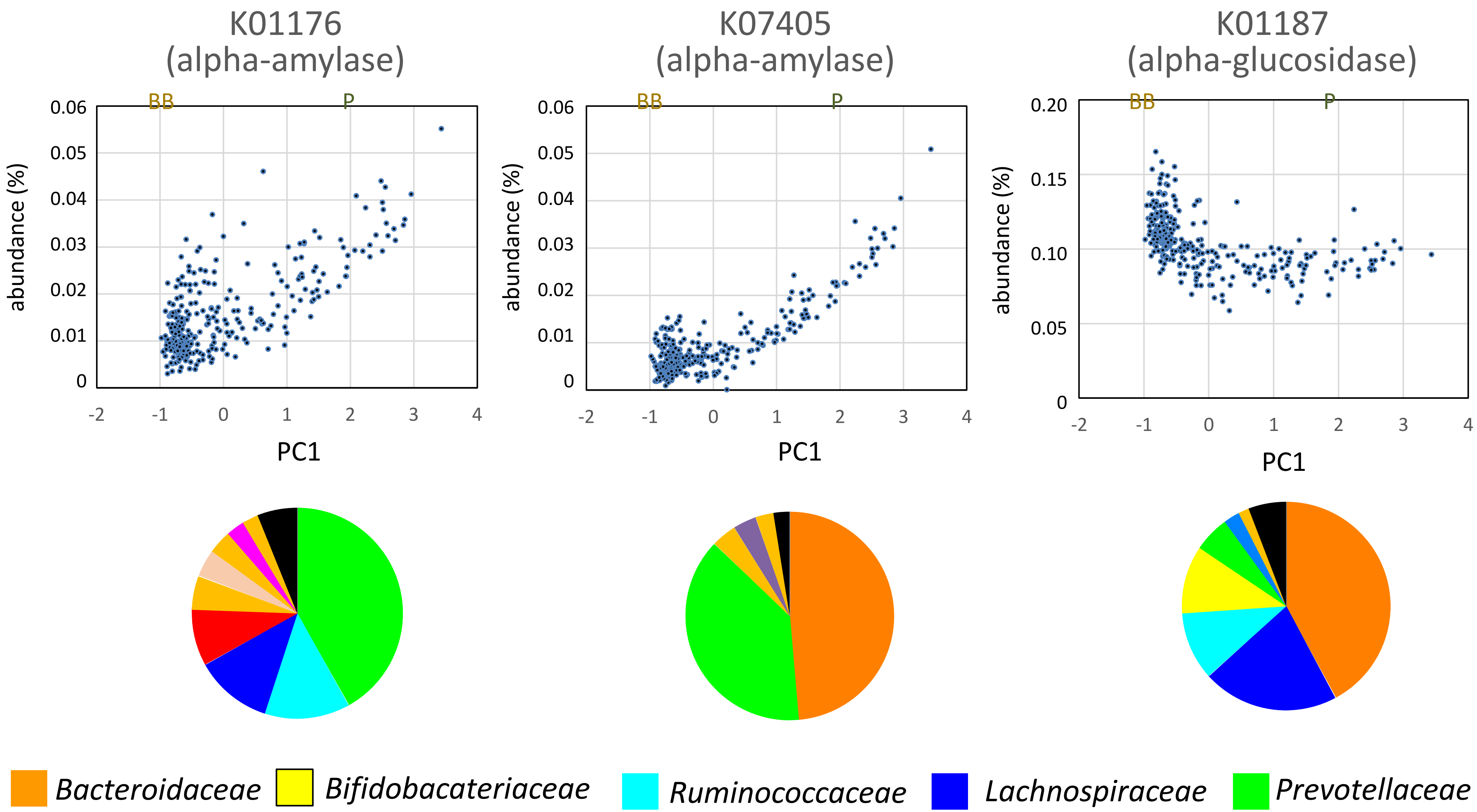


Indica
Javanica

Resistant Starch
(6.6%)

>: higher than other cities (*p*<0.05); >>: higher than other cities (*p*<0.001)
<: lower than other cities (*p*<0.05); <<: lower than other cities (*p*<0.001)

Predicted metagenome (PICRUSt) suggests non-digested amylose in the colon of P-type



*Pie chart represents contribution of bacteria family to these genes

WORKING HYPOTHESIS

Relative proportion of dietary fat & resistant carbohydrate

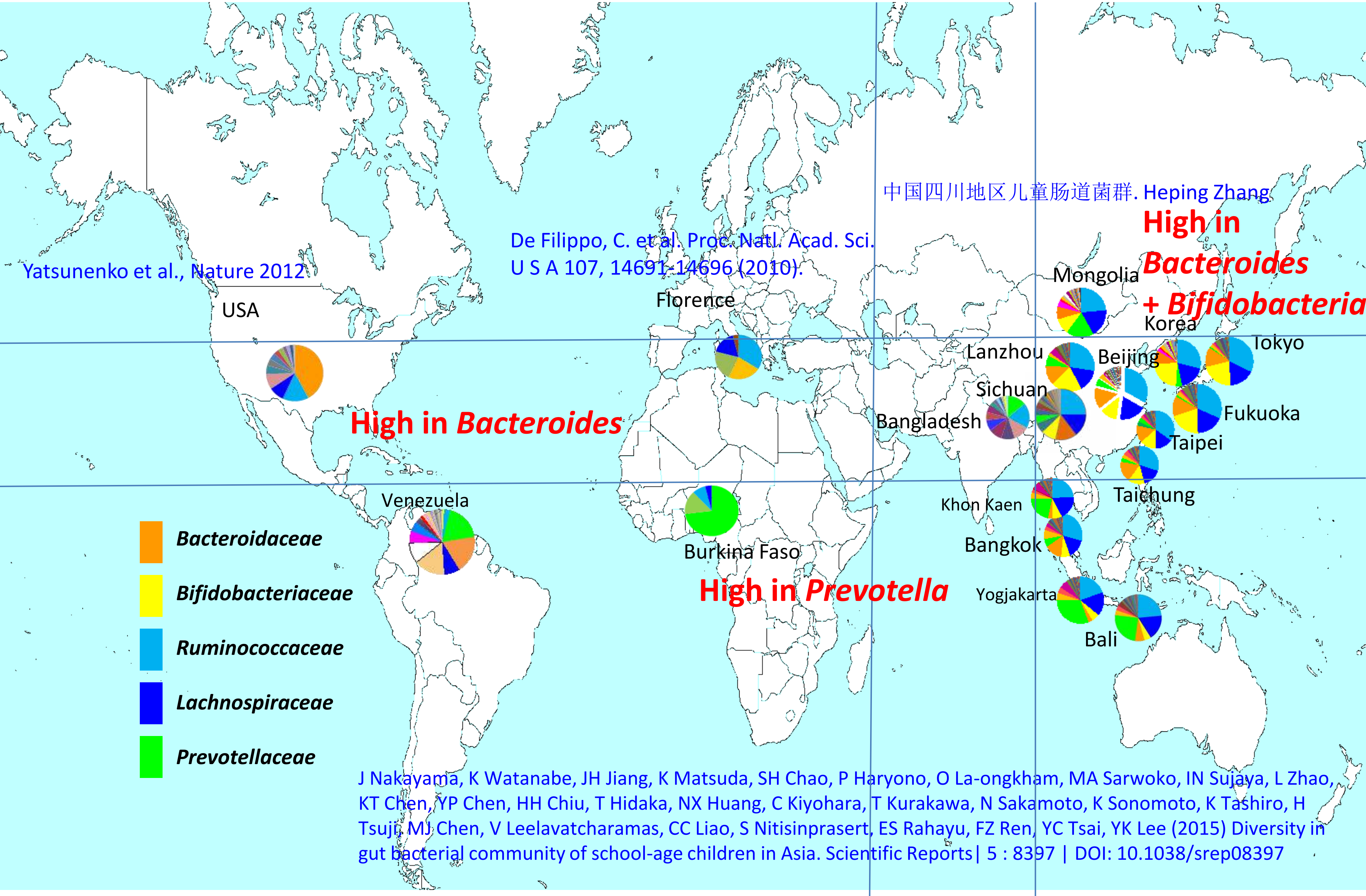
BB-type

Less resistant starch ➡ ↑ Bile acid in colon ➡ Kill *Prevotella* + bile sensitive species ➡ ↓Diversity

P-type

High resistant starch ➡ ↓ Bile acid in colon ➡ Promote *Prevotella* + bile sensitive species ➡ ↑Diversity

Microbial heritage: enhanced by Mother to infant transfer?



Take Home Message

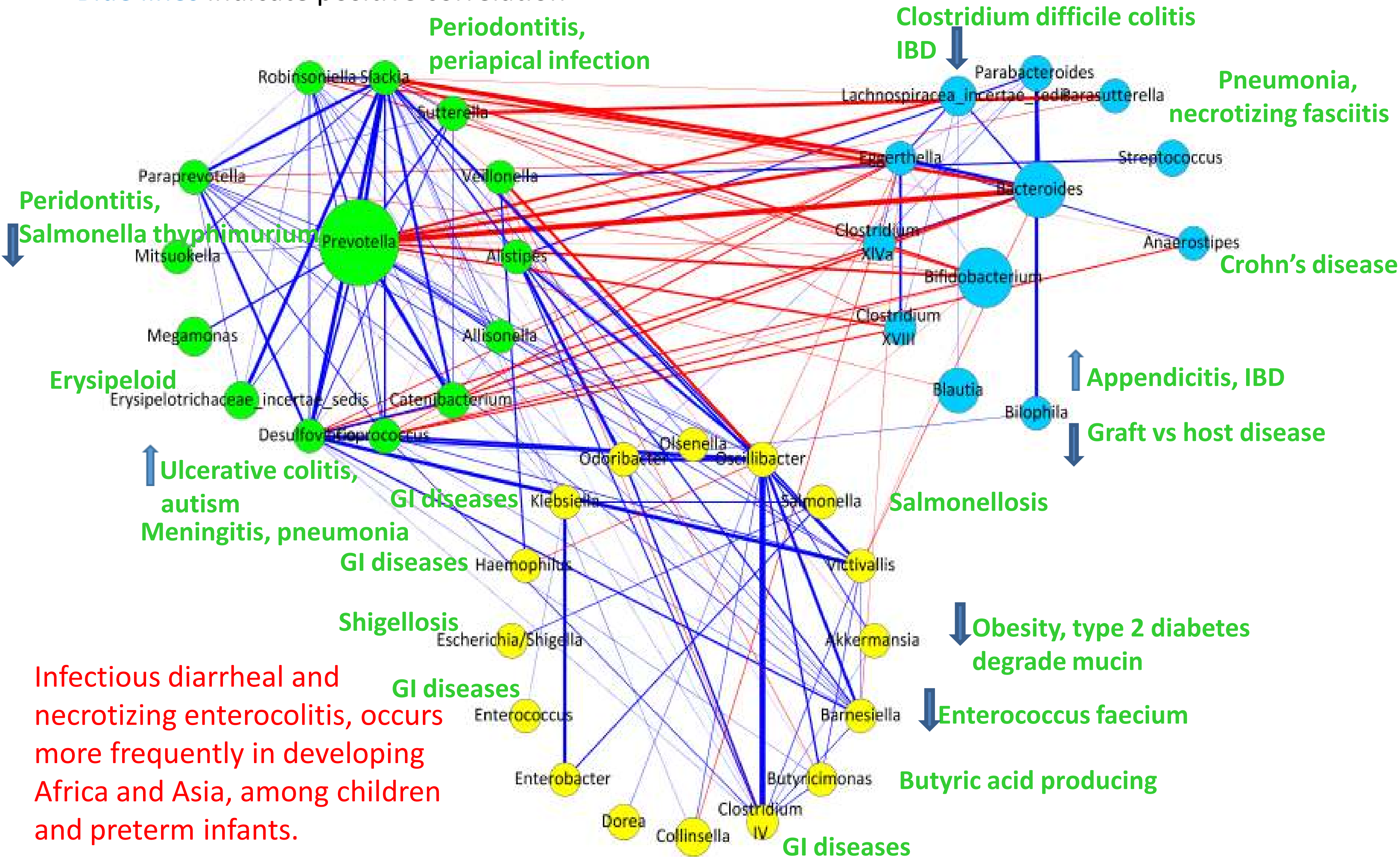
- Diet determines enterotype.
- Which is the healthier enterotype,

- *Prevotella* enterotype caries GI pathogens !?

Correlation between gut commensal and pathogens

Red line indicate negative correlation
Blue lines indicate positive correlation

Diet induced cancers & circular-vascular diseases occurs more frequently in Europe and North America

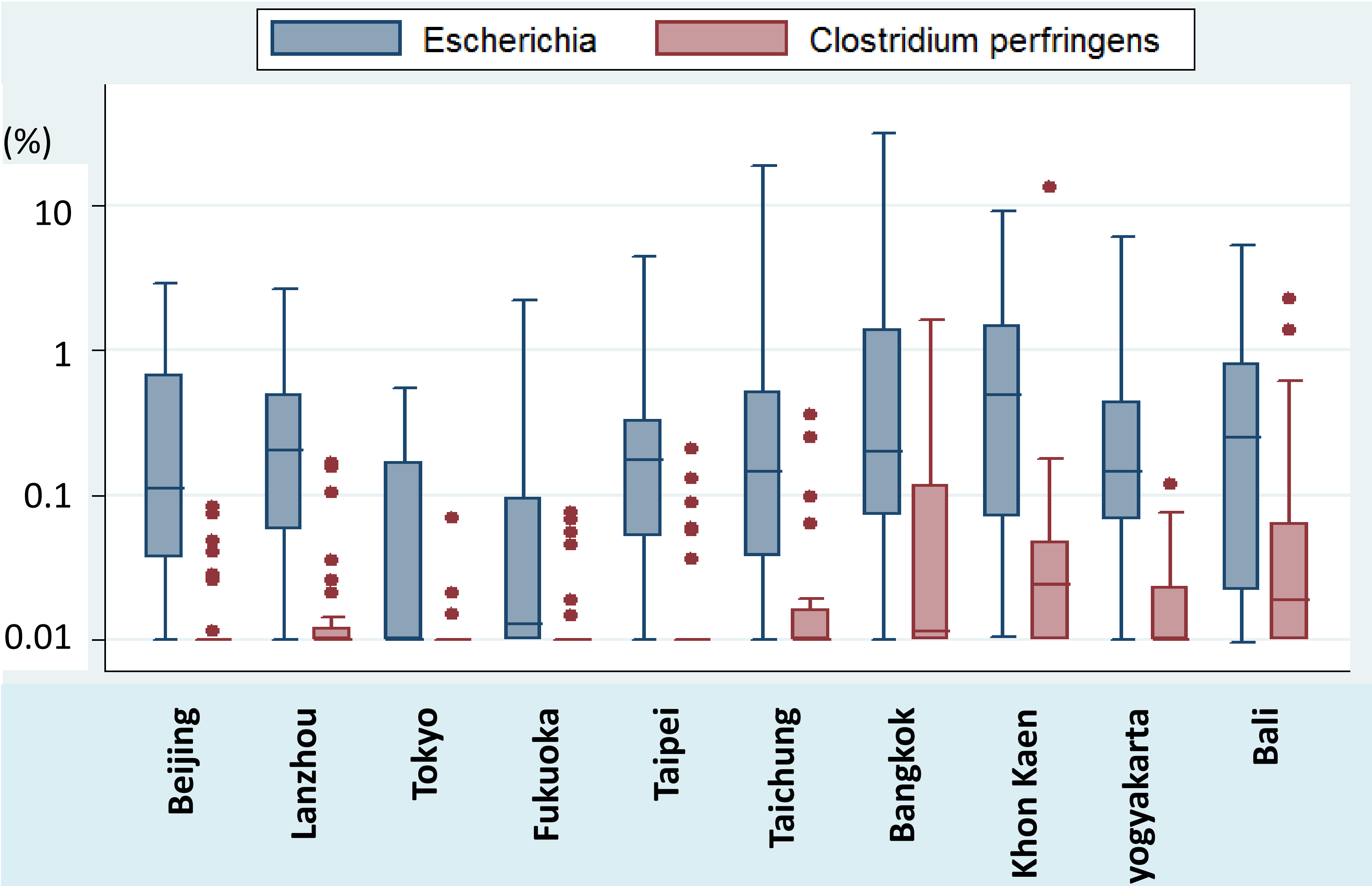


Infectious diarrheal and necrotizing enterocolitis, occurs more frequently in developing Africa and Asia, among children and preterm infants.

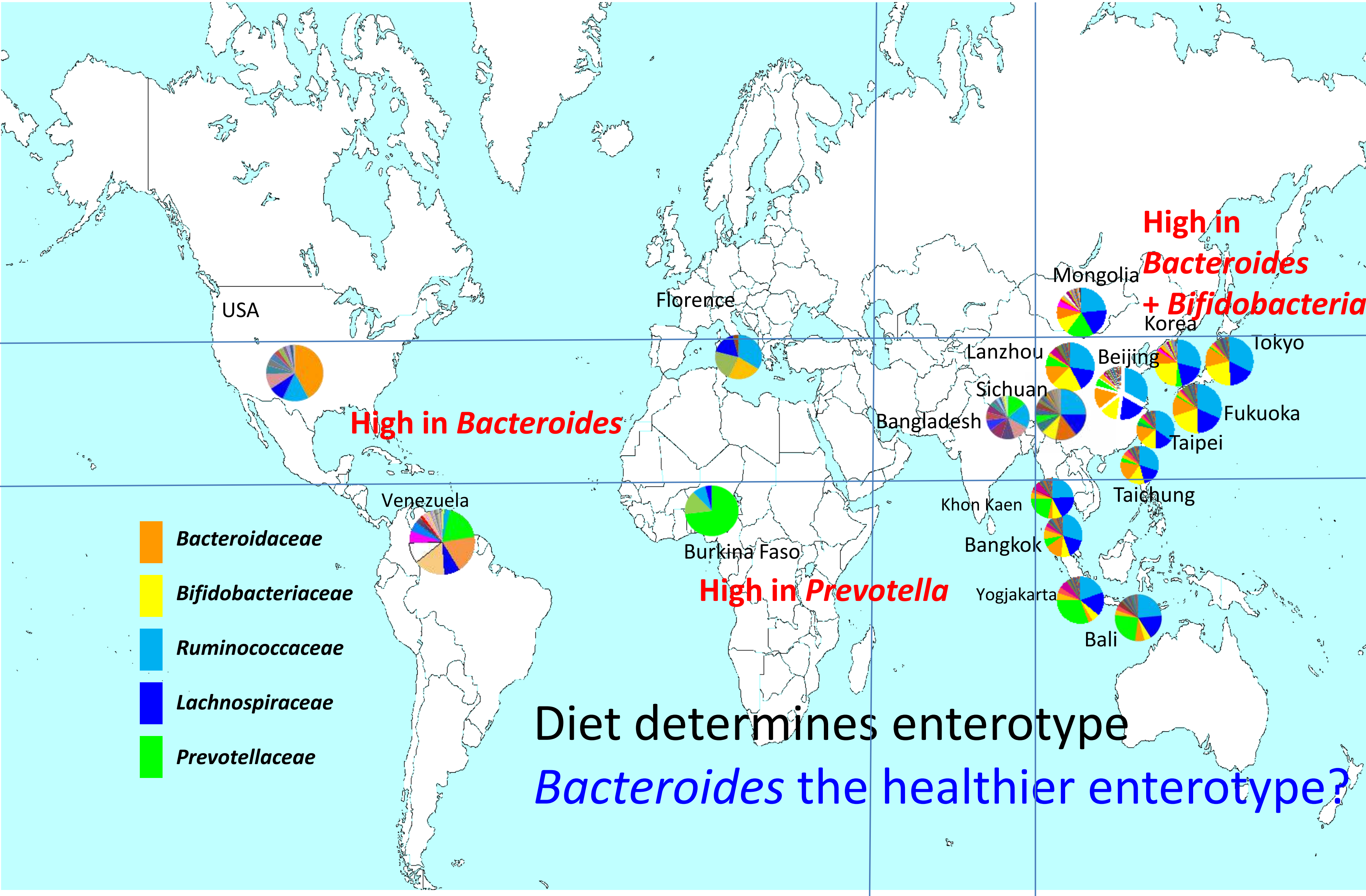
Relative abundance of potentially pathogenic bacteria in the 10 cities

"East Asian youngsters harbor less amount of potentially pathogenic bacteria"

Hygiene?

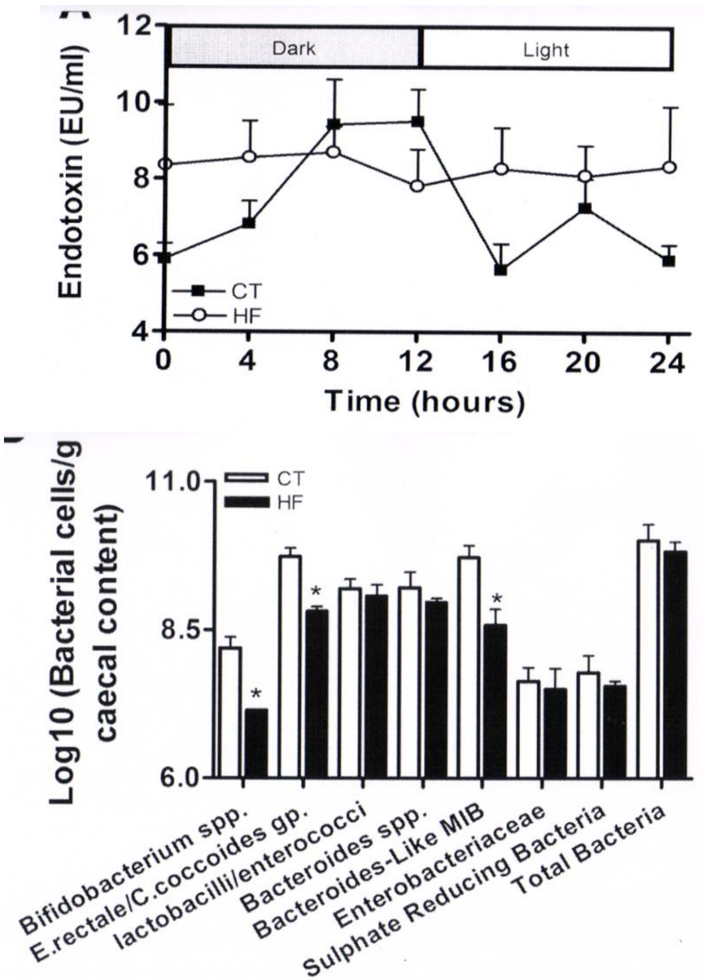


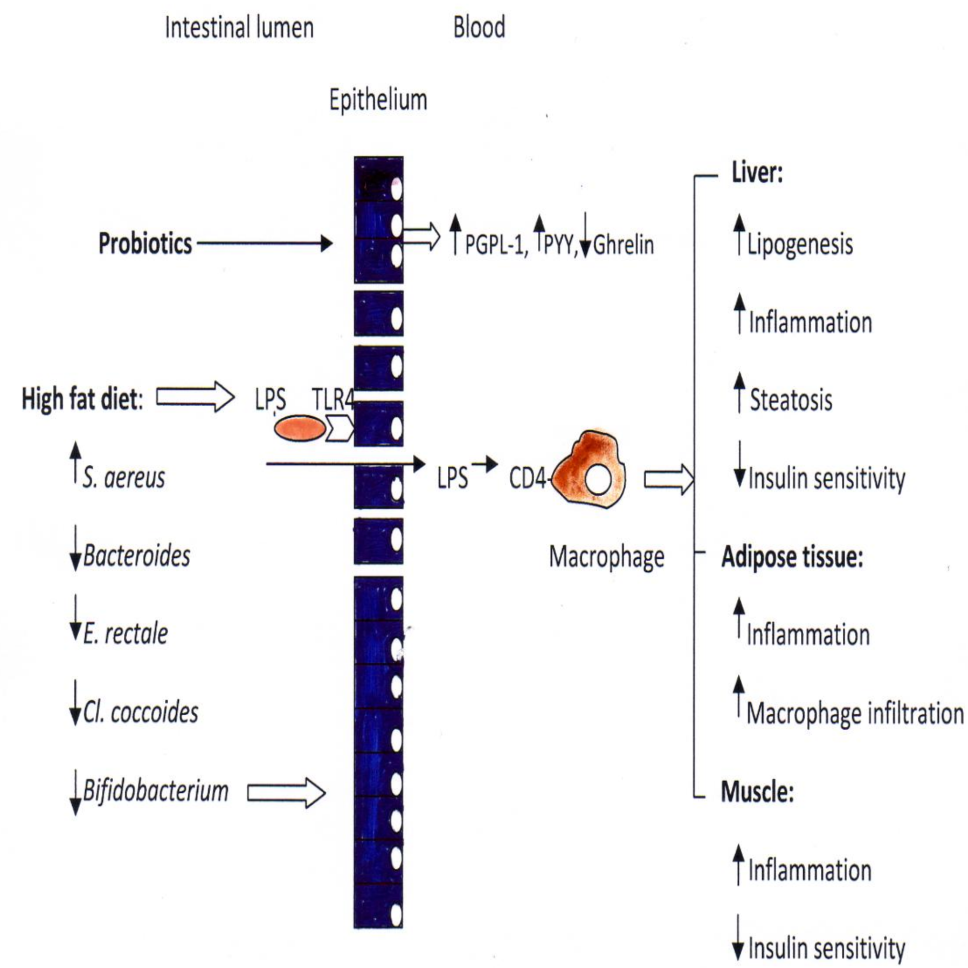
Gut microbiota of healthy population worldwide



But, high-fat **feeding increased endotoximia (high plasma bacterial lipopolysaccharide) and changed intestinal microbiota.** Cani et al. Diabetes 2007, 56: 1761-72.

Commensal strengthen epithelial layer tight-junction (increase expression of zonula occludens-1 & myosin light-chain kinase), preventing crossover of pathogen and LPS, chronic inflammation and type-2 diabetes.





WORKING HYPOTHESIS

Relative proportion of dietary fat & resistant carbohydrate determine enterotype

P-type

High resistant starch ➡ ↓ Bile acid in colon ➡ Promote *Prevotella* + bile sensitive species ➡ ↑Diversity

BB-type

Less resistant starch ➡ ↑ Bile acid in colon Kill *Prevotella* + bile sensitive species ↓Diversity

Over consumption of fat led to obesity

Pathogen-enriched

High fat ➡ ↑ Bile acid/ fatty acids in colon ➡ Kill commensal, weaken tight junction ➡ ↑Chronic inflammation

Does obesity plays any role in Type-2 Diabetes in Asia?

Over consumption of carbohydrate could lead to obesity!

Starch interfere fat digestion in the gut

WORKING HYPOTHESIS

Relative proportion of dietary fat & resistant carbohydrate determine enterotype

P-type

High resistant starch → ↓ Bile acid in colon → Promote *Prevotella* + bile sensitive species → ↑Diversity

BB-type

Less resistant starch → ↑ Bile acid in colon → Kill *Prevotella* + bile sensitive species → ↓Diversity

Over consumption of fat led to obesity

Pathogen-enriched

High fat → ↑ Bile acid/ fatty acids in colon → Kill commensal, weaken tight junction → ↑Chronic inflammation

Over consumption of carbohydrate led to obesity

High carbohydrate → ↓ Bile acid/ fatty acids → Commensal remained Strengthen tight junction → No chronic inflammation

Implication?

balance

High fat-low resistant starch (wheat, potato) consumers eat more resistant starch (Indica rice, bailey, oat, millet) to prevent type-2 diabetes.

High resistant starch-low fat consumers switch to low resistant starch or eat more fat to prevent MCI/dementia and improve on longevity.

(hypertension, cardiovascular diseases?!)

(Working hypothesis for intervention study!)

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