Supplementary Figure 1: The usual dietary intakes are different between rural Africans and African Americans

Photographic illustrations of key differences in usual food preparation and cooking methods between rural South Africans in KwaZulu-Natal, and westernized American populations in Pittsburgh, USA, with a comparative analysis of key macronutrient differences (g/d) based on dietary recall in the last 11 African American subjects and in 20 rural Africans with significance testing by Mann-Whitney U test. Not included for reasons of scale, was the significantly higher fibre intake in Africans 28g/d fiber, plus an estimated 38g/d resistant starch generated in cooking 'putu' as discussed under Supplementary Methods and shown on Supplementary Table 2, vs. 14g/d in African Americans, $p<0.0001$. Photographs by SJDOK.

Supplementary Figure 2: **Changes in Epithelial Proliferation in Different Regions of the Colon**

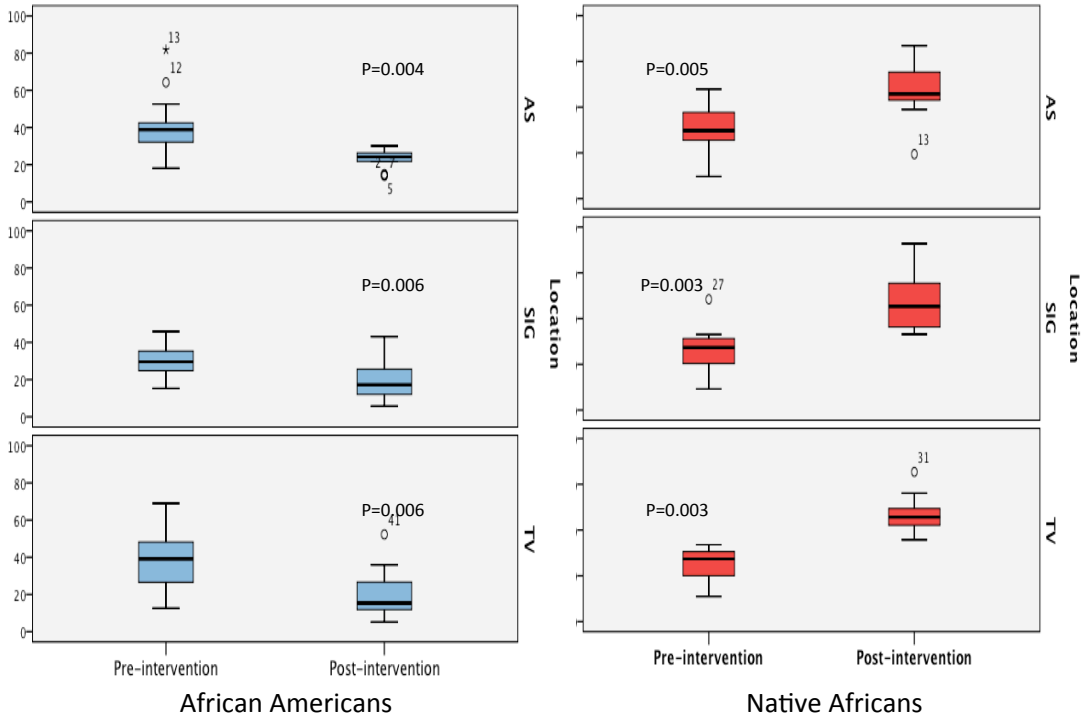
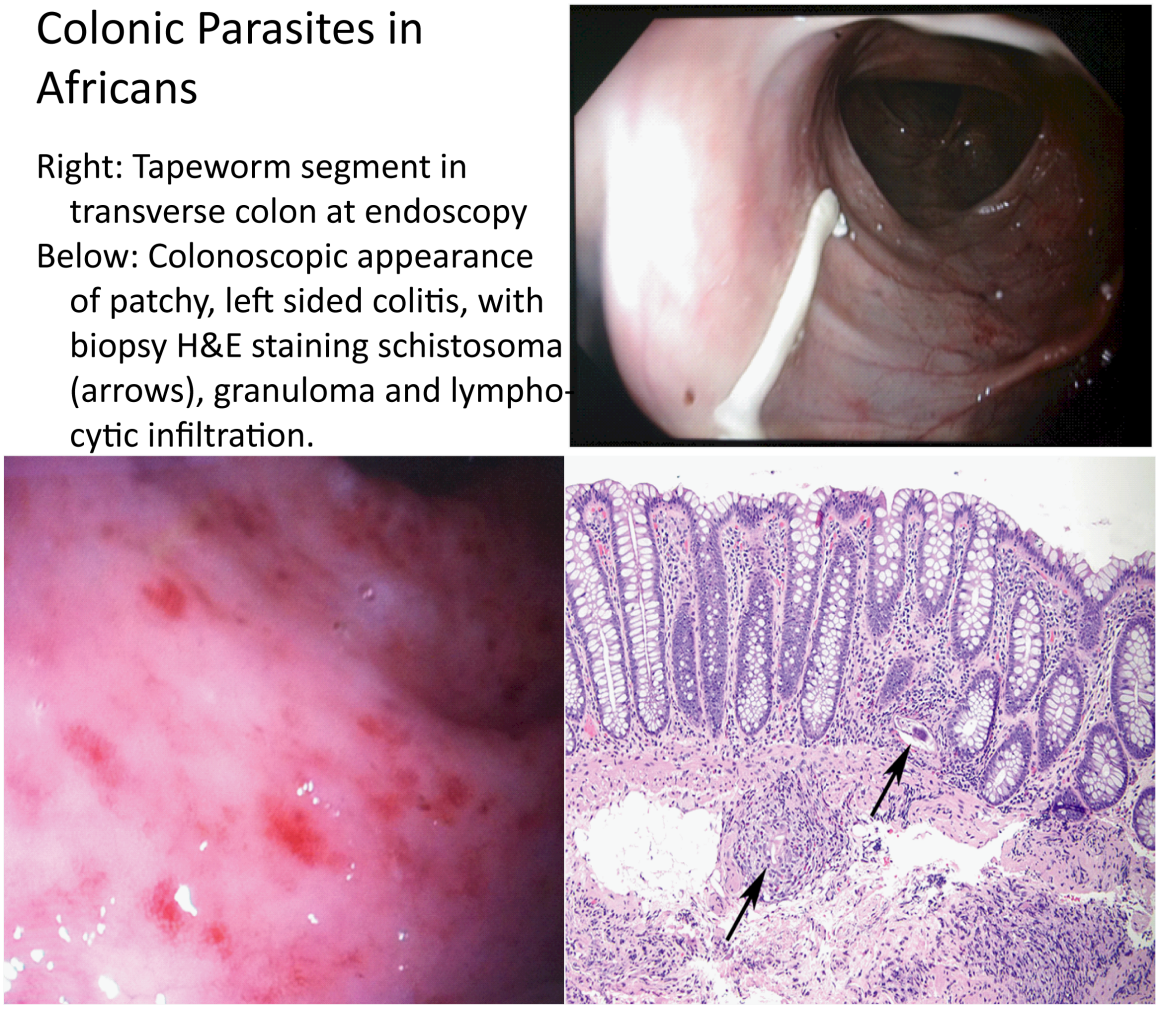


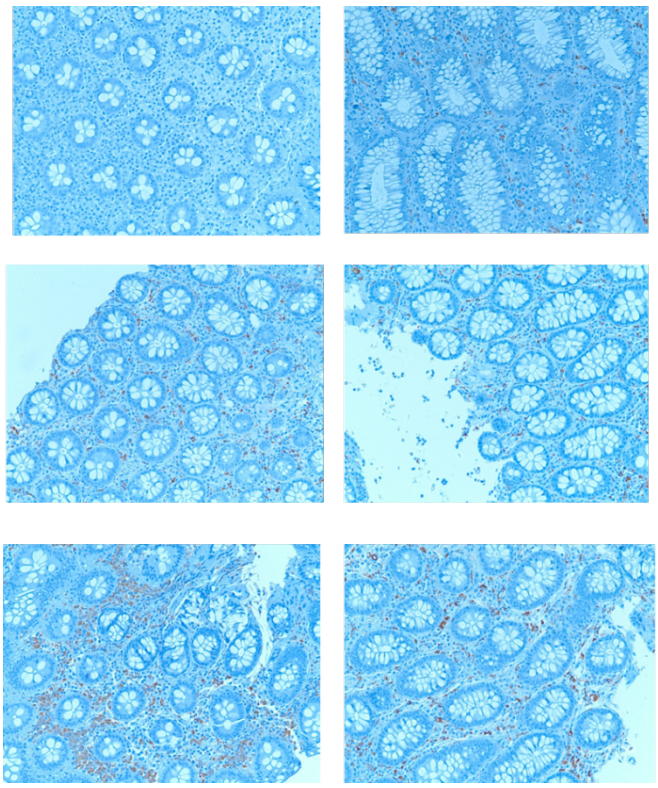
Illustration of the changes in epithelial proliferation measured by Ki67 crypt staining in mucosal biopsy samples from different regions of the colon in 20 African Americans and 12 rural Africans after dietary switch showing similar changes throughout the colon, where AS = ascending colon, SIG = sigmoid colon, and TV = transverse colon. Statistical testing by Wilcoxon Signed Rank test.

Supplementary Figure 3: **Colonoscopic and Histological Evidence of Parasitic Infections in rural Africans**



Colonoscopy findings in rural Africans, illustrating the high background of inflammation (H&E staining) and parasites

Supplementary Figure 4: Grading for Colonic Mucosal Macrocytic Infiltration



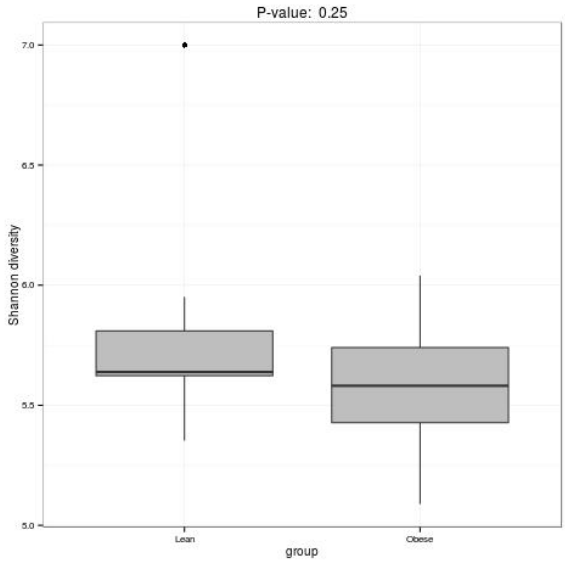
Grade 1: No/ Week
<15 +ve cell/ HPF

Grade 2: Moderate
15 -40+ve cell/ HPF

Grade 3: Strong/ Robest
>40+ve cell/ HPF

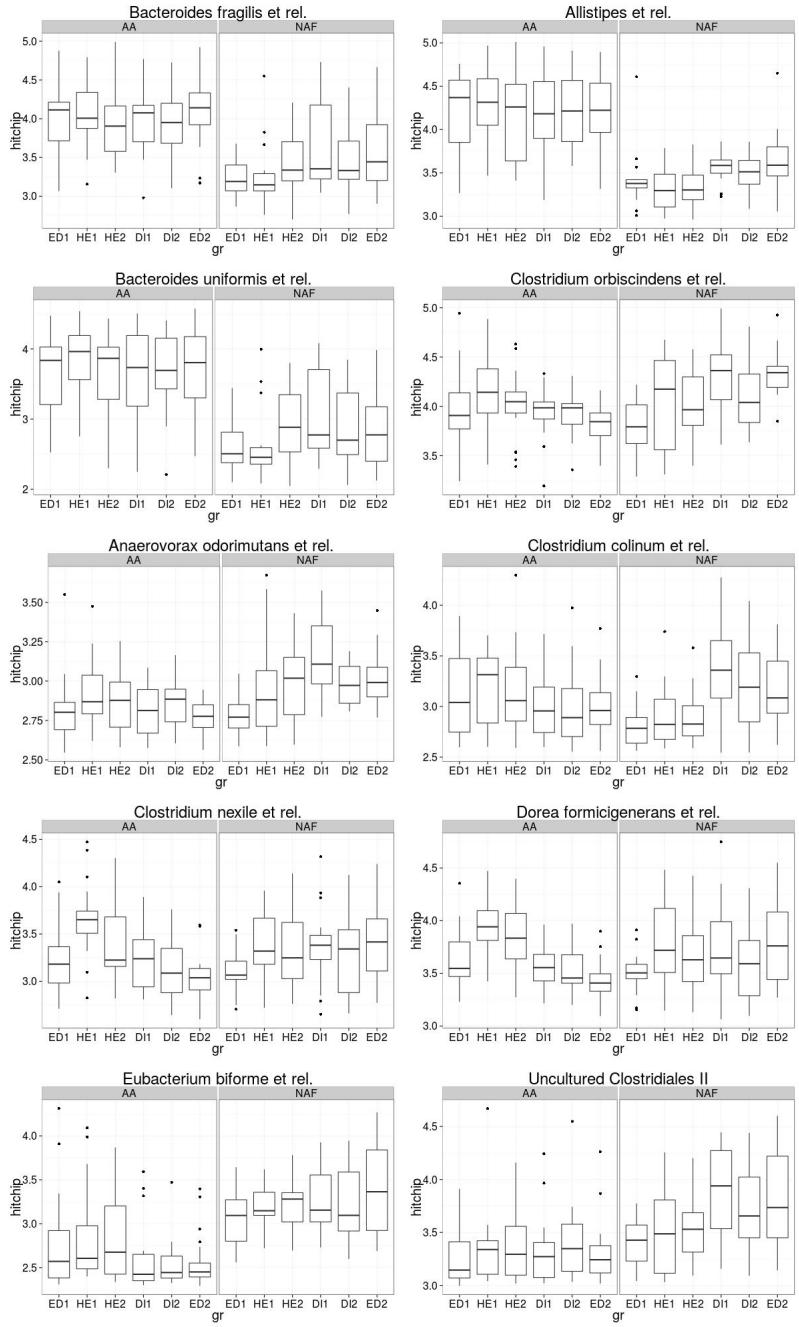
The number of CD68 positive cells (macrophages, stained brown) within the lamina propria were counted and graded on a scale from 1-3: Grade 1 (None/rare), Grade 2 (scattered superficial collections) and Grade 3 (strong, diffuse or band-like infiltrate in the superficial lamina propria) as shown above.

Supplementary Figure 5: The Effect of Obesity on the Microbiota



Nine African Americans and seven Africans were obese with BMI >30 kg/m^2 (p=ns, Chi-squared testing). There were no significant differences (Wilcoxon test) in microbiota diversity, shown by the Shannon diversity index, in our data between obese (BMI >30kg/m^2) and lean individuals as illustrated.

Supplementary Figure 6: Notable additional significant microbe changes during the study



Supplemental Figure 6 illustrates the significant changes in specific bacteria during the time course of the study, as measured by global HITChip analysis, to complement those detected by targeted qPCR analysis shown in Figure 2.

Supplementary Tables

Supplementary Table 1: Summary of Macronutrient and Fibre Compositions Before and After Diet Switch

Group	Period	Fat %	Carbohydrate %	Protein %	Fiber g/d
African American	Usual	35	47	15	14
Rural Africans	Usual	16	72	11	66
African American	Intervention	16	70	14	55
Rural Africans	Intervention	52	21	27	12

The macronutrient composition as % total energy for the usual and intervention diets in Africans and Americans before and after dietary change.

Supplementary Table 2: Group mean values for the estimations of nutrient compositions of the Usual Diets in the African and American populations

	Africans	African Americans
Energy (Kcal)	2353	2393
Total protein (g)	68.5	86
Plant protein (g)	46.2	26
Animal protein (g)	22.3	60
Total fat (g)	42.4	96
Carbohydrate, avail. (g)	388.1	287
Total dietary fibre (g)	28*	14
Insoluble dietary fibre (g)	3.2	9
Soluble dietary fibre (g)	2.8*	6
Ca (mg)	279	734
Fe (mg)	10.7	15.5
Vitamin A (RE) (mcg)	966	4617
Total carotenoids (mcg)	5667	4617
B-Carotene (mcg)	5252	1948
A-Carotene (mcg)	788	411
Thiamin (mg)	1.41	1.9
Riboflavin (mg)	0.69	2.2
Niacin (mg)	12.9	27
Vitamin B6 (mg)	1.186	2
Folate (mcg)	348	486
Vitamin B12 (mcg)	1.3	4.4
Pantothenate (mg)	4.45	5
Biotin (mcg)	24.7	2
Vitamin C (mg)	55	104
Vitamin D (mcg)	1.61	4.2
Vitamin E (mg)	10.57	10.5
α-Tocopherol (mg)	4.62	9
Vitamin K (mcg)	276.42	177
Saturated fatty acids (FA) (g)	8.75	33
Mono-unsaturated FA (g)	13.61	32
Polyunsaturated FA (g)	16.28	22
Cholesterol (mg)	82	323
Choline	253	353

* Excludes resistant starch, estimated to contribute an additional 38g/d, making a total of 66g/d; see above discussion[1].

Group mean values for dietary analysis based on 3 day recalls in the home environment on usual diets (data from 12 rural Africans and 11 African Americans)

Supplemental Table 3: Intervention Diets

Intervention Diet Analysis	**African Americans**	**Africans**
Nutrients **Basic Components**	Actual intakes Daily mean	
Gram Weight (g)	2292.7	1550.4
Calories (kcal)	2205.8	2526.2
Calories from Fat (kcal)	368.4	1299.8
Calories from Sat Fat (kcal)	67.6	502.8
Protein (g)	85.7	170.2
Carbohydrates (g)	383.5	128.1
Dietary Fiber (g)	44.0*	9.0
Soluble Fiber (g)	3.6	1.6
Total Sugars (g)	115.0	31.7
Monosaccharides (g)	28.0	5.9
Disaccharides (g)	27.0	12.1
Other Carbs (g)	94.6	81.5
Fat (g)	41.5	145.2
Saturated Fat (g)	7.5	55.9
Mono Fat (g)	17.7	53.0
Poly Fat (g)	6.9	15.0
Trans Fatty Acid (g)	0.6	5.0
Cholesterol (mg)	273.7	1108.6
Water (g)	1676.6	1043.5
Vitamin A - IU (IU)	13698.5	25601.9
Vitamin A - RAE (RAE)	817.3	6816.6
Carotenoid RE (RE)	1323.9	301.3
Retinol RE (RE)	137.5	6672.0
Beta-Carotene (mcg)	5330.9	1746.3
Vitamin B1 (mg)	1.8	1.4
Vitamin B2 (mg)	1.4	4.2
Vitamin B3 (mg)	16.0	46.7
Vitamin B3 - Niacin Equiv (mg)	26.7	65.6
Vitamin B6 (mg)	1.6	3.3
Vitamin B12 (mcg)	2.2	61.7
Biotin (mcg)	18.9	16.4
Vitamin C (mg)	118.4	33.2
Vitamin D - IU (IU)	108.3	363.3
Vitamin D - mcg (mcg)	2.7	9.0

Vitamin E - Alpha-Toco (mg)	5.1	4.8
Folate (mcg)	760.2	450.4
Folate, DFE (mcg)	818.2	458.3
Vitamin K (mcg)	282.1	102.0
Pantothenic Acid (mg)	4.9	10.1
Calcium (mg)	593.7	574.9
Chromium (mcg)	2.5	5.7
Copper (mg)	1.6	10.4
Fluoride (mg)	1.5	0.1
Iodine (mcg)	88.6	56.2
Iron (mg)	15.8	22.4
Magnesium (mg)	377.7	203.7
Manganese (mg)	4.5	1.2
Molybdenum (mcg)	59.1	24.2
Phosphorus (mg)	943.0	1817.5
Potassium (mg)	3857.5	2839.2
Selenium (mcg)	87.1	164.4
Sodium (mg)	2423.3	3490.3
Zinc (mg)	7.7	29.8
Omega 3 Fatty Acid (g)	0.8	1.1
Omega 6 Fatty Acid (g)	4.1	6.5
Alcohol (g)	0.0	0.0
Caffeine (mg)	352.5	86.1
Choline (mg)	286.4	922.0

* Excludes resistant starch as discussed above[1]

Group mean actual dietary intakes (SDs available) during dietary switch (food given minus food returned)**:** The table shows the analysis of the major nutrient components given each day to the 2 groups during the 14 day dietary switch, highlighting the low animal protein and fat, and high carbohydrate and fibre content of the African American intervention, and the high animal protein and fat, low fibre content of the African intervention. Note that the actual fibre intake in the African American intervention diet was higher as the content of resistant starch was not added (estimated to be an additional 9 g/day[1], making an average total of 53g/d).

Supplementary Table 4: Intervention Menu Examples

a) High Fat, Low Fibre Intervention Diet for Africans

	Breakfast	Lunch	Dinner
Day 1	Beef Sausage Links Pancakes	Hamburger French Fries	Meatloaf Rice
Day 2	Beef Kielbasa Grits	Meatballs Spaghetti	Salisbury Steak Noodles
Day 3	Breakfast Steak Hash Browns	Chili w Meat Rice	Roast Beef Mashed Potatoes & Gravy
Day 4	Corned Beef Hash Potatoes	Beef Hotdog Baked Beans	T-Bone Steak Macaroni & Cheese
Day 5	Beef Bacon Rice Krispies	Beef Stew Potatoes	Fried Liver & Onions Rice
Day 6	Beef Sausage Patty Biscuits	Stuffed Bell Peppers Rice	Beef BBQ Ribs Steak Fries

b). High Fibre, Low Fat Diet for African Americans

	Breakfast	Lunch	Dinner
Day 1	Hi-Maize Corn Fritters	Hi-Maize Corn Dogs w Veggie Dog	Okra/Tomatoes/Hi-Maize Meal
	Salmon Croquettes w Hi-Maize RS	Homemade Tater Tots	Hi-Maize RS Corn Muffins Black-eye Peas
	Spinach/Red Pepper & Onions	Mango slices	Pineapple Black Tea

Day 2	Buttermilk Corn Biscuits	Catfish Nuggets breaded with	Lentils
	Banana	Hi-Maize RS	Rice
	Hi-Maize RS Cheese Grits	Hi-Maize Hushpuppies	Hi-Maize Cornbread
	Scrambled Egg Substitute	Kale Salad w Hi-Maize Croutons	African Potato Salad Guava Juice
Day 3	ProNutro Cereal	Navy bean soup	Fish Taco (Tilapia)

c). Detailed Example of Day 1 High Fibre, Low Fat Menu for the Dietary Intervention in African Americans, based on 2000kcal/day

		Weigh and record edible portion for items with 'X'	Weigh and record leftover portion
Breakfast			
50 g (raw weight)	South African Maize Meal	X	
50 g	Buttermilk, 1% fat (bring 250 g water to a boil, slowly add South African maize meal while constantly stirring to prevent lumps. Add buttermilk and cook on low heat for 1 hour)		
1 large	Large egg (fried in sunflower oil with salt and pepper)		
1 slice	Schwebel's Enriched White Bread		
10 g raw	Tomato slice (fry in oil with egg, place on top)		
300 ml	Coffee		
8 g	Half and Half		
4 g	Sugar (for coffee)		
4 g	Sugar (for phutu)		
1 medium	Banana (remove peel and weigh and record weight)	X	
Mid-morning			
300 ml	Coffee		
8 g	Half and Half		
4 g	Sugar		
Lunch			
100 g cooked	Cooked potatoes, peeled, diced		
100 g cooked	Swiss chard		
10 g cooked	Onions (sautee in sunflower oil)		
5 g	Sunflower oil (for sauteeing onions)		
0.5 g	Salt (for potatoes, swiss chard & onion mixture)		
100 g cooked	White rice		
0.5 g	Rice spice seasoning		
70 g cooked	Chicken breast, boneless, skinless		
5 g raw	Chopped onion (put on chicken before baking)		
0.2 g	black pepper		
0.5 g	salt (brush chicken with sunflower oil & bake in oven)		
150 g	Pineapple juice		

Mid-Afternoon		
100 g raw	Samp (raw Samp soaked for 6 hours)	X
100 g raw	Sugar Beans / Cranberry Beans (raw beans soaked for 6 hours)	X
7 g	Sunflower oil	
10 g raw	Onions	
0.5 g	Curry Powder	
0.5 g	Salt	
0.2 g	Black Pepper	
	(Boil beans for 1 hour. Add samp, cook another hour. Add onions, oil, spices, then cook 1 hour more. Record weight when all items cooked and mixed together).	X
	Weight of Mid Afternoon Samp and Beans	X
Dinner		
	Samp & Beans	X
300 ml	Roobios Tea	
4 g	Sugar	
4 g	Lemon juice (for tea)	
Evening		
1 medium	Orange (remove peel and weigh)	X
1 slice	Schwebel's White Bread (toasted)	
7 g	Apricot Jam	

Supplementary Table 5: Histological staining of colonic biopsies

a) Scoring criteria for the histological assessment of mucosal biopsies

Key	Scoring criteria	Lamina Propria Chronic Inflammation	Intra-epithelial lymphocytes
0	Normal	Normal density and distribution	<5 /100
1	mild	Scattered foci of deep chronic inflammation	5-10/100
2	moderate	Diffuse superficial and deep chronic inflammation without expansion of the lamina propria	11-20/100
3	marked	Diffuse superficial and deep with expansion of the lamina propria with basal lymphoplasmacytosis	>20/100

b) Illustration of the higher densities of inflammatory cells within the lamina propria in Africans at baseline

Baseline Differences		African Americans		Africans		
		N	%	N	%	p-value
Lamina Propria (LP) inflammation	Normal	21	36.8%	0	0.0%	0.0001
	Mild	33	57.9%	18	50.0%	
	Moderate	3	5.3%	18	50.0%	
Total		57	100.0%	36	100.0%	

c) Illustration of the higher densities of intraepithelial lymphocytes in Africans at baseline

		African Americans		Africans		
		N	%	N	%	P-value
Intraepithelial Inflammation	Normal/Mild	51	89.5%	2	5.6%	0.0001
	Moderate	6	10.5%	5	13.9%	
	Marked	0	0.0%	29	80.6%	
Total		57	100.0%	36	100.0%	

d) Eosinophil counts from biopsies taken from the sigmoid colon were non-significantly higher in Africans at baseline

Location: Sigmoid colon						
		African Americans		Africans		
		N	%	N	%	
Increased eosinophils in LP	No	5	27.8%	2	16.7%	P=0.7
	Yes	13	72.2%	10	83.3%	
Total		19	100.0%	12	100.0%	

Supplementary Table 5 summarizes the H&E histological staining light microscopy results from the biopsies taken from the sigmoid, transverse, and ascending colon, which show significantly higher grades of inflammation in the lamina propria, and intraepithelial lymphocyte counts in Africans, which persisted following dietary switch. The scoring system used is shown on the first table. Note that 3 sets of biopsies were taken from each subject, hence the maximum number of measurements were 20x3 for lamina propria and intraepithelial assessments. Unfortunately some samples were lost during transport, preparation or staining. Of note, the formalin preserved samples for the first 8 African participants were lost in transportation from the rural areas. Findings from the different regions of the colon showed the same pattern of differences. Left sided eosinophilic infiltration (measured only in the sigmoid colon as changes in the other regions of the colon are considered less clinically significant) was noted in 83% of Africans and 72% of African Americans. In addition to schistosoma, intestinal spirochaetosis was also identified in the biopsies of three African subjects.

Supplementary Table 6: Targeted Faecal Short Chain Fatty Acid and Bile Acid Analysis

	African Americans			Rural Africans		
	ED1	ED2	p value	ED1	ED2	p value
Acetate	17.2	29.9	0.01	73.2	41.4	0.02
Propionate	5.3	9.2	0.001	20.1	10.6	0.003
Butyrate	4.2	7.3	0.01	13.4	6.6	0.01
Total bile acids	64.4	40.7	0.009	5.5	9.5	0.0001

Group median values for the major fecal short chain fatty acids and total bile acids (all in μmol/g faeces) for 20 Africans and 20 Americans before (period ED 1, Table 1) and after dietary switch (period ED 2), statistical evaluation across the time points by Kruskal Wallis test. See **Figure 2** for box plots.

Supplementary Table 7: **Colonic Evacuate Analysis**

mmoles	African American (AA)			African (A)			p Value
	Before	After	p Value	Before	After	p Value	Baselines
Acetate	14.51±3.29	32.97±8.07	0.040	49.76±9.41	25.48±3.71	0.039	0.0002
Propionate	3.97±0.83	8.53±2.08	0.048	12.58±1.93	8.20±0.82	0.068	0.0000
Butyrate	3.56±0.96	8.61±2.10	0.034	12.30±2.42	6.66±0.97	0.038	0.0005
Lithocholic acid	0.08±0.01	0.03±0.01	0.019	0.01±0.002	0.06±0.02	0.033	0.0001
Cholic acid	0.46±0.13	0.17±0.06	0.073	0.04±0.01	0.18±0.06	0.036	0.0030
Deoxycholic acid	0.52±0.12	0.16±0.05	0.020	0.04±0.01	0.14±0.04	0.038	0.0004

Measurements of short chain fatty acid and bile acid contents in colonic evacuates (mmoles/total evacuate) showing significant population differences at baseline (Mann-Whitney), followed by significant (Wilcoxon signed rank test) reciprocal changes in African Americans and rural Africans following diet switch. Total evacuate quantities were 1.50±0.13 litres in 20 African Americans and 1.63±0.10 litres in 20 Africans (p=0.17). Using these figures plus measurements of SCFA and BA concentrations in the evacuates to calculate total colonic quantities showed that, in general, faecal concentrations reflected the same changes as colonic contents.

Supplementary Table 8: Baseline Differences in Faecal Microbial Genera

Phylum/Class	Genus-like group	FDR	African Americans (%)	Africans (%)
Actinobacteria	*Collinsella*	<0.01	0.0	0.1
Bacilli	*Enterococcus*	0.02	0.0	0.1
Bacteroidetes	*Bacteroides uniformis* et rel.	<0.01	1.4	0.1
Bacteroidetes	*Allistipes* et rel.	<0.01	3.9	0.7
Bacteroidetes	*Bacteroides fragilis* et rel.	<0.01	2.0	0.3
Bacteroidetes	*Bacteroides ovatus* et rel.	<0.01	1.1	0.3
Bacteroidetes	*Bacteroides vulgatus* et rel.	<0.01	15.1	1.8
Bacteroidetes	*Parabacteroides distasonis* et rel.	<0.01	1.1	0.4
Bacteroidetes	*Bacteroides stercoris* et rel.	<0.01	0.5	0.1
Bacteroidetes	*Bacteroides intestinalis* et rel.	<0.01	0.2	0.0
Bacteroidetes	*Bacteroides plebeius* et rel.	<0.01	0.6	0.3
Bacteroidetes	*Prevotella melaninogenica* et rel.	<0.01	11.7	48.5
Bacteroidetes	*Prevotella oralis* et rel.	<0.01	2.0	7.3
Bacteroidetes	*Bacteroides splachnicus* et rel.	<0.01	0.9	0.4
Bacteroidetes	*Prevotella ruminicola* et rel.	<0.01	0.0	0.1
Bacteroidetes	*Tannerella* et rel.	<0.01	0.4	0.2
Clostridium cluster I	*Clostridia*	<0.01	0.2	0.4
Clostridium cluster III	*Clostridium stercorarium* et rel.	0.02	0.1	0.2
Clostridium cluster IV	*Subdoligranulum variable* et rel.	0.01	2.5	1.0
Clostridium cluster IX	*Mitsuokella multiacida* et rel.	<0.01	0.1	0.4
Clostridium cluster IX	*Megasphaera elsdenii* et rel.	0.02	0.1	0.4
Clostridium cluster IX	Uncultured Selenomonadaceae	0.03	0.1	0.0
Clostridium cluster IX	*Dialister*	0.047	4.6	0.1
Clostridium cluster XI	*Clostridium difficile* et rel.	<0.01	0.1	0.4
Clostridium cluster XIVa	*Clostridium symbiosum* et rel.	<0.01	2.6	1.0
Clostridium cluster XIVa	*Anaerostipes caccae* et rel.	<0.01	0.7	0.2
Clostridium cluster XIVa	*Eubacterium ventriosum* et rel.	<0.01	0.2	0.1
Clostridium cluster XIVa	*Bryantella formatexigens* et rel.	<0.01	1.5	0.4
Clostridium cluster XIVa	*Ruminococcus obeum* et rel.	0.02	1.8	1.3
Uncultured Clostridiales	Uncultured Clostridiales II	0.03	0.3	0.7
Verrucomicrobia	*Akkermansia*	0.02	1.4	0.2

The genus-like groups that differed between Africans and African Americans at baseline. The most significantly different taxa between 20 Africans and 20 African Americans are shown (False Discovery Rate FDR<5%). The fraction of total HITChip signal is used as a proxy for relative abundance, and the average over the samples is provided for each comparison. In line with our previous observations[2] (same populations, different individuals), of the Bacteroidetes phylum, *Bacteroides* is the dominant genus in African Americans, while Africans are dominated by the genus *Prevotella*.

Supplementary Table 9: Plasma Amino Acids in Africans and African Americans Before and After Dietary Change

	African Americans			Rural Africans		
	Pre: ED 1	Post: ED 2	p value	Pre: ED 1	Post: ED 2	p value
Total	1358±98	1355±40	Ns	1209±34	1393±87	ns
Alanine	325±23	320±21	Ns	237±20	347±30	0.01

p=0.009

Group mean ± SE values for plasma amino acid concentrations (µmol/l) showing significantly lower values of the most abundant amino acid, alanine, in 20 rural Africans compared to 20 African Americans at baseline (ED 1, Table 1) (Mann-Whitney). The group mean differences in the other amino acids were not significant. Following diet switch (ED 2), alanine significantly increased in rural Africans (Wilcoxon signed rank test).

Supplementary Table 10: Demographics of Participants

	Age (yr)	Weight (kg)	Height (cm)	Body mass index (kg/m^2)
African Americans	55.6±0.8	87.1±4.0	172.5±2.4	29.4±0.8
Rural Africans	54.8±1.0	73.1±3.3*	163.5±2.2**	27.7±1.5

Summary of the demographic features of the 2 groups. Age and body mass index were similar for the two groups, but Africans were significantly shorter (p=0.009, Mann-Whitney) and lighter (p=0.01). Nine African Americans and seven Africans were obese with BMI >30 kg/m^2 (p=ns, Chi-squared testing).

Supplementary Table 11: List of abbreviations and full names for metabolites in the networks shown in Figure 5.

Abbreviated name	Full Name
(3S)-Cit-CoA	(3S)-Citryl-CoA
1,2-Propanediol	1,2-Propanediol
1DeO-D-xylulose 5P	1-Deoxy-D-xylulose 5-phosphate
2(OH-Et)-2-oxobutanoate	2-Aceto-2-hydroxybutanoate
2(OH-Et)TPP	2-Hydroxyethyl-TPP
2,3,4,5-TetraH-dipicolinate	2,3,4,5-Tetrahydrodipicolinate
2,3DiOH-3Me-valerate	2,3-DiOH-3Me-valerate
2,3DiOH-isovalerate	2,3-Dihydroxyisovalerate
2,4DiOH-hept-2-enedioate	2,4-Dihydroxyhept-2-enedioate
2,5DiOH-pyridine	2,5-Dihydroxypyridine
2,5-Dioxopentanoate	2,5-Dioxopentanoate
2,6-DiAm-pimelate	2,6-Diaminopimelate
2-[2Cx-4Methiazol-5(2H)-ylidene]Et P	2-[2-Carboxy-4Methiazol-5(2H)-ylidene]ethyl phosphate
2-Acetolactate	2-Acetolactate
2Am-3Cx-muconate semiAl	2-Amino-3-carboxymuconate semialdehyde
2Am-6-oxopimelate	2-Amino-6-oxopimelate
2DeH-3deO-6P-D-galactonate	2-Dehydro-3-deoxy-6-phospho-D-galactonate
2DeH-pantoate	2-Dehydropantoate
2DeO-D-ribose 5P	2-Deoxy-D-ribose 5-phosphate
2Me-1(OH-Bu)TPP	2-Methyl-1-hydroxybutyl-TPP
2Me-1(OH-Pr)TPP	2-Methyl-1-hydroxypropyl-TPP
2Me-butanoyl-CoA	2-Methyl-butanoyl-CoA
2Me-citrate	2-Methylcitrate
2OH-glutarate	2-Hydroxyglutarate
2-Oxo-3deO-6P-gluconate	2-Keto-3-deoxy-6-phosphogluconate
2-Oxobutyrate	2-Oxobutyrate
2-Oxoglutarate	2-Oxoglutarate
2-Oxoisocaproate	2-Oxoisocaproate
2-Oxoisovalerate	2-Ketovaline
2Ph-acetamide	2-Phenylacetamide
3,4DiOH-mandelaldehyde	3,4-Dihydroxymandelaldehyde
3,4DiOH-mandelate	3,4-Dihydroxymandelate
3Cx-1(OH-Pr)TPP	3-Carboxy-1-hydroxypropyl-TPP
3DeH-sphinganine	3-Dehydrosphinganine
3Fum-pyruvate	3-Fumarylpyruvate
3HIV	3-Hydroxyisovalerate
3HIV-CoA	3-Hydroxyisovaleryl-CoA
3IsoPr-malate	3-Isopropylmalate

Abbreviated name	Full Name
3Me-1(OH-Bu)TPP	3-Methyl-1-hydroxybutyl-TPP
3Me-2-oxopentanoate	3-Methyl-2-oxopentanoate
3Me-crotonyl-CoA	3-Methyl-crotonyl-CoA
3Me-TLA SO	3-Methylthiolactic acid sulfoxide
3Me-TPA SO	3-Methylthiopyruvic acid sulfoxide
3OH-3Me-2-oxopentanoate	3-Hydroxy-3-Methyl-2-oxopentanoate
3OH-anthranilate	3-Hydroxyanthranilate
3OH-mandelate	3-Hydroxymandelate
3OH-Tyr	3-Hydroxy-tyrosine
3-Oxopropanoate	3-Oxopropanoate
3-Ureidopropionate	3-Ureidopropionate
4-Cresol	4-Cresol
4CS	4-Cresyl sulfate
4-Guanidinobutanoate	4-Guanidinobutanoate
4HPA-CoA	4-Hydroxyphenylacetyl-CoA
4HPA-Glu	4-Hydroxyphenylacetylglutamate
4OH-2-oxoglutarate	4-Hydroxy-2-oxoglutarate
4OH-2-oxohexanoate	4-Hydroxy-2-oxohexanoate
4OH-2-oxopimelate	4-Hydroxy-2-ketopimelate
4OH-2-oxovalerate	4-Hydroxy-2-oxovalerate
4OH-benzaldehyde	4-Hydroxybenzaldehyde
4OH-benzoate	4-Hydroxybenzoate
4OH-benzoyl-CoA	4-Hydroxybenzoyl-CoA
4OH-hippurate	4-Hydroxyhippurate
4OH-phenacyl alcohol	4-Hydroxyphenacyl alcohol
4-Oxobutanoate	4-Oxobutanoate
5,10My-THF	5,10Methylene-THF
5DeH-4deO-D-glucarate	5-Dehydro-4-deoxy-D-glucarate
5Me-3-oxo-4-hexenoyl-CoA	5-Methyl-3-oxo-4-hexenoyl-CoA
5Me-THF	5-Methyltetrahydrofolate
5OH-isourate	5-Hydroxyisourate
5P-ribosylamine	5-Phosphoribosylamine
6ASA	6-Aminosalicylic acid
6OH-3-succinoylpyridine	6-Hydroxy-3-succinoylpyridine
6OH-nicotinate	6-Hydroxynicotinate
Ac-adenylate	Acetyl adenylate
Ac-choline	Acetylcholine
Ac-CoA	Acetyl-CoA
Acetate	Acetate
Adenine	Adenine
Adenylosuccinate	Adenylosuccinate
ADMA	Nω,Nω-Dimethyl-arginine

Abbreviated name	Full Name
ADP-ribose	ADP-ribose
Adrenaline	Adrenaline
Ala	Alanine
Allantoate	Allantoate
Allantoin	Allantoin
AMP	Adenosine 5-monophosphate
Anthranilate	2-Aminobenzoate
Anthraniloyl-CoA	Anthraniloyl-CoA
Arachidonate	Arachidonate
Arachidonyl-CoA	Arachidonyl-CoA
Arg	Arginine
Argininosuccinate	Argininosuccinate
Arterenol	Arterenol
Asp	Aspartate
Betaine	Betaine
Betaine aldehyde	Betaine aldehyde
Biocytin	Biocytin
Biotin	Biotin
Biotinyl-5AMP	Biotinyl-5-adenosine monophosphate
Butyrate	Butyrate
Butyryl-CoA	Butyryl-CoA
Carbamate	Carbamate
Carbamoyl P	Carbamoyl phosphate
Carnitine	Carnitine
Catechol	Catechol
Choline	Choline
Choline P	Phosphocholine
Choloyl-CoA	Choloyl-CoA
Chorismate	Chorismate
Citicoline	Citicoline
Citrate	Citrate
Citrulline	Citrulline
CMP	Cytidine-5-monophosphate
CoA	Coenzyme A
Creatine	Creatine
Creatinine	Creatinine
Cys	Cysteine
CysGly	Cysteinylglycine
Cystathionine	Cystathionine
Cytidine	Cytidine
Cytosine	Cytosine
D-arabino-6P-hex-3-ulose	D-arabino-6-Phospho-hex-3-ulose

Abbreviated name	Full Name
D-Arabinose	D-Arabinose
Deamido-NAD	Deamido-NAD
DeP-CoA	Dephospho-CoA
D-Fructose 6P	D-Fructose 6-phosphate
D-Glucosamine P	D-Glucosamine phosphate
DHF	Dihydrofolate
DiH-LipE	Dihydrolipoamide-E
DMA	Dimethylamine
DMF	N,N-Dimethylmethanamide
DMG	Dimethylglycine
Dopamine	Dopamine
D-Ribose	D-Ribose
D-Ribulose	D-Ribulose
D-Ribulose 5P	D-Ribulose 5-phosphate
D-Xylose	D-Xylose
D-Xylulose	D-Xylulose
D-Xylulose 5P	D-Xylulose 5-phosphate
Ethanal	Ethanal
FA	Fatty acid
For-kynurenine	Formylkynurenine
Formate	Formate
Formylanthranilate	Formylanthranilate
Fumarate	Fumarate
GABA	gamma-Aminobutyric acid
GAR	Glycinamide ribonucleotide
Gln	Glutamine
Glu	Glutamate
Glu 5-semiAl	Glutamate 5-semialdehyde
Gly	Glycine
Glyceraldehyde 3P	Glyceraldehyde 3-phosphate
Glycerone P	Glycerone phosphate
Glycerophosphoric acid	Glycerophosphoric acid
Glycocholate	Glycocholate
Glycolaldehyde	Glycolaldehyde
Glycolate	Glycolate
Glyoxylate	Glyoxylate
GMP	Guanosine 5-monophosphate
GPC	Glycerophosphocholine
GSH	Glutathione
GTP	Guanosine 5-triphosphate
Guanidinoacetate	Glycocyamine
hCys	Homocysteine

Abbreviated name	Full Name
Homocitrate	Homocitrate
HTPA	4-Hydroxy-2,3,4,5-tetrahydrodipicolinate
Hydrouracil	Hydrouracil
Hypoxanthine	Hypoxanthine
IAA	Indole-3-acetic acid
Ile	Isoleucine
IminoAsp	Iminoaspartate
IminoGly	Iminoglycine
IMP	Inosine 5-monophosphate
Indole-3-acetamide	Indole-3-acetamide
Indoleglycerol P	Indoleglycerol phosphate
Inosine	Inosine
Isobutyryl-CoA	Isobutyryl-CoA
Isocitrate	Isocitrate
Isovaleryl-CoA	Isovaleryl-CoA
KDO	2-Dehydro-3-deoxy-D-octonate
Kynurenine	L-Kynurenine
Lactaldehyde	Lactaldehyde
Lactate	Lactate
Lecithin	Lecithin
Leu	Leucine
Linoleate	Linoleate
Linolenate	Linolenate
Linoleoyl-CoA	Linoleoyl-CoA
LipE	Lipoamide-E
LTA4	Leukotriene A4
LTC4	Leukotriene C4
L-Xylulose	L-Xylulose
Lys	Lysine
Malate	Malate
Mal-CoA	Malyl-CoA
Me-corrinoid	Methylcorrinoid
MeOH	Methanol
meso-2,6-DiAm-pimelate	meso-2,6-Diaminopimelate
Methanal	Methanal
Methyl-CoM	Methylcoenzyme M
MMA	Methylamine
N2Cit-N6Ac-N6OH-Lys	N2-Cityl-N6-Acetyl-N6-hydroxylysine
N6Ac-2,6-diAm-pimelate	N6-Acetyl-2,6-diaminopimelate
N6Ac-Lys	N6-Acetyl-lysine
N6Ac-N6-Indol-3-yl-Lys	N6-[(Indol-3-yl)acetyl]-lysine
N6Ac-N6OH-Lys	N6-Acetyl-N6-hydroxylysine

Abbreviated name	Full Name
N6OH-Lys	N6-hydroxylysine
NA	Nicotinamide
NAc-Asp	N-Acetylaspartate
NAc-citrulline	N-Acetylcitrulline
NAc-D-glucosamine 6P	N-Acetyl-D-glucosamine 6-phosphate
NAc-D-mannosamine	N-Acetyl-D-mannosamine
NAc-Orn	N-Acetyl-ornithine
NAc-SMCSO	N-Acetyl-S-Methyl-L-cysteine sulfoxide
NAD	Nicotinamide adenine dinucleotide
NANA	N-Acetyl neuraminic acid
N-Car-Asp	N-Carbamoyl-aspartate
N-For-Asp	N-Formylaspartate
N-For-Glu	N-Formylglutamate
N-For-maleamic acid	N-Formylmaleamic acid
Nicotinate	Nicotinate
Nicotinate ribonucleotide	Nicotinate ribonucleotide
NMN	Nicotinamide mononucleotide
NMNA	Trigonelline
N-Ribosyl NA	N-Ribosylnicotinamide
N-Suc-Glu	N-Succinylglutamate
Nω-(ADP-D-ribosyl)Arg	Nomega-(ADP-D-ribosyl)-arginine
OAc-carnitine	O-Acetylcarnitine
OAc-Ser	O-Acetylserine
Orn	Ornithine
O-Suc-hSer	O-Succinylhomoserine
Oxaloacetate	Oxaloacetate
PAG	Phenylacetylglutamine
Palmitoylcarnitine	Palmitoylcarnitine
Palmitoyl-CoA	Palmitoyl-CoA
Pantoate	Pantoate
Pantothenate	Pantothenate
PAP	Phosphoadenosine phosphate
PhAc	Phenylacetate
PhAc-CoA	Phenylacetyl-CoA
Phe	Phenylalanine
Phenol	Phenol
Propanal	Propanal
Propionate	Propionate
Propionyladenylate	Propionyladenylate
Propionyl-CoA	Propanoyl-CoA
PRPP	PRPP
Psi 5P	Pseudouridine 5-phosphate

Abbreviated name	Full Name
PtdSer	Phosphatidylserine
Pyruvate	Pyruvate
Quinolinate	Quinolinate
Ribose 5P	Ribose 5-phosphate
S-(2Me-Bt)diH-LipE	S-(2-Methyl-butanoyl)-DiH-LipE
S-(2Me-Pp)diH-LipE	S-(2-Methyl-propanoyl)-DiH-LipE
S-(3Me-Bt)diH-LipE	S-(3-Methyl-butanoyl)-DiH-LipE
S-(MeOH)GSH	S-(Hydroxymethyl)glutathione
Saccharopine	Saccharopine
S-Adenosyl-hCys	S-Adenosylhomocysteine
Sarcosine	Sarcosine
SelenoCys	Selenocysteine
Selenocystathionine	Selenocystathionine
Ser	Serine
S-For-GSH	S-Formylglutathione
SMCSO	S-Methyl-L-cysteine sulfoxide
S-Suc-diH-LipE	S-SuccinylDiH-LipE
Succinate	Succinate
Suc-CoA	Succinyl-CoA
tBA	tert-Butanol
TCE	Trichloroethylene
Thr	Threonine
TMA	Trimethylamine
TMAO	Trimethylamine N-oxide
TPP	Thiamin pyrophosphate
Trp	Tryptophan
Tyr	Tyrosine
Tyramine	Tyramine
UDP-3-O-(βOH-myristoyl)-NAc-glucosamine	UDP-3-O-(beta-hydroxymyristoyl)-N-Acetyl-glucosamine
UDP-NAc-glucosamine	UDP-N-Acetyl-glucosamine
UMP	UMP
Uracil	Uracil
Urate	Urate
Urea	Urea
Ureidoperacrylic acid	Ureidoperacrylic acid
Uridine	Uridine
Val	Valine
Valerate	Valerate
Valeryl-CoA	Pentanoyl-CoA
Xanthine	Xanthine
Xylitol	Xylitol
Xylulose 1P	Xylulose 1-phosphate

Abbreviated name	Full Name
αIsoPr-malate	alpha-Isopropylmalate
α-Linolenoyl-CoA	alpha-Linolenoyl-CoA
βAla	beta-Alanine
βAlaArg	beta-Alanyl-arginine
βAlaLys	beta-Alanyl-lysine
βMe-Mal-CoA	beta-Methyl-malyl-CoA
γGluCys	gamma-Glutamylcysteine

Explanation for the abbreviations used for metabolites measured by ^{1}H-NMR and shown in the networks in Figure 5.

Supplementary Notes

Supplementary Note 1: Additional Study Details

Study Design: Subjects were not housed and fed their usual diets for the home environment study as validation studies had been previously conducted in both communities to verify that the diets, microbiome, metabolome and mucosal biomarkers of cancer risk, i.e. epithelial proliferation measured by Ki67staining were distinct, particularly with regard to the dietary macronutrient composition, rates of colonic saccharolytic fermentation, bile acid deconjugation and mucosal proliferation[2,3]. Recruitment would have been problematic for a 4-week in-house study, because in rural Africa, healthy middle-aged members of the population conventionally look after grandchildren while their parents work, and in America it would be difficult for employed African Americans to take 4 weeks off, thus biasing selection.
Recruitment: Overall, the study was well accepted by both communities and recruitment followed the estimated timelines. Only 6 African Americans who satisfied the inclusion and exclusion criteria decided not to join the study. Recruitment was easier in rural Africa, as more potential candidates were unemployed, and only one interviewed potential candidate decided not to join the study.

Inclusion criteria
1. Informed consent
2. Ages 50-65 years, inclusive
3. BMI between 20-35 Kg/m^2: In our last study, average BMI was in the overweight-moderately obese category for both groups, i.e. 30.5(3.0) Kg/m^2 in AAs and 28.0(1.2) in Africans. To maintain representation of the sample to the general population we will limit our inclusion criteria to the weight range of the previous study, i.e. BMI 20-35, avoid severe (Class II) and very severe obesity (Class III), and balance the 2 groups.

Exclusion criteria

1. Previous GI surgery resulting disturbed gut function due to in loss of bowel or altered anatomy
2. Any form of chronic GI disease resulting in disturbed gut function, diarrhea, and malabsorption
3. Any form of acute GI disease disturbing GI function and needing current medication, e.g. gastroenteritis, peptic ulcer disease
4. Abnormal blood tests: CBC, ESR, urea and electrolytes, LFTs
5. The detection of previously unrecognized ulceration (with depth and >0.5cm), stricture, severe inflammation, and polyps >1cm diameter during screening endoscopy
6. History of any GI malignancy
7. Present GI malignancy, previously known or detected at screening endoscopy
8. Presence of any other form of cancer or malignancy
9. Oral or IV antibiotic therapy within the last 6 weeks
10. Unable or unwilling to modify dietary intake
11. Insulin or steroid therapy that may result in altered gut function or immunity
12. Chronic non-steroidal anti-inflammatory medication, or use of short-term NSAIDS within 4 weeks of study.
13. Known HIV disease
14. Severe obesity with BMI>35kg/m^2

Supplementary Note 2: African Living Conditions "HOME ENVIRONMENT"

The environment and living conditions of the African and African American populations are quite different. The rural South Africans live in small family communities of several traditional 'pole and dagga' (wooden poles plastered with clay) thatched circular huts ('rondavels'), now being gradually replaced with more robust brick and tin roof structures. Each community has about 5 acres of land, leased from the local chief, which supports small seasonal (during the 'rainy season' November to March) vegetable gardens that grow limited supplies of corn, pumpkins, watermelons, spinach and papayas, and a variety of animals, chickens, goats, and maybe a few cattle. Cattle are considered a sign of wealth and are used for milk and only slaughtered on ceremonial occasions. Consequently, milk products are consumed, but rarely fresh: it is left outside the huts to ferment, and then consumed with relish as 'maas'. Eggs are also eaten when available, but meat in any form is scarce and generally added as flavouring rather than forming the signature component. Foods are generally boiled, not fried, and cooked in cast iron pots on open wood fires in a separate hut. Electricity is becoming more available, but is still very rudimentary and unreliable. The diet consists chiefly of 'putu', a stiff porridge made from refined commercial corn flour called 'mielie meal', with salt and vegetables added for flavouring. It is eaten communally, and forms the bulk of the 2-3 meals consumed each day. Water is usually obtained from community wells, but also from the rivers. Roads consist of rough tracks through the bush and most people have to walk between settlements and to the closest main road to catch public transport (private minicab taxis) to the towns.

Thus, there are many environmental differences that could explain the differences in disease patterns. In this study, we focus on the differences in dietary intakes, as epidemiological surveys have concluded that they most influence colon cancer risk, and they are most modifiable.

Supplementary Note 3: Colonoscopy findings: Colonoscopy was considered normal in four Americans and ten Africans. Adenomatous polyps were found and removed in nine Americans and no Africans. Hyperplastic polyps were confirmed by biopsy in eight Americans and in two Africans: four Americans had both adenomatous and hyperplastic polys. Diverticula were seen in 14 Americans and no Africans. On the other hand, endoscopic evidence of mucosal inflammation was only seen in Africans: visual evidence of mild-moderate asymptomatic patchy colitis was seen and confirmed by histology in seven Africans. In five it involved the proctosigmoid region, in one the left colon and in one other, the whole colon. In the latter two subjects, the histology revealed dense lymphocytic infiltration associated with schistosoma. In one patient with macroscopically normal appearing mucosa, a 6 cm segment of a tapeworm was seen in the transverse colon.

Supplementary Discussion

Potential Confounders

Effect of Obesity: Subgroup analysis did not show any distinct differences between the moderately obese and non-obese, but our study was not powered to answer this question, and the subgroup numbers are too few to closely examine the effect of obesity. It is important to note that we used each subject as his/her own control and have reported only those bacterial groups that change systematically and significantly following the dietary intervention, detected with paired statistical testing to control host factors, such as BMI and antibiotic exposure > 6weeks prior to study, that remain approximately constant within each individual during the study period. However, we confirmed that there were no significant differences ($p=0.25$; Wilcoxon test) in microbiota diversity in our data between obese and lean individuals (Supplementary Figure 5).

Antibiotic Exposure: From the published evidence, 6 weeks antibiotic-free was a reasonable cut-off to use, as although short-term use of antibiotics may have some long-term influence on microbiota composition, its functional significance is doubtful. The topic has been recently reviewed by Keeney et al.[4] with some studies showing complete recovery within 4 weeks and

others long term losses of specific OTUs. The functional consequence of these losses was not detected, as there were no clinical manifestations, which is not surprising given the large overlap in metabolic activity between genetically distinct microbes. Again, we need to stress that the use of each subject as his/her own control should prevent this and other factors, such as the use of antibiotics in childhood, from being a significant confounder in the interpretation of our results, namely that increasing fibre increases saccharolytic fermentation and butyrogenesis whereas increasing fat increases secondary bile aid production by the microbiota. One might also argue that taking antibiotics is part of the way of life in westernized society, and this might be one of the reasons why westernized diseases, including colon cancer, are so much more common. Finally, it should be noted that the paper by Relman's group concluded that inter-individual variation was the major source of variability between samples[5] again emphasizing the importance of using each subject as his own control.

Microbial and Metabolite Stability after Colonoscopy

Although we have generally presented the results of our analyses at two points during the study, namely prior to the first colonoscopy ('home environment' sample whilst subjects consumed their usual food, and prior to the last colonoscopy after two weeks of diet exchange, we analyzed fecal samples at 6 different time points in order to discriminate diet effect from temporal variation and the potential disturbance due to bowel washout and colonoscopy:

1. Whilst on their usual diet prior to the initial colonoscopy (ED1)
2. 1 week after the first colonoscopy (HE1)
3. 2 weeks after the first colonoscopy (HE2)
4. 1 week after the diet intervention (DI1)
5. 2 weeks after the diet intervention (DI2)
6. Prior to the final colonoscopy (ED2).

Part of the reason why we took multiple samples was because of theoretical concerns we had that colonoscopy and bowel preparation might affect the microbiota (as suggested by Gorkiewicz et al[6] and Harrell et al[7] but refuted by O'Brien et al[8]) and their metabolism. Examination of the results of our targeted qPCR measurements of microbes (functional genes) of interest and metabolites (short chain fatty acids and bile acids) shown on Figure 2, and global HITChip phylogenetic analyses shown on Figure 3 and Supplementary Figure 6, indicate that there were no significant differences between time points 1 and 3, whilst there were between 1 and 6. Evaluation across the repeat measures by Kruskal Wallis test indicated that dietary exchange had the predominant effect.

Supplementary Methods

Home Environment Dietary Analysis: Estimated usual average daily dietary intakes for the African Americans were based on 3-day recalls and computerized analysis. With rural Africans, visits were made to the participants' homes in addition to dietary recalls and computerized analysis. Dietary analysis was conducted by the collection of individual data by 3-day recall method by a trained local dietician and interpreter and compositional analysis with the aid of locally produced computer software. The Nutrition Data System for Research Software, developed by the Nutrition Coordinating Center, University of Minnesota, Minneapolis, MN (database version 4.02–30, released July 1998), was used for the analysis of the African American diets. For African subjects, data collection was similar and analysis was performed using MRC FoodFinder, computerized software containing analysis of local South African foods[9]. It should be noted that the analysis shown on Supplementary Table 3 does not include resistant starch, which we would estimate as contributing a further 38 g of soluble fibre from our previous measurements of carbohydrate malabsorption of 10% in rural Africans[10]. The figure might have been higher as Ahmed and Segal[1] calculated that approximately 18% of maize meal converts to resistant starch after traditional African food preparation and cooking. The analyses on Supplementary Table 3 must be considered best estimates as recalls were only completed in the last 11/20 African Americans and 12/20 rural Africans, and considerable variation was reported in the 3-day recalls, necessitating exclusion of recalls <1000 kcal/d as all subjects were healthy and active, and were subsequently shown to need >2000 kcal to maintain their body weights when in the exchange study. The same pattern of dietary differences are seen when all recalls are used, but it seems more correct to exclude readings of <1000 kcal/d and put more weight on the other 2 readings. Dietary recall is known to underestimate actual intakes and is notoriously imprecise. Perhaps of more importance were the calculated differences in macronutrient distribution shown on **Table 1**, which are less dependent on the accuracy of dietary recall.

Dietary Interventions: The dietary intervention for African Americans at the University of Pittsburgh's Clinical and Translational Research Center included a rotating three-day menu cycle for 14 days (Supplementary Table 4). The composition of the intervention diet for African Americans was similar to that of traditional Africans, namely high complex carbohydrate, low meat and fat. The diet for each subject was calculated based on the following: 30-35 kcal/kg IBW, 14% protein, 16% fat, 70% carbohydrate, 55 g dietary fiber.

Traditional African foods provided on the menus included Phutu and Samp & Beans. Phutu, a porridge made from Hi-Maize corn meal, is high in resistant starch. Samp is dried corn kernels and the beans used were sugar beans. The Phutu was provided every other day and the Samp & Beans were provided daily. In the Phutu recipe, all subjects received the same amount of Hi-Maize meal (50 g raw weight). In addition, all subjects received the same amount of Samp & Beans daily (100 g raw weight of both Samp and beans). The amounts of the other foods served varied depending on the subjects' calorie needs. The vegetables provided included sweet and white potatoes, cabbage, and Swiss chard. Fruits included mango, banana, pineapple, orange, apple juice and apricot mango nectar. Small portions of protein foods were provided which included eggs, peanut butter, chicken thigh, chicken breast and tilapia. Small amounts of fats

were used in cooking which included sunflower oil and tub margarine. Other carbohydrate sources included whole wheat bread, white bread and white rice. Other foods such as apricot jam, sugar, half and half were calculated into the menus to achieve calorie needs.

Cooking methods were similar to traditional African preparation. Phutu was cooked by adding it slowly to boiling water stirring constantly to prevent lumps. Buttermilk was also added to the recipe. The Phutu continued to simmer in a pot on low heat for one hour. The Samp & Beans were soaked overnight in water. First the beans were boiled for an hour in water and then the Samp was added. The Samp & Beans cooked for another hour before adding other ingredients (onion, tomato, curry, salt, pepper). Once all the ingredients were added, the Samp & Beans cooked on low heat in a covered pot for an additional four hours. The chicken and fish were baked in the oven. Eggs were either hard cooked or fried in a small amount of sunflower oil. The cabbage was sautéed in oil with onions and spices. The Swiss chard was cooked with beet stems. Other foods like potatoes and rice were boiled. Subjects were encouraged to consume all foods however foods that were not consumed were weighed back and documented. Copies of the menus with the total amounts of foods served and returned were given to the study dietitian for analysis. Overall, subjects consumed the majority of foods provided.

Weights were obtained on admission and daily thereafter. If the subject had a weight loss of 2 kg the calorie level of the menus was adjusted. Most subjects were able to maintain their weight within 2 kg throughout the study. However, for those few subjects who did have weight loss of 2 kg, extra calories were provided by additional juice or fruit to bring them back to within 2kg of baseline.

At screening potential subjects were asked about their food preferences and dislikes. Particularly in regards to those foods on the intervention diet menus. When possible, potential subjects were given a sample of Samp & Beans to try at screening. Once admitted to the study and the menus were in progress if subjects had palatability concerns attempts were made to improve the acceptance of the foods. For instance additional spices could be added (garlic powder, extra salt and pepper, extra curry powder, hot sauce, etc.) adding Splenda to the Phutu resulted in better consumption for those subjects who found it difficult to eat.

On occasion, some subjects would make special requests regarding meal timing, additional foods and/or beverages. The dietary staff would address these requests with the study nutritional specialist, Dr. Ruder, and every attempt was made to accommodate the subjects' request while keeping within the study protocol.

The procedure followed in the dietary interventions in Africa was similar, with the overall dietary composition consisting of 52% fat, 21% carbohydrate, 27% protein and 12g fiber per day. Foods were purchased from the supermarket in Empangeni, the closest large town, and either used immediately for the cooked meals, or frozen. All components were common to what is available in the USA and what are usually used in westernized cooking (Supplementary Table 4).

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