Supporting Tables

Table S1. *Eigenstrat* principal component statistics. The program uses unsupervised Tracy-Widom (TW) statistics to test if the means of the eigenvector coordinates associated to each individual in each population differ significantly.

Eigenvector	Eigenvalue	TW Statistic	TW *p*-value
1	2.005631	3.503	0.000627
2	1.666154	1.709	0.016769
3	1.389458	-1.513	0.577793
4	1.201761	-4.663	0.999032
5	1.148618	-5.237	0.999895
6	1.108053	-5.567	0.999976
7	1.069332	-5.872	0.999995
8	1.054077	-5.647	0.999984
9	1.035545	-5.468	0.999962
10	1.016427	-5.278	0.999911

Table S2. Significance results. Lists of significance (*P* and *Q* values) for differential expression for each of the three pairwise comparisons of nomadic, rural, and urban lifestyles, as well as the joint analysis of all three lifestyles and of sex. Pairwise comparisons include estimates of fold change (log base2 units) as the difference in mean relative abundance from the unadjusted and SV-adjusted analyses. The table consists of 5 Excel worksheets in one file.

Table is packaged in a single compressed archive:

http://statgen.ncsu.edu/ggibson/SupplInfo/ Idaghdourextsupptables.zip

Also available as single Excel spreadsheets at:

http://statgen.ncsu.edu/ggibson/SupplInfo/SupplInfo15.htm

Table S3. Surrogate variables. Lists of surrogate variables and fixed effects for each individual in the three pairwise comparisons of nomadic, rural, and urban lifestyles, as well as the joint analysis of all three lifestyles and of gender. Pairwise comparisons each shows five significant SVs while the three-way comparison and gender each shows six SVs. The table consists of 5 Excel worksheets in one file. Fixed effects are coded 1, 2 or 3 for Lifestyle, 1 or 2 for Gender, and 1 or 2 for Batch.

Table is packaged in a single compressed archive:

http://statgen.ncsu.edu/ggibson/SupplInfo/ Idaghdourextsupptables.zip

Also available as single Excel spreadsheets at:

http://statgen.ncsu.edu/ggibson/SupplInfo/SupplInfo15.htm

Table S4. List of transcripts. The 10,177 transcripts considered expressed in PBMC.

Table is packaged in a single compressed archive:

http://statgen.ncsu.edu/ggibson/SupplInfo/ Idaghdourextsupptables.zip

Also available as single Excel spreadsheets at:

http://statgen.ncsu.edu/ggibson/SupplInfo/SupplInfo15.htm

Table S5. List of individuals and analyses. 52 unique individuals were samples from the three life style shown in the table. Samples used for each experiment (gene expression, genotyping, and methylation) as well as the samples that were replicated are also shown.

#	Sample_ID	Expression	Exp_ID	Array_ID	Batch	Genotype	Methylation	Sex	Lifestyle
1	A03	YES	FA8B	1743113118_C	A	YES	YES	FEM	URBAN
2	A09	YES	MA8D	1743113118_E	A	YES	YES	MAL	URBAN
3	A11	YES	MA9C	1743113119_C	A	YES	YES	MAL	URBAN
4	A12	YES	FA9F	1743113119_G	A	NO	YES	FEM	URBAN
5	A16	YES	MA4A	1743113134_A	A	YES	YES	MAL	URBAN
6	A18	YES	FA4C	1743113134_C	A	NO	YES	FEM	URBAN
7	A15	YES	MA4D	1743113134_D	A	YES	YES	MAL	URBAN
8	A14	YES	MA4E	1743113134_E	A	NO	YES	MAL	URBAN
9	A8	YES	FA6C	1743113136_D	A	NO	YES	FEM	URBAN
10	A6	YES	FA6D	1743113136_E	A	NO	YES	FEM	URBAN
11	A17	YES	MA2E	1743113062_E	B	YES	YES	MAL	URBAN
12	A22	YES	MA2G	1743113062_G	B	YES	YES	MAL	URBAN
13	A21	YES	MA3B	1743113063_B	B	NO	YES	MAL	URBAN
14	A01	YES	MA3C	1743113063_C	B	YES	YES	MAL	URBAN
15	A13	YES	FA3E	1743113063_E	B	NO	YES	FEM	URBAN
16	A07	YES	FA5D	1743113076_D	B	NO	YES	FEM	URBAN
17	A19	YES	MA5G	1743113076_G	B	NO	YES	MAL	URBAN
18	A20	YES	MA7E	1743113077_E	B	NO	YES	MAL	URBAN
19	E13	YES	MD8A	1743113118_A	A	YES	YES	MAL	NOMAD
20	E10	YES	MD8E	1743113118_F	A	NO	YES	MAL	NOMAD
21	E09	YES	MD9A	1743113119_E	A	YES	YES	MAL	NOMAD
22	E01	YES	MD9E	1743113119_H	A	YES	YES	MAL	NOMAD
23	E12	YES	FD4B	1743113134_B	A	YES	YES	FEM	NOMAD
24	E6	YES	FD4H	1743113134_H	A	NO	YES	FEM	NOMAD
25	E11	YES	FD6E	1743113136_F	A	NO	YES	FEM	NOMAD
26	E14	YES	MD6F	1743113136_H	A	YES	YES	MAL	NOMAD

27	E05	YES	MD7H	1743113077_H	B	YES	YES	MAL	NOMAD
28	E03	YES	FD2D	1743113062_D	B	NO	NO	FEM	NOMAD
29	E17	YES	MD2F	1743113062_F	B	YES	YES	MAL	NOMAD
30	E07	YES	FD2H	1743113062_H	B	NO	YES	FEM	NOMAD
31	E16	YES	FD3A	1743113063_A	B	NO	YES	FEM	NOMAD
32	E04	YES	MD3H	1743113063_H	B	YES	YES	MAL	NOMAD
33	E08	YES	FD5H	1743113076_H	B	NO	NO	FEM	NOMAD
34	E15	YES	MD7F	1743113077_F	B	NO	YES	MAL	NOMAD
35	SN1	YES	FV8C	1743113118_D	A	YES	YES	FEM	RURAL
36	SN10	YES	FV8F	1743113118_H	A	NO	YES	FEM	RURAL
37	SN16	YES	MV9B	1743113119_B	A	YES	YES	MAL	RURAL
38	SN3	YES	FV9D	1743113119_D	A	NO	YES	FEM	RURAL
39	SN17	YES	MV4A	1743113134_F	A	YES	YES	MAL	RURAL
40	SN18	YES	MV4G	1743113134_G	A	YES	YES	MAL	RURAL
41	SN12	YES	FV6A	1743113136_A	A	NO	YES	FEM	RURAL
42	SN2	YES	FV6B	1743113136_C	A	NO	YES	FEM	RURAL
43	SN13	YES	MV2B	1743113062_B	B	YES	YES	MAL	RURAL
44	SN11	YES	FV3G	1743113063_G	B	NO	YES	FEM	RURAL
45	SN14	YES	MV7A	1743113077_A	B	YES	YES	MAL	RURAL
46	SN7	YES	FV7B	1743113077_B	B	YES	YES	FEM	RURAL
47	SN5	POOR	---	1743113077_G	B	YES	YES	FEM	RURAL
48	SN15	POOR	---	1743113076_E	B	NO	YES	MAL	RURAL
49	A4	POOR	---	1743113077_C	B	NO	YES	MAL	URBAN
50	A23	POOR	---	1743113076_B	B	NO	NO	MAL	URBAN
51	E2	POOR	---	1743113076_C	B	NO	NO	MAL	NOMAD
52	A08_rep	POOR	FA6C	1743113076_F	B	NO	YES	FEM	URBAN
53	SN17_rep	YES	MV3F	1743113063_F	B	YES	YES	MAL	RURAL
54	SN13_rep	YES	MV3D	1743113063_D	B	YES	YES	MAL	RURAL
55	E03_rep	YES	FD5A	1743113076_A	B	NO	NO	FEM	NOMAD
56	E05_rep	YES	MD2A	1743113062_A	B	YES	YES	MAL	NOMAD
57	SN8	NO	---	---		NO	YES	FEM	RURAL

Table S6. List of genes in Fos and Myc networks shown in Figure 3. Fold change and *P* value from surrogate variable analysis followed by mixed model analysis of variance as described in material and methods are shown.

Name	Entrez_ID	Fold Change	*P*-value	Location
ACTG1	71	-1.5294026	0.00605659	Cytoplasm
ALPP	250	-1.278339	0.00114771	Extracell. Space
ANKS1A	23294	-1.1743818	2.05E-05	Cytoplasm
ANXA2	302	-1.1844711	0.00299349	Plasma Memb.
ARL6IP1	23204	-1.1324935	0.00119596	Cytoplasm
BAT1	7919	1.34768336	4.91E-04	Nucleus
BOP1	23246	-1.3220285	3.00E-09	Nucleus
CDR2	1039	1.21897037	3.18E-05	Cytoplasm
CHMP6	79643	-1.2052507	1.29E-05	Cytoplasm
COTL1	23406	-1.1483082	2.16E-04	Cytoplasm
CPD	1362	-1.3318136	1.40E-06	Extracell. Space
EAF1	85403	-1.1383807	6.71E-04	Nucleus
ELL	8178	-1.3741125	2.04E-06	Nucleus
EMB	133418	1.31891314	1.70E-05	Plasma Memb.
FARS2	10667	1.10651023	0.00228784	Cytoplasm
FOS	2353	3.67294184	2.47E-05	Nucleus
GAK	2580	-1.3105464	5.70E-09	Nucleus
GM2A	2760	-1.6517571	0.00184158	Cytoplasm
H3F3A	3020	1.07691646	0.00331633	Nucleus
H3F3B	3021	1.4959445	1.27E-04	Nucleus
HGS	9146	-1.2682638	6.41E-07	Cytoplasm
HIVEP2	3097	1.10719351	0.0021508	Nucleus
LRSAM1	90678	-1.3993772	1.00E-10	Cytoplasm
MFAP1	4236	-1.0909704	7.20E-04	Extracell. Space
MGST3	4259	-1.2119304	5.90E-04	Cytoplasm
MYC	4609	1.16830351	1.94E-04	Nucleus
NOL5A	10528	1.30772704	2.78E-04	Nucleus
NOP5/NOP58	51602	1.27398178	1.40E-08	Nucleus
PA2G4	5036	1.2514751	1.10E-05	Nucleus
PARP10	84875	-1.3587708	1.04E-05	Nucleus

POLE	5426	-1.2175069	1.43E-05	Nucleus
PPP1R16A	84988	-1.0816162	0.0036466	Plasma Memb.
PRDX3	10935	-1.1246358	0.00294685	Cytoplasm
RFX1	5989	-1.1928743	2.74E-04	Nucleus
RNH1	6050	-1.1262036	0.00559963	Cytoplasm
RPL12	6136	1.42007109	1.00E-11	Cytoplasm
RPL19	6143	1.14053192	5.94E-05	Cytoplasm
RPL27	6155	1.19911635	1.85E-05	Cytoplasm
RPL30	6156	1.3444361	2.00E-10	Cytoplasm
RPL34	6164	1.17708518	3.89E-06	Cytoplasm
RPL35	11224	1.31008932	7.38E-08	Cytoplasm
RPS12	6206	1.14229077	1.35E-05	Cytoplasm
RPS18	6222	1.24545327	3.57E-04	Cytoplasm
RPS20	6224	1.30484429	2.11E-05	Cytoplasm
RPS7	6201	1.18451853	7.56E-06	Cytoplasm
RPS9	6203	1.15786488	0.0017371	Cytoplasm
SCPEP1	59342	-1.2233267	1.30E-04	Cytoplasm
SEC23B	10483	-1.2177539	3.22E-07	Cytoplasm
SIAHBP1	22827	-1.2650019	5.09E-07	Nucleus
SLC11A1	6556	-1.4352495	3.60E-04	Plasma Memb.
SLC25A19	60386	-1.1533171	3.83E-04	Cytoplasm
SLC25A5	292	-1.1427435	0.00131215	Cytoplasm
SMARCD2	6603	-1.2446635	1.44E-06	Nucleus
SNF8	11267	-1.4052659	3.75E-05	Nucleus
SPTBN1	6711	1.24295752	0.00198691	Plasma Memb.
SQRDL	58472	-1.1583783	0.00199505	Cytoplasm
STX12	23673	-1.1135745	7.53E-04	Plasma Memb.
TCEA1	6917	1.19374442	1.94E-07	Nucleus
TGFBI	7045	-1.417562	0.00114392	Extracell. Space
TSG101	7251	1.13423903	1.15E-04	Nucleus
TSPO	706	-1.3148237	4.99E-06	Cytoplasm
VDAC1	7416	-1.1159642	0.00303239	Cytoplasm
VDAC2	7417	-1.1526311	3.15E-04	Cytoplasm
VPS36	51028	1.21219122	0.00438165	Cytoplasm
VPS37C	55048	-1.2345254	0.00359611	Cytoplasm
ZNF33A	7581	1.09598622	0.00125708	Nucleus
ZNF467	168544	-1.3810602	1.51E-04	Nucleus

Table S7. Top 15 networks generated by Ingenuity from the list of genes differentially expressed (1% FDR) for each lifestyle pairwise comparison. The genes called Focus Genes are genes that meet the 1% FDR cutoff in addition to the presence of at least one other full-length, wild-type gene or protein in the IPKB that interacts (directly or indirectly) with these genes. The networks are sorted by their score that is based on the likelihood that the Focus Genes that are part of a network are found therein by random chance alone.

Network	Analysis	Score	Focus Genes	Top Functions
1	Nomadic_vs_Rural	43	30	Cell Cycle, Cancer, Gastrointestinal Disease
1	Nomadic_vs_Urban	41	31	Protein Synthesis, Cancer, Cell Cycle
1	Rural_vs_Urban	38	35	RNA Post-Transcriptional Modification, Cellular Assembly and Organization, Protein Synthesis
2	Nomadic_vs_Urban	41	31	Cancer, Cell Cycle, Reproductive System Disease
2	Nomadic_vs_Rural	40	29	Gene Expression, Cell Morphology, Connective Tissue Development and Function
2	Rural_vs_Urban	35	34	Cell Morphology, Cellular Assembly and Organization, Cellular Development
3	Nomadic_vs_Urban	39	30	Cellular Development, Post-Translational Modification, Cellular Growth and Proliferation
3	Nomadic_vs_Rural	36	27	Cellular Assembly and Organization, Cancer, Cell Death
3	Rural_vs_Urban	35	34	Viral Function, Cellular Function and Maintenance, Post-Translational Modification
4	Nomadic_vs_Urban	37	29	Nucleic Acid Metabolism, Gene Expression, Cancer
4	Nomadic_vs_Rural	36	27	Cancer, Cellular Growth and Proliferation, Cell Signaling
4	Rural_vs_Urban	35	34	Protein Degradation, Gene Expression, DNA Replication, Recombination, and Repair
5	Nomadic_vs_Urban	37	29	Cell Signaling, Immune Response, Carbohydrate Metabolism
5	Nomadic_vs_Rural	34	26	Vitamin and Mineral Metabolism, Lipid Metabolism, Cancer

5	Rural_vs_Urban	33	33	Cellular Development, Reproductive System Development and Function, Cellular Assembly and Organization
6	Nomadic_vs_Urban	37	29	Cancer, Cell Death, Reproductive System Disease
6	Rural_vs_Urban	33	33	Immune Response, Hematological System Development and Function, Cellular Development
6	Nomadic_vs_Rural	30	24	Post-Translational Modification, Gene Expression, Cell Cycle
7	Nomadic_vs_Urban	35	28	DNA Replication, Recombination, and Repair, Cell Cycle, Cellular Assembly and Organization
7	Rural_vs_Urban	33	33	Cardiovascular System Development and Function, Protein Degradation, Cell Signaling
7	Nomadic_vs_Rural	28	23	Cell-To-Cell Signaling and Interaction, Cellular Assembly and Organization, Hematological System Development and Function
8	Nomadic_vs_Urban	35	28	Molecular Transport, Protein Trafficking, Cell Death
8	Rural_vs_Urban	31	32	RNA Post-Transcriptional Modification, Cellular Assembly and Organization, Carbohydrate Metabolism
8	Nomadic_vs_Rural	26	22	Cancer, Hematological Disease, Cellular Development
9	Nomadic_vs_Urban	35	28	Protein Synthesis, Gene Expression, Cell Cycle
9	Rural_vs_Urban	31	32	Cellular Assembly and Organization, Vitamin and Mineral Metabolism, Lipid Metabolism
9	Nomadic_vs_Rural	19	18	Immune Response, Neurological Disease, Cardiovascular System Development and Function
10	Nomadic_vs_Urban	33	27	Hematological System Development and Function, Immune and Lymphatic System Development and Function
10	Rural_vs_Urban	31	32	Gene Expression, Cardiovascular System Development and Function, Cell-To-Cell Signaling and Interaction
10	Nomadic_vs_Rural	18	17	Cancer, Reproductive System Disease, Renal and Urological Disease
11	Rural_vs_Urban	31	32	Post-Translational Modification, Cell Cycle, Protein Degradation
11	Nomadic_vs_Urban	27	24	Cell Signaling, Tissue Development, Cardiovascular System Development and Function
11	Nomadic_vs_Rural	18	17	Ophthalmic Disease, Cellular Function and Maintenance, Cellular Assembly and Organization
12	Rural_vs_Urban	31	32	Cardiovascular Disease, Metabolic Disease, RNA Post-Transcriptional Modification
12	Nomadic_vs_Urban	27	24	Cardiovascular System Development and Function, Tissue Morphology, Lipid Metabolism
12	Nomadic_vs_Rural	16	16	Lipid Metabolism, Small Molecule Biochemistry, Molecular Transport
13	Rural_vs_Urban	31	32	Cell Signaling, Gene Expression, Cancer
13	Nomadic_vs_Urban	25	23	Cellular Assembly and Organization, Cellular Movement, Gene Expression

13	Nomadic_vs_Rural	16	16	Cell Signaling, Immune Response, Hematological System Development and Function
14	Rural_vs_Urban	31	32	Gene Expression, Carbohydrate Metabolism, Cancer
14	Nomadic_vs_Urban	19	19	Immune Response, Cancer, Tumor Morphology
14	Nomadic_vs_Rural	16	16	Cancer, Cell Cycle, Gene Expression
15	Rural_vs_Urban	29	31	Cellular Growth and Proliferation, Hematological System Development and Function, Immune Response
15	Nomadic_vs_Rural	16	16	Dermatological Diseases and Conditions, Gene Expression, Cell Signaling
15	Nomadic_vs_Urban	14	16	Cellular Development, Cellular Growth and Proliferation, Reproductive System Disease