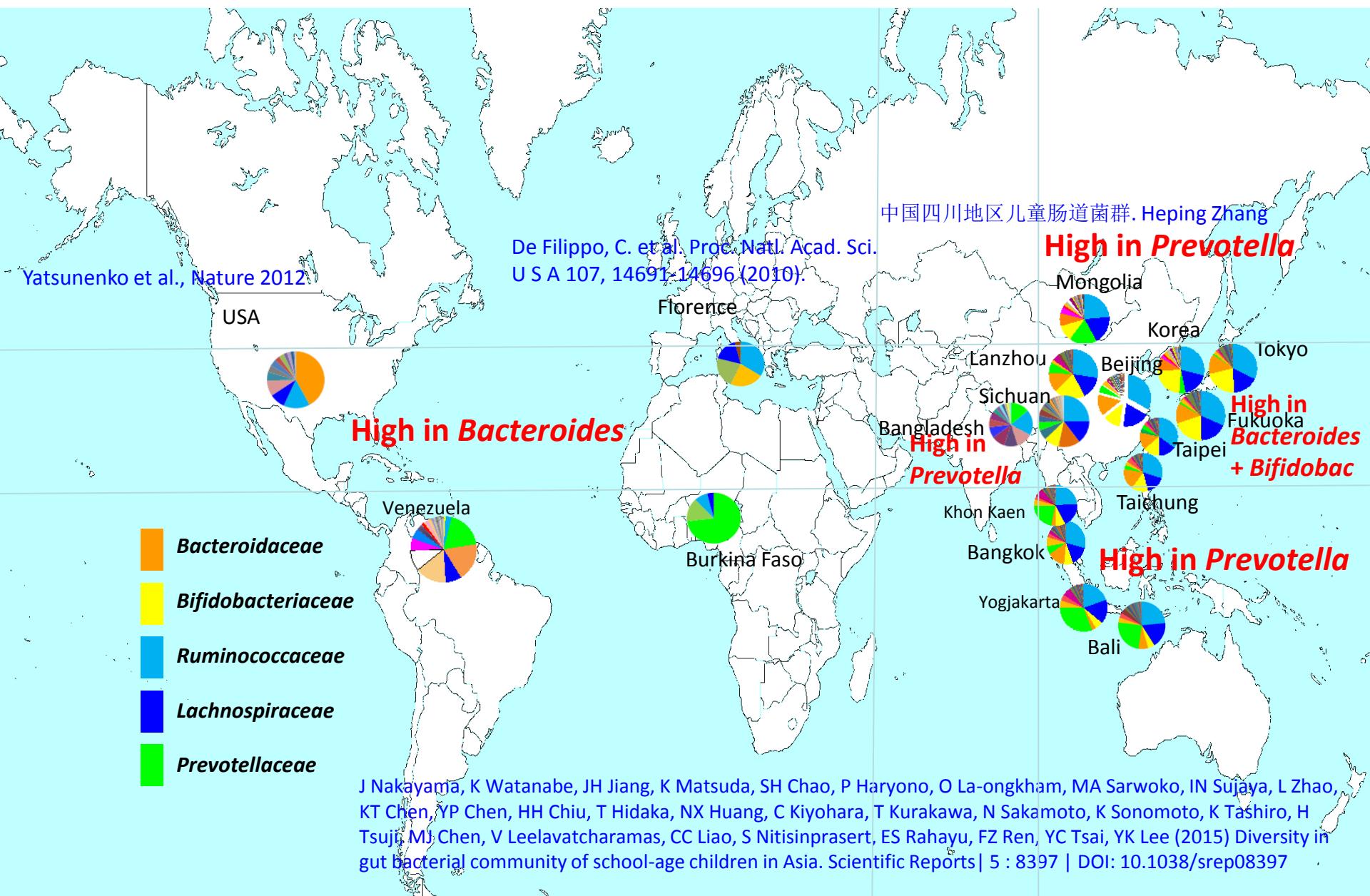
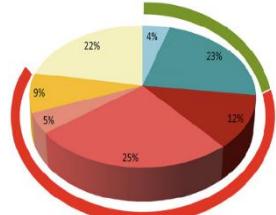


Probiotics in a World Where Dietary Habits Collide

Yuan Kun LEE
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5 Science Drive 2, Singapore 117597

Gut microbiota of healthy children worldwide



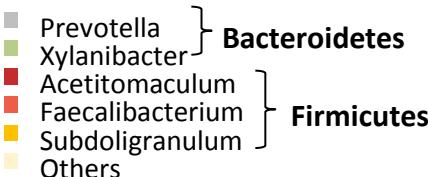
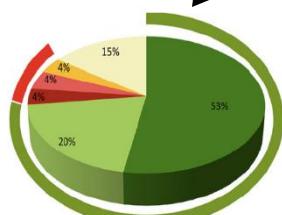


EU children (n=15, 1~6 y.)



Children in

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



Diet determines gut microbiome

Enterotypes:

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

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

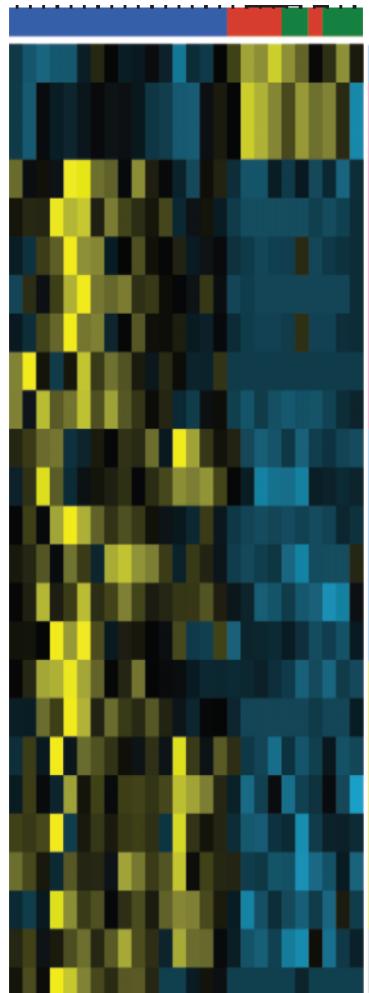
Type 3: Diet rich in carbohydrates- favored *Prevotella*

Linking long-term dietary patterns with gut microbial enterotypes

Wu GD, Chen J, Hoffman C, et al. Science 2011, DOI: 10.1126/Science 1208344

Overrepresenting genes in Southeast Asia/East Asia and US/Africa

Yatsunenko et al.
2012, Nature
US Malawi



amyA, malS; alpha-amylase
 gltB; glutamate synthase (NADPH/NADH)
 gltD; glutamate synthase (NADPH/NADH)
 1-pyrroline-5-carboxylate dehydrogenase
 glsA, GLS; glutaminase
 gadB, gadA, GAD; glutamate decarboxylas
 asdA; aspartate 4-decarboxylase
 PRODH; proline dehydrogenase
 rocD; ornithine--oxo-acid transaminase
 kamA; lysine 2,3-aminomutase
 AXY8, FUC95A, afcA; alpha-L-fucosidase 2
 SHPK; sedoheptulokinase
 SORD, gutB; L-iditol 2-dehydrogenase
 pfkA, PFK; 6-phosphofructokinase 1
 G6PD, zwf; glucose-6-phosphate 1-dehydro
 alpha-mannosidase
 MANBA, manB; beta-mannosidase
 bioA; adenosylmethionine-8-amino-7-oxo
 lipB; lipoyl(octanoyl) transferase
 cbiB, cobD; adenosylcobinamide-phospho
 cobB-cbiA; cobyrinic acid a,c-diamide synt
 cobQ, cbiP; adenosylcobyrinic acid synthase
 cobU, cobT; nicotinate-nucleotide--dimet
 choloylglycine hydrolase
 paaK; phenylacetate-CoA ligase

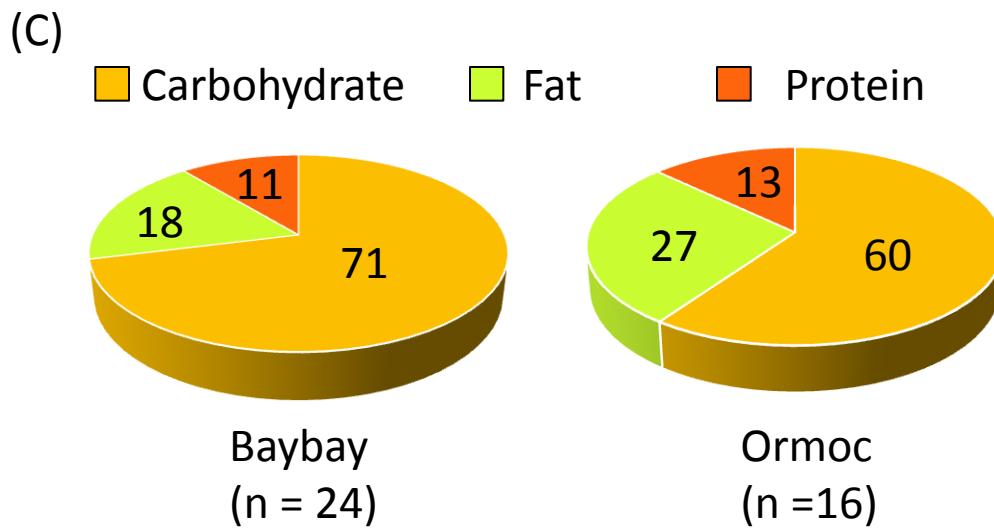
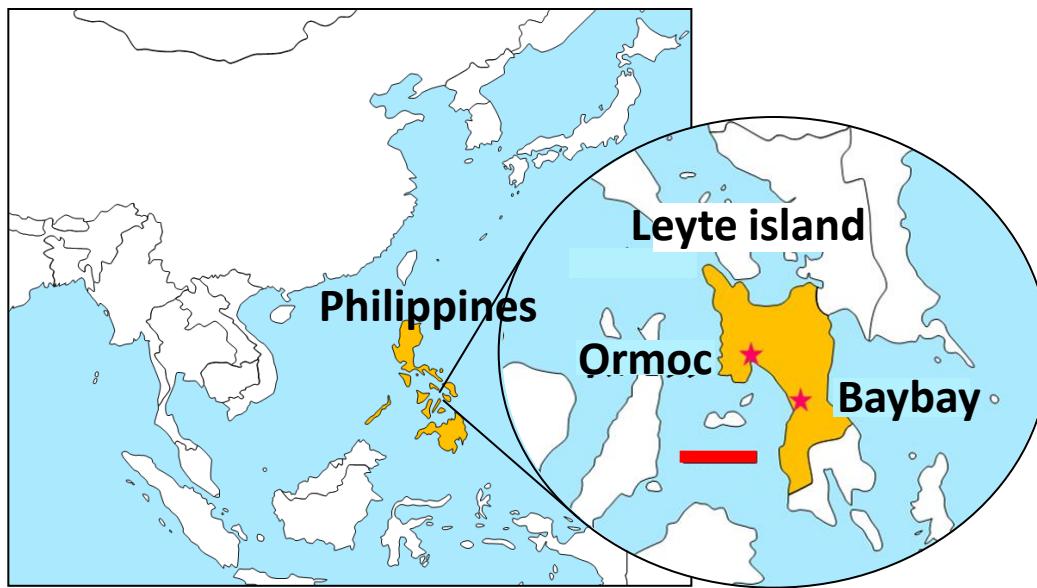
Asian Microbiome Program

East Asia-type Southeast Asia-type

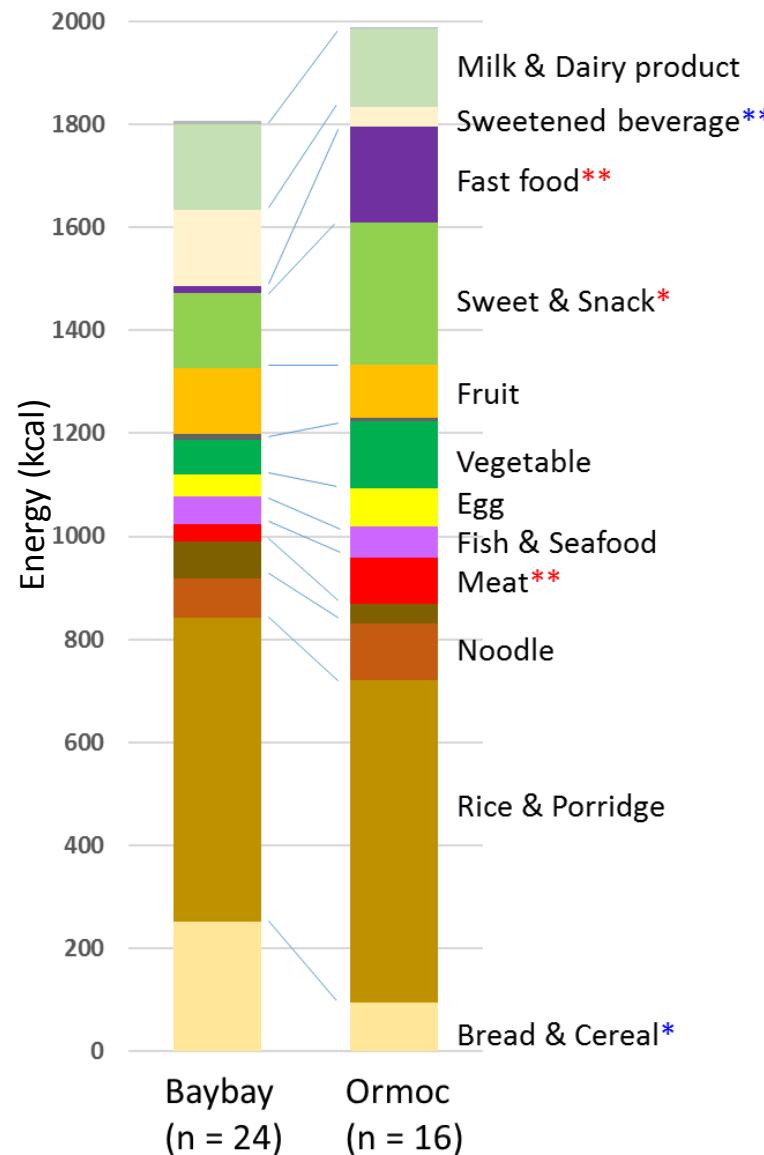
0395	0513	0243	0244	0361	0167	0174	0279	0423	0147	0454	0176	0265	0618	0569	0415	0276	0762	0782	1.35	0.959	0436	0494	1.01	0.952	17028	18389	16704	15262	14525	13886	0261	
0399	0503	0369	0504	0508	0422	0358	1.6387	0382	0442	0376	0237	0285	0713	0782	0495	0271	1.8204	1.817	2.3709	2.1001	1.048	1.054	1.963	1.6538	2.037	1.549	2.3088	2.4524	0389	2.3893	1.8861	
19862	2238	1.7813	1.7557	1.7442	2.1297	2.029	1.29	1.807	1.6592	1.3361	1.545	2.0283	1.98	2.075	1.95	1.7716	1.8728	2.3225	2.7682	2.6549	2.1613	1.9828	1.874	2.5471	1.8398	2.0404	2.6381	2.3925	1.940	2.5429	2.4265	
03	0052	00246	00216	00157	00221	0.014	0.0211	0.0188	0.0252	0.0405	0.023	0.0217	0.028	0.0113	0.02	0.0211	0.0476	0.0191	0.0247	0.0103	0.0111	0.0301	0.0265	0.0232	0.0113	0.0105	0.0083	0.0053	0.0211	0.0043	0.0003	
07413	0293	0168	0355	0077	0136	0.1568	0.213	0.0031	0.0362	0.269	0.29	0.193	0.237	0.27	0.183	0.293	0.22	0.031	0.058	0.0466	0.141	0.123	0.045	0.0308	0.0291	0.0771	0.0265	0.1588	0.0777	0.0265		
07491	02825	0152	02709	0.091	0.105	0.1685	0.4385	0.349	0.225	0.221	0.393	0.193	0.246	0.297	0.1484	0.1663	0.211	0.074	0.026	0.0117	0.07	0.089	0.0495	0.0144	0.1608	0.467	0.0316	0.0299	0.241	0.0988	0.0907	
0374	00765	00676	0.1798	0.0601	0.0663	0.1653	0.273	0.0588	0.2168	0.1637	0.163	0.1688	0.1784	0.031	0.0873	0.018	0.1265	0.0418	0.048	0.021	0.0412	0.0425	0.048	0.0238	0.0223	0.0105	0.0089	0.0126	0.0181	0.0372	0.0021	
00749	0002	00018	0051	0029	0.0007	0.0072	0.0083	0.0057	0.008	0.0215	0.007	0.0082	0.008	0.0078	0.006	0.0058	0.0074	0.0061	0.0066	0.0017	0.0062	0.0057	0.008	0.0059	0.0058	0.0031	0.0012	0.0072	0.0066	0.0007		
0221	043	0275	0.0917	0.0665	0.0051	0.007	0.013	0.0338	0.023	0.0497	0.073	0.019	0.0588	0.021	0.058	0.012	0.037	0.0206	0.022	0.042	0.024	0.028	0.0165	0.019	0.0412	0.024	0.0036	0.0094	0.0429	0.0093	0.0094	
03497	02895	0125	0235	0.1652	0.1094	0.1616	0.221	0.0939	0.1769	0.1722	0.003	0.2378	0.189	0.1681	0.1168	0.0493	0.1893	0.074	0.054	0.0261	0.0686	0.1119	0.0885	0.0171	0.017	0.0285	0.0089	0.0214	0.1185	0.0223		
12765	0373	053	0321	02691	0.0536	0.1758	0.0555	0.0559	0.045	0.031	0.024	0.0298	0.29	0.1553	0.1493	0.174	0.1678	0.158	2.4468	2.7744	0.9755	1.6319	1.145	2.0504	0.8564	1.304	2.1559	0.3517	0.575	2.7055	2.2665	
01179	00458	00531	00444	00278	0.0871	0.0183	0.003	0.018	0.0394	0.0611	0.037	0.0144	0.0658	0.058	0.0088	0.0249	0.021	0.0237	0.008	0.0222	0.007	0.067	0.0449	0.0561	0.0334	0.0198	0.0159	0.0378	0.048	0.0281	0.0242	
0046	00313	0.0537	0.049	0.0367	0.034	0.035	0.0033	0.0057	0.0999	0.0711	0.0418	0.1963	0.0835	0.038	0.0854	0.0325	0.0459	0.0294	0.0427	0.052	0.0374	0.0289	0.0165	0.0553	0.0319	0.0149	0.0498	0.0282	0.0243			
23945	2057	2.045	2.0558	2.1554	2.2	2.455	2.2214	1.9015	2.1413	1.9481	2.5467	2.7353	2.2782	2.41	2.003	1.7689	1.8035	1.8075	1.5698	1.7409	2.3224	1.8689	2.0103	1.2458	1.2655	1.0821	1.216	1.277	1.658	1.408	1.345	
03894	0104	0.271	0.2341	0.1659	0.1271	0.145	0.24	0.3639	0.2529	0.5241	0.2977	0.2262	0.278	0.058	0.108	0.1111	0.1324	0.106	0.0692	0.0117	0.0038	0.165	0.1763	0.0591	0.5604	0.3103	0.0507	0.0716	0.2531	0.0602	0.0007	
06976	10419	0.6333	0.5728	0.3227	0.3707	0.4167	1.7268	1.2055	0.892	1.693	1.3176	0.7518	1.297	0.291	0.345	0.375	1.4222	0.921	0.988	0.1878	0.4085	0.2967	0.3981	0.999	1.0676	0.7945	0.1958	0.79	0.2444	0.2311	0.1453	
07859	04369	0.032	0.0487	0.0161	0.0498	0.0103	0.0379	0.0387	0.0385	0.0408	0.1287	0.047	0.051	0.0284	0.0455	0.0289	0.0277	0.0267	0.0087	0.107	0.245	0.052	0.103	0.4510	0.244	0.0314	0.0285	0.0086	0.0168	0.0701	0.1568	0.0772
03497	01481	0.1982	0.1576	0.4551	0.218	0.2665	0.0207	0.1359	0.0359	0.2123	0.5035	0.2856	0.3396	0.2495	0.2448	0.2756	0.2455	0.1614	0.1446	0.155	0.2569	0.2057	0.4244	0.0388	0.1236	0.0935	0.0544	0.0266	0.1901	0.1666	0.0002	
02843	0.1775	0.1048	0.1842	0.1829	0.1379	0.1561	0.2204	0.0204	0.103	0.2451	0.1866	0.2387	0.0392	0.0927	0.0982	0.1418	0.0475	0.0511	0.0357	0.0465	0.0714	0.2574	0.0308	0.0268	0.0303	0.0086	0.0296	0.0694	0.0225	0.0093		
03833	0.0833	0.0493	0.0123	0.048	0.0564	0.0223	0.0228	0.0464	0.0478	0.029	0.0161	0.0183	0.0192	0.0285	0.0289	0.0463	0.0326	0.0368	0.0281	0.0257	0.0285	0.0483	0.0359	0.1034	0.1258	0.1809	0.1288	0.1778	0.1367	0.2276	0.1743	
07006	0.0405	0.0574	0.0762	0.0662	0.0242	0.0564	0.0167	0.0236	0.0103	0.0484	0.0308	0.0588	0.0474	0.0506	0.0364	0.0404	0.0274	0.027	0.049	0.0569	0.0178	0.0214	0.0271	0.2803	0.0203	0.1923	0.0743	0.267	0.2223			
05682	0.0309	0.0548	0.0517	0.0515	0.0542	0.0322	0.0307	0.0382	0.0175	0.0495	0.0603	0.7826	0.542	0.535	0.0711	0.5528	0.0474	0.0478	0.0314	0.0345	0.0568	0.0579	0.5024	0.0251	0.2703	0.2415	0.1478	0.2386	0.0521	0.0287	0.2103	
03805	0.042	0.051	0.0568	0.0517	0.0525	0.05	0.0585	0.0479	0.0477	0.0363	0.7413	0.5761	0.4956	0.4946	0.478	0.3891	0.3625	0.3651	0.323	0.454	0.4581	0.4582	0.1938	0.2802	0.2281	0.1833	0.2195	0.3495	0.24	0.1665		
10675	0.0276	0.0333	1.05	0.789	1.202	1.1228	1.008	0.6875	0.566	0.923	1.1601	0.8827	1.077	0.6453	0.6345	0.5055	0.5567	0.5203	0.4088	0.6781	0.6943	0.4772	0.2531	0.0878	0.5085	0.2942	0.3571	0.7105	0.0386	0.2715		
03830	0.0409	0.0525	0.0421	0.0563	0.0571	0.0435	0.0376	0.0447	0.0044	0.0748	0.0598	0.575	0.611	0.0312	0.032	0.0283	0.0325	0.0464	0.0142	0.0553	0.0321	0.0303	0.0262	0.0115	0.0246	0.1423	0.0366	0.1503	0.0330	0.0141	0.0166	

Collision of dietary habits: Impact of Western high-fat, low carbohydrate diet on gut microbiota in youngsters on Leyte island Philippines

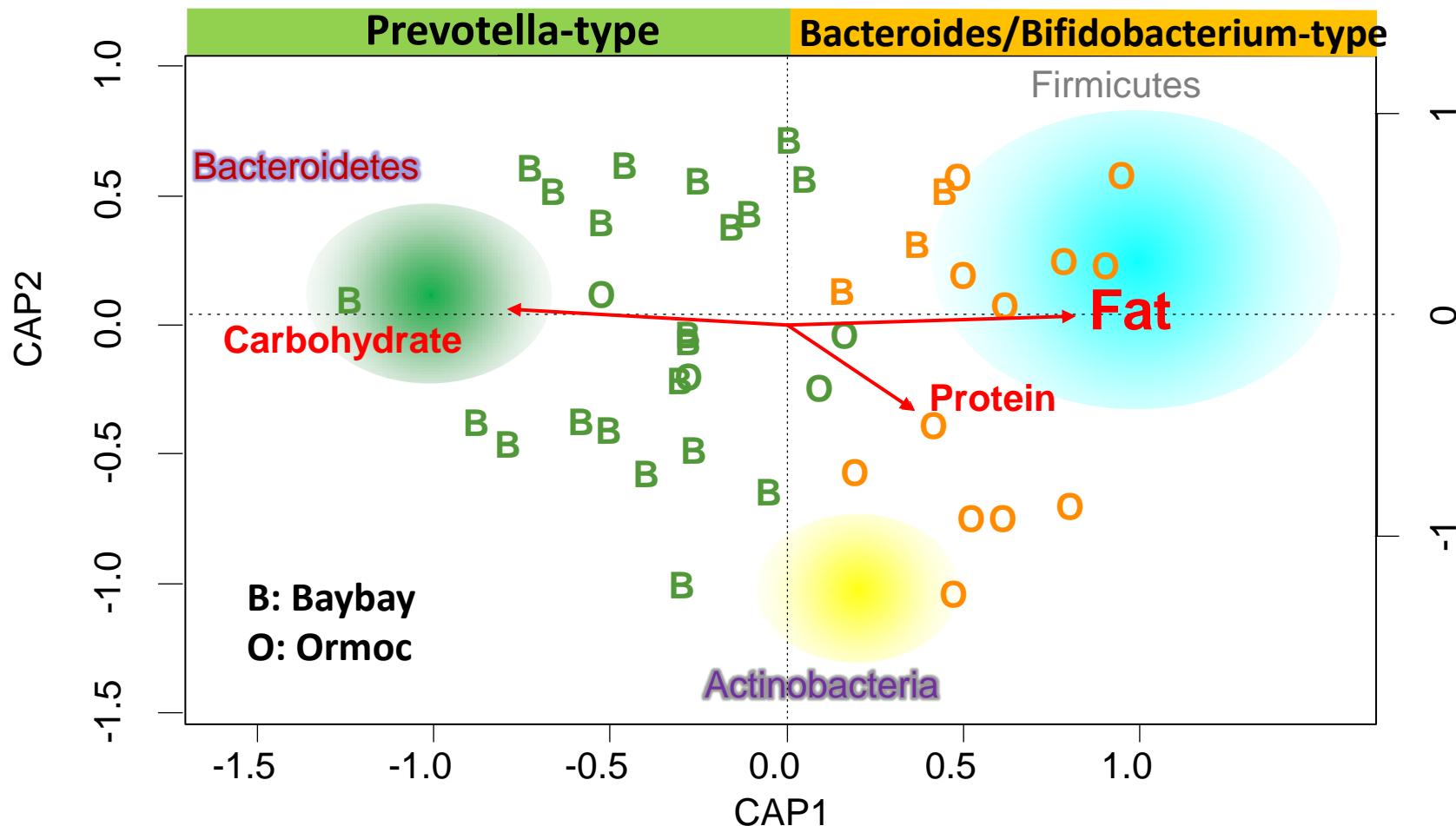
(A)



(B)



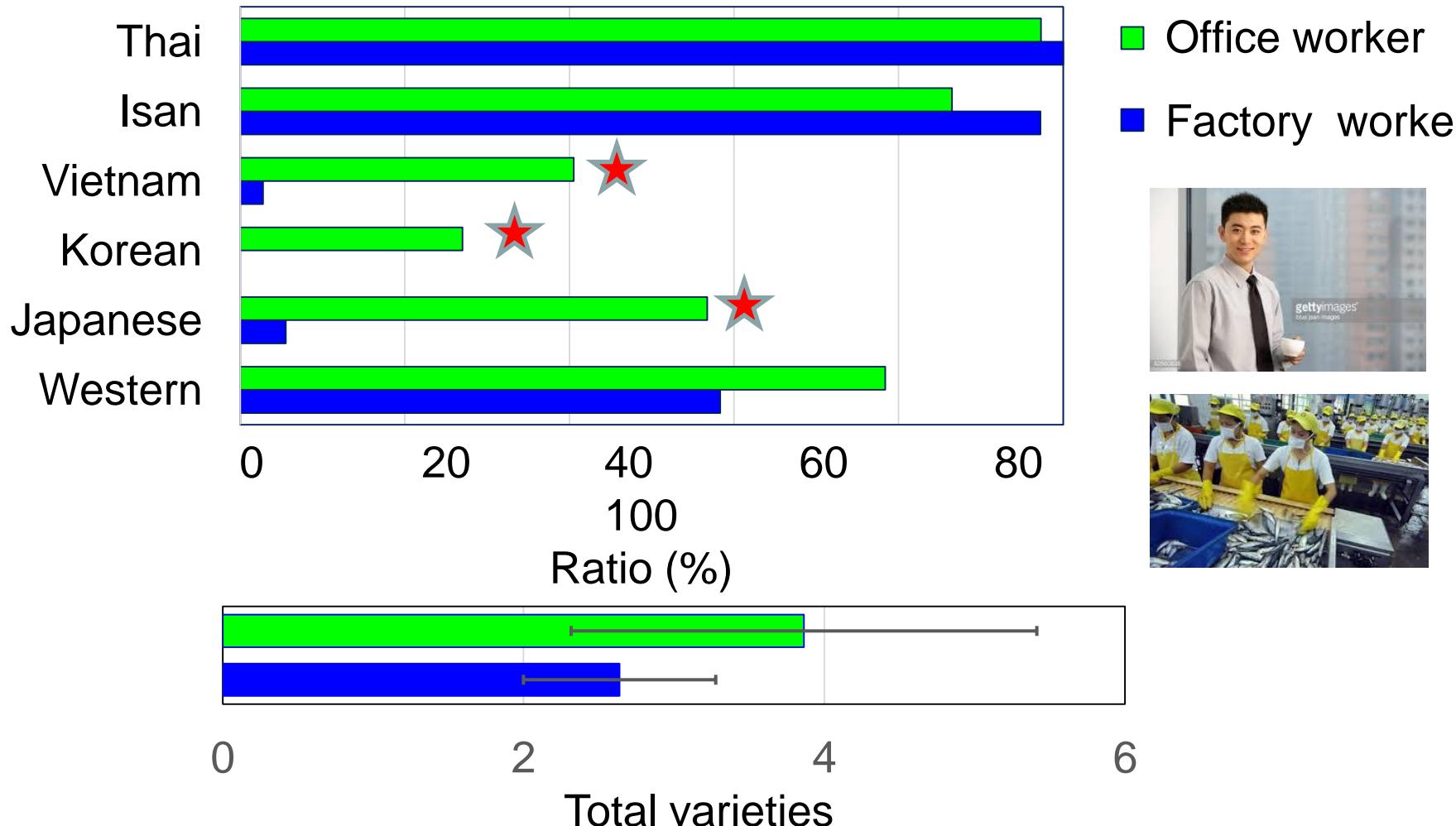
Redundancy analysis to correlate macronutrient intake with gut microbiota



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

Collision of dietary habits: globalization of diet in Bangkok Thailand

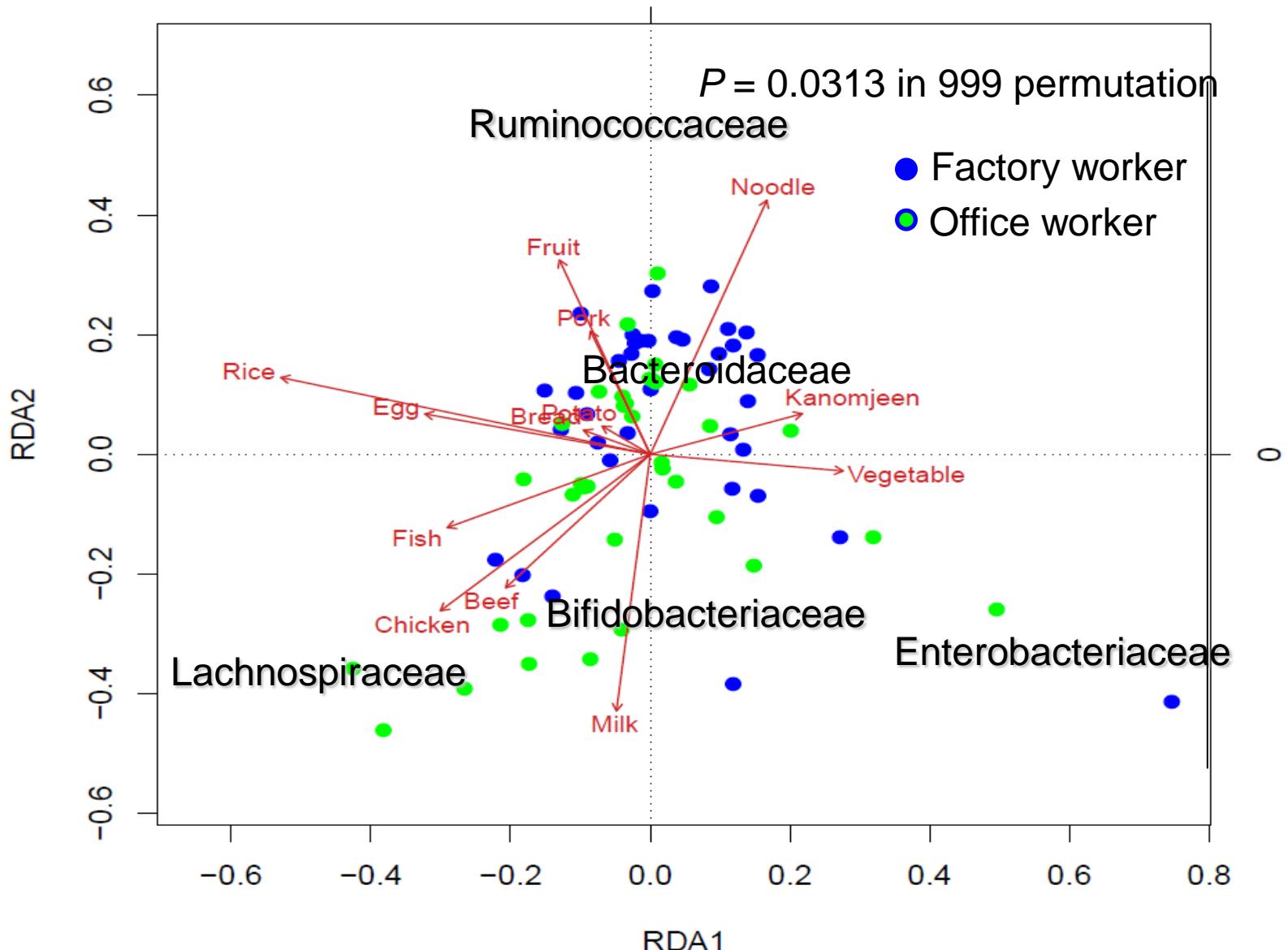
Type of meal



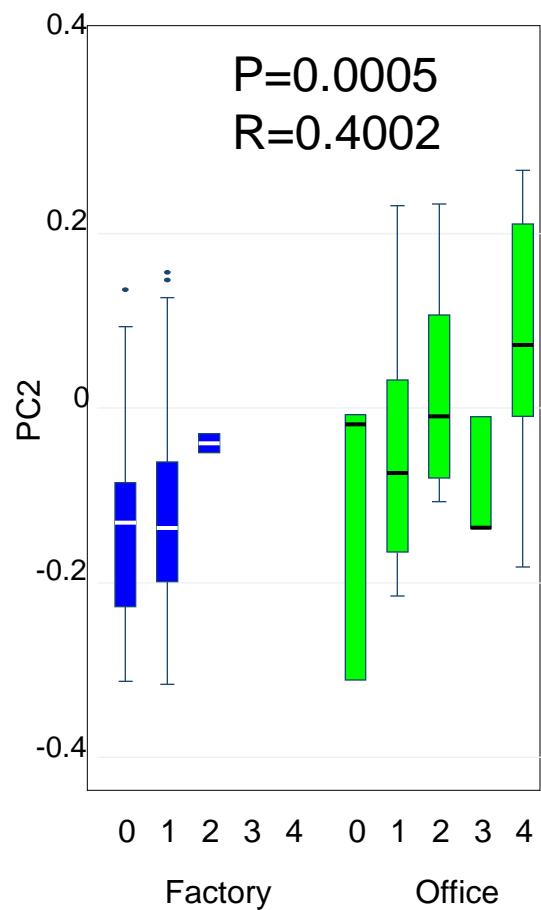
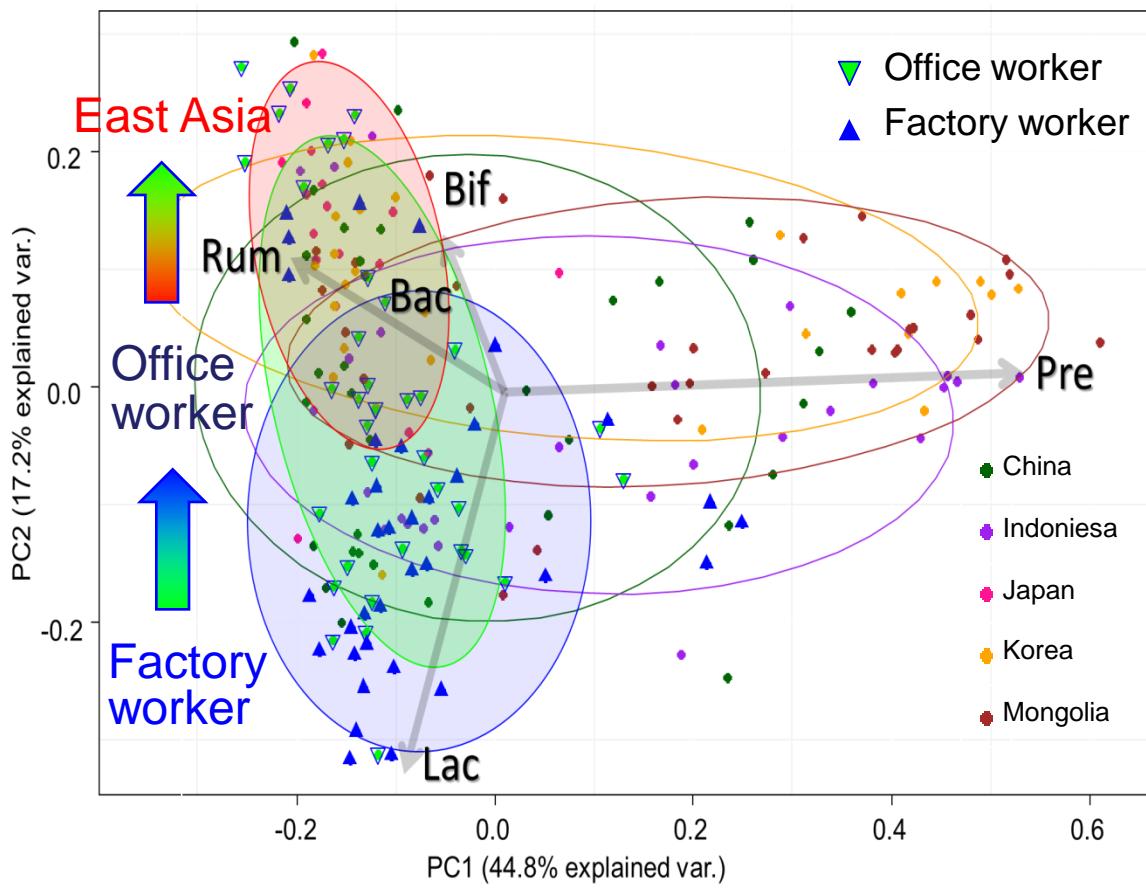
- Office worker
- Factory worker



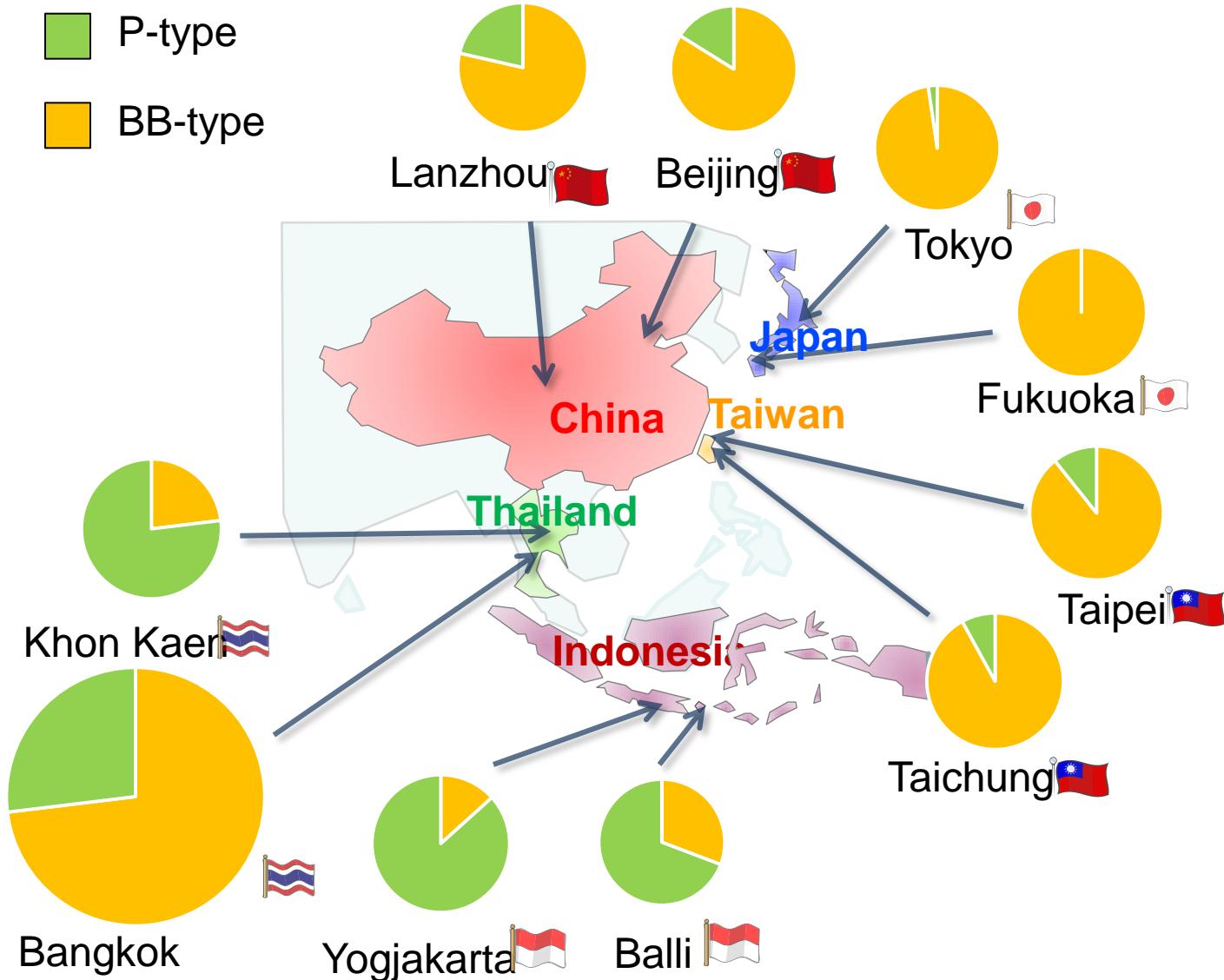
Redundancy analysis showing correlation between dietary habit and microbiota



Shift of Bangkok Thai gut microbiota to East Asia gut microbiota with intake of international diets



Microbiota profile in Asian cities



**Are changes
in microbiome
profile
bidirectional?**

Southern
Chinese migrated

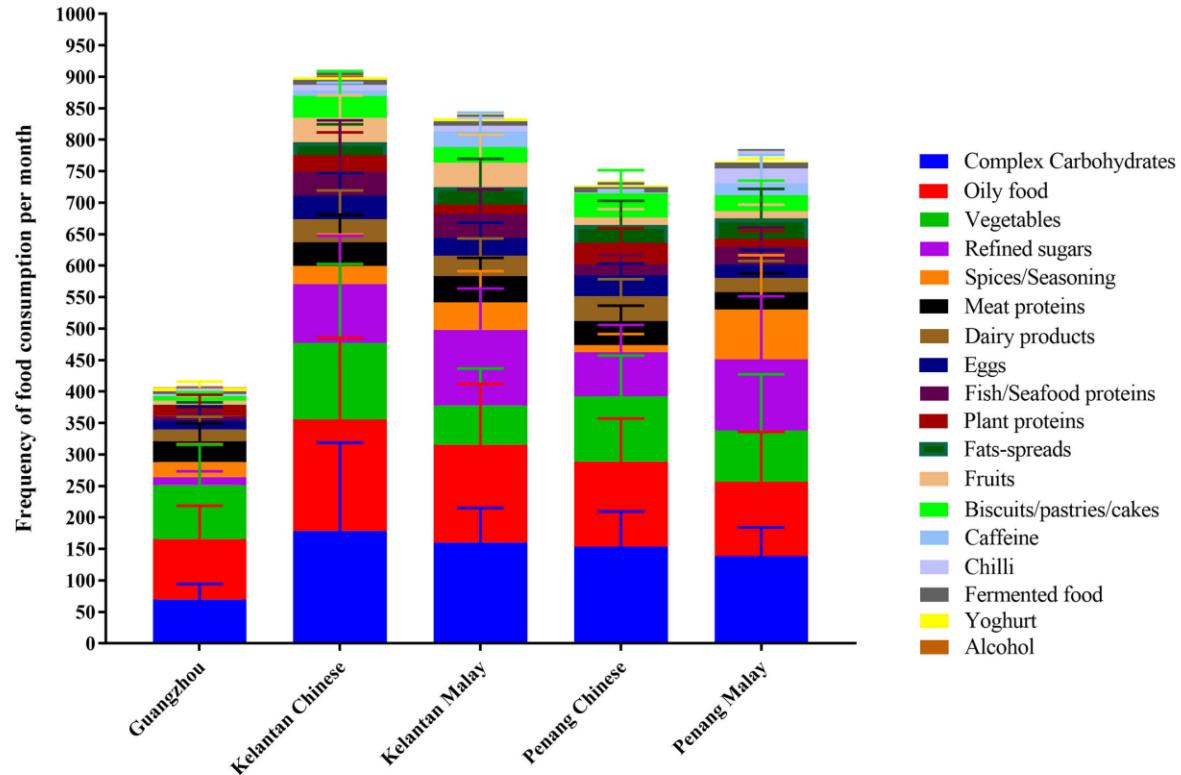
to

Penang, Kelantan
Malaysia



Figure 3.13

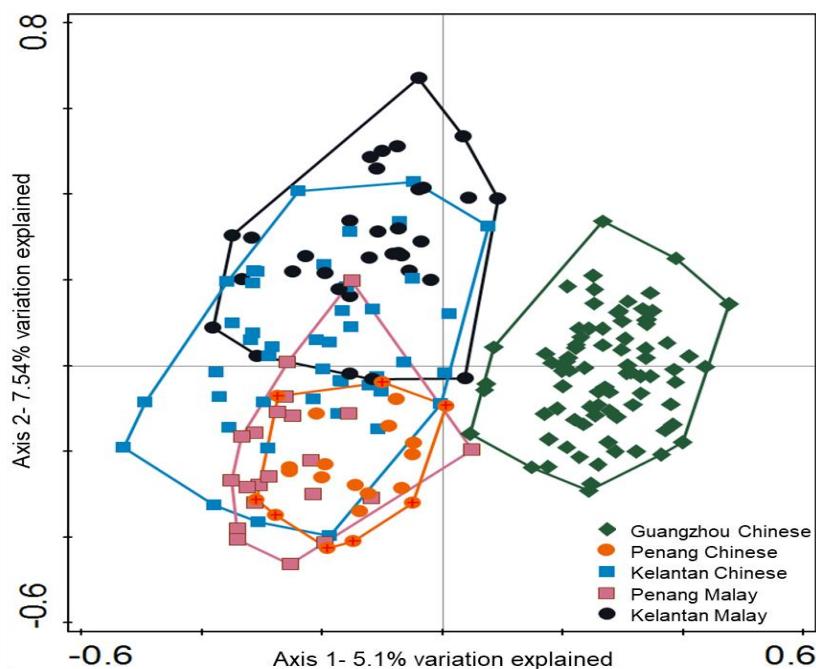
© H. J. de Blij, P. O. Muller, and John Wiley & Sons, Inc.



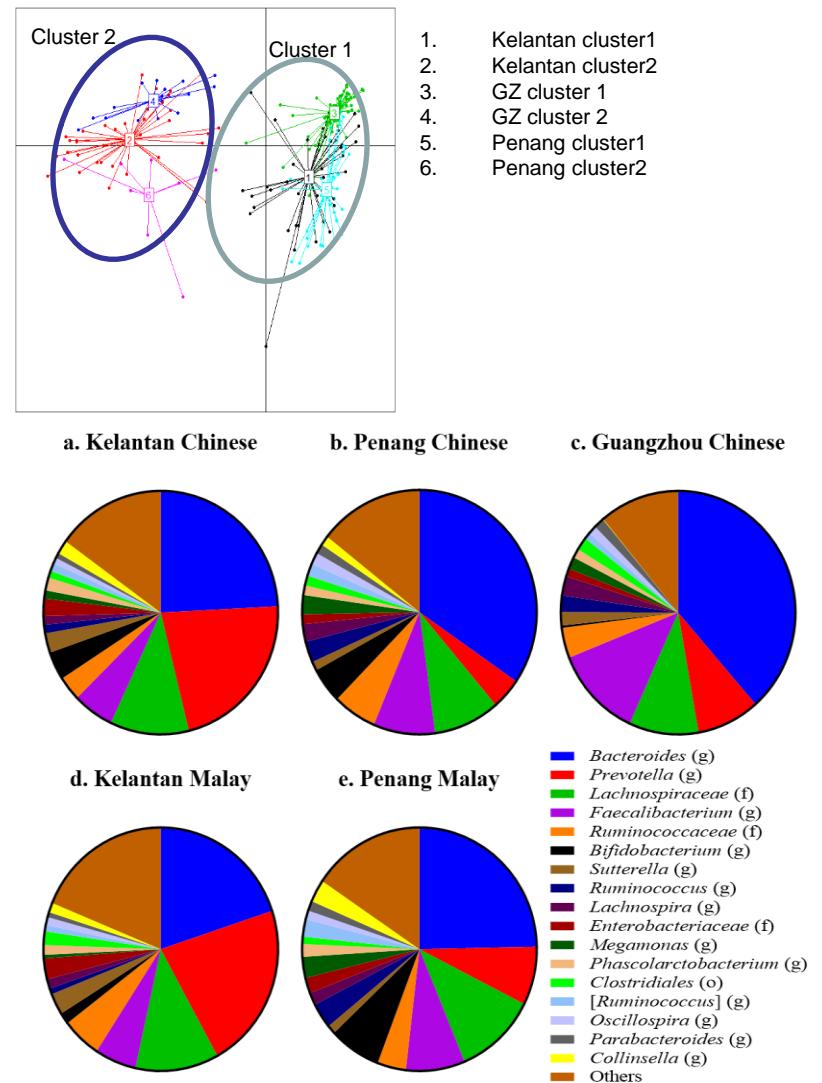
Guangzhou Chinese diet is largely different from Penang & Kelantan Chinese diet

Penang Chinese diet similar to Penang Malay diet, and Kelantan Chinese & Malay

Human migration: Impact of dietary changes on gut microbiota of Southern Chinese



Distance-based redundancy analysis (db-RDA) comparing similarities of two races from three cities. The percentage of variation explained for each axis is shown and Monte Carlo permutation test is significant at $p=0.002$.



Major gut microbiota are determined largely by diet & life style.

Scientific & clinically demonstrated probiotic effects:



1. Probiotics digest dietary components which are not digestible by the human, and intervene energy metabolism & storage.
2. Probiotics prevent formation of carcinogens from dietary components.
3. Probiotics produce vitamins and other growth factors essential for the host.
4. Through competition and production of inhibitory factors, probiotics suppress growth and colonization of gut pathogens.
5. Probiotics strengthen epithelial layer tight-junction, preventing crossover of pathogen and endotoxin, preventing chronic inflammation & related diseases.
6. Probiotics regulate immunity development at young age and enhance immunity in the adults.
7. Through gut-brain axis, probiotics regulate mental stage and functions.

Effect of diet on probiotic effects??

On adhesion, colonization, host-probiotic cross-talk, microbe-microbe interactions

Adhesive Polymers (adhesion of probiotics on GI surface)

Bacteria	Adhesin	Receptor on intestinal surface
<i>Escherichia coli</i>	Type 1 fimbriae Type P fimbriae Type K99 fimbriae Type CFA/I fimbriae Type F-41 fimbriae Flagella-MS	Oligomannoside Galabiose Sialic acid Sialic acid GalNAc, mucin Mannose
<i>Vibrio cholerae</i>	Flagella	L-Fucose
<i>Streptococcus sobrinus</i>	Protein	Glucan
<i>Klebsiella pneumoniae</i>	NFA I protein	GalNAc β 1
<i>Lactobacillus plantarum</i>	Protein	Mannose
<i>Lactobacillus johnsonii</i>		Oligomannoside Gangliotri/tetra-osylcer amides

The type of carbohydrate we eat affects the colonization of probiotics in our gut:

Lactobacillus rhamnosus GG (isolated in US, developed in Europe)

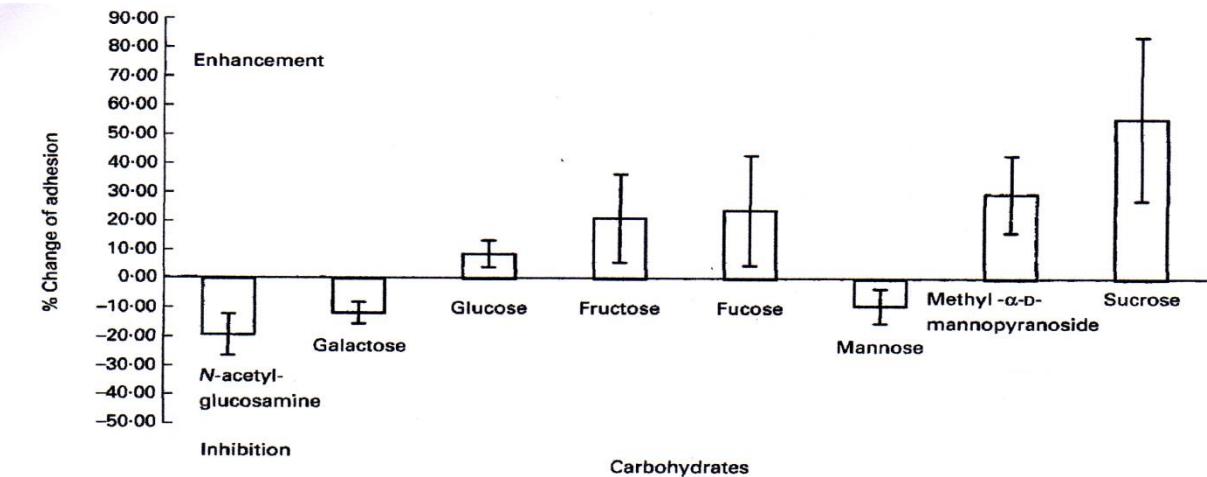


Fig. 1. The effect of carbohydrates on the adhesion of *Lactobacillus rhamnosus GG* to Caco-2 cells. The vertical bars represent the standard deviation.

Lactobacillus casei Shirota (isolated & developed in Japan)

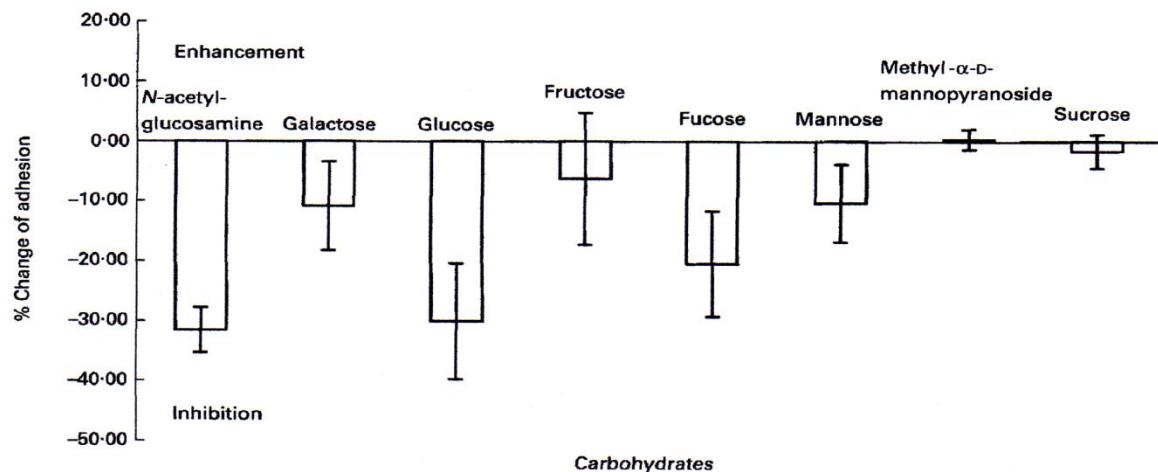
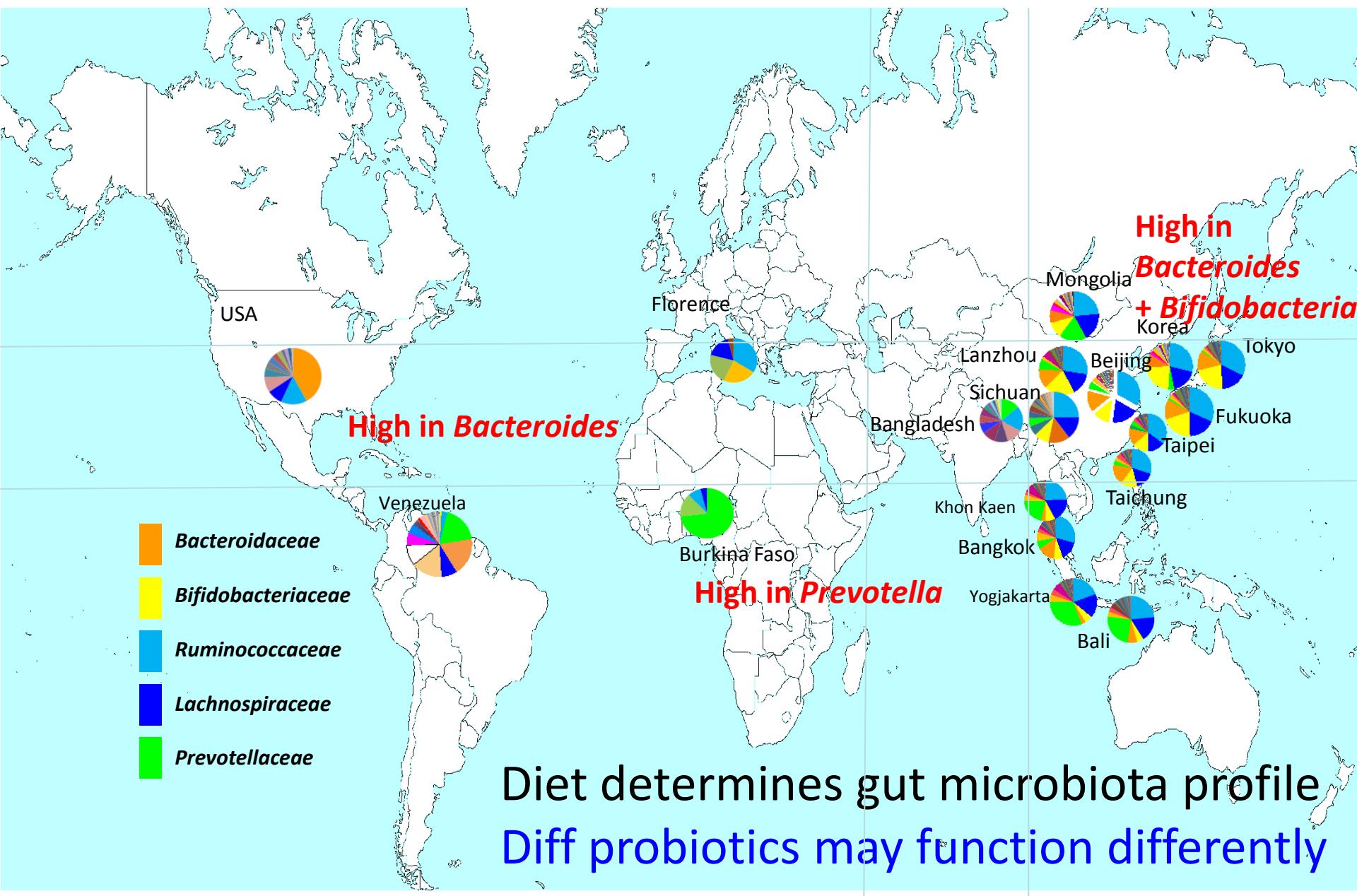


Fig. 2. The effect of carbohydrates on the adhesion of *Lactobacillus casei Shirota* to Caco-2 cells. The vertical bars represent the standard deviation.

Gut microbiota of healthy population worldwide



thank you!