

Appendix Table 1 Impact of TB on the significant pathways

Pathway		Gene GK-vs-GK- TB (431)	Gene_All (7708)	Gene_Pvalue	Gene_Qvalue	Metabolites Count (2812)	Pathway ID	Genes
Insulin pathway	signaling	19	127	7.32E-05	0.005345768	9	ko04910	Acacb;Mapk1;Srebf1;Prkacb;Pygb;Prkaa2;Socs2;Flot2;Foxo1;Rapgef1;Sorbs1;Fbp2;Ptprf;Mapk8;Prkar2a;Pklr;Crk;Pck1;Fasn
Thyroid signaling pathway	hormone	16	113	0.000507806	0.021182748	4	ko04919	Notch4;Slc16a10;Mapk1;Slc16a2;Prkacb;Med1;Ncoa3;Ncoa2;Tbc1d4;Rxra;Med12l;Foxo1;Actg1;Itgb3;LOC100361457;Ctnnb1
Glycerophospholipid metabolism		14	97	0.00092564	0.027211821	229	ko00564	Cds1;Lpin1;Lpgat1;Pnpla7;Pla2g6;Etnk1;Lpin2;Pisd;Pld2;Dgkd;Etnk2;Lclat1;Etnppl;Pla2g12a
Vascular muscle contraction	smooth	16	121	0.001086261	0.027211821	2	ko04270	Itpr2;Mapk1;Adcy5;Prkeh;Prkacb;Gna11;Kenma1;Arhgef12;Cyp4a1;Pla2g6;Cyp4a2;Adcy9;Ppp1r12b;Itpr3;Ppp1r12c;Pla2g12a
Apoptosis		17	133	0.001128762	0.027211821	1	ko04210	Csf2rb;Itpr2;Mapk1;Tuba4a;Xiap;Fos;Eif2s1;Cflar;Gadd45g;Casp2;Gadd45b;Mapk8;Map3k5;Actg1;Pidd1;Itpr3;LOC100361457
FoxO pathway	signaling	16	122	0.001187659	0.027211821	7	ko04068	Foxo3;Bcl6;Mapk1;Prkaa2;Gadd45g;Tgfbr2;Foxo1;Stat3;Gadd45b;Mapk8;Usp7;Agap2;Pck1;Sgk3;Smad4;Cnd2
Pathways in cancer		45	510	0.001354603	0.027211821	34	ko05200	Csf2rb;Notch4;Lama4;Mapk1;Adcy5;Lamc2;Prkacb;Gna11;Ncoa3;Lrp6;Xiap;Fos;Traf3;Pml;Arhgef12;Rxra;Lpar2;Ednrb;Gadd45g;Il13ra1;Tgfbr2;Foxo1;Il6st;Fgfr1;Fgfr2;Tpm3;Stat3;Gadd45b;Mapk8;Il6r;Col4a2;Ccdc6;Tert;Crk;Arnt;Rasgrp3;Adcy9;Smad4;Met;Lama5;Ctnnb1;Gsta3;Gnai1;Cnd2;Lamc3
GnRH pathway	signaling	13	90	0.001386032	0.027211821	2	ko04912	Itpr2;Mapk1;Adcy5;Map2k6;Prkacb;Gna11;Mmp14;Map3k1;Egr1;Pld2;Mapk8;Adcy9;Itpr3

Adipocytokine signaling pathway	11	69	0.00141297	0.027211821	1	ko04920	Acacb;Prkaa2;Adipor2;Rxra;Cpt1b;Cpt1a;Stat3;Mapk8;Pck1;Ptpn11;RGD1565355
Bile secretion	11	70	0.001594212	0.027211821	81	ko04976	Adcy5;Slc4a4;Prkacb;Abcg5;Abcg8;Rxra;Abcc4;Nceh1;Slc4a2;Slc5a1;Adcy9
Insulin resistance	14	103	0.001677099	0.027211821	26	ko04931	Acacb;Srebf1;Pygb;Prkaa2;Tbc1d4;Cpt1b;Foxo1;Cpt1a;Stat3;Ptprf;Mapk8;Pck1;Ptpn11;RGD1565355
AMPK signaling pathway	15	120	0.002706305	0.039512053	21	ko04152	Foxo3;Acacb;Srebf1;Prkaa2;Adipor2;Cpt1b;Ppp2r1b;Foxo1;Scd;Cpt1a;Fbp2;Pfkfb3;Pck1;RGD1565355;Fasn

Appendix Table 2 Intergroup differentially expressed genes

GK_ mean	GK-TB _mean	log2(fc)_GK -vs-GK-TB	Symbol	Description
3.40	13.79	**2.02	Abcg5	ATP binding cassette subfamily G member 5
0.41	1.28	**1.63	Abcg8	ATP binding cassette subfamily G member 8
2.10	12.44	**2.56	Acadsb	acyl-CoA dehydrogenase, short/branched chain
0.01	0.18	**3.75	Ace	angiotensin I converting enzyme
1.60	3.56	**1.16	Acot9	acyl-CoA thioesterase 9
12.65	25.7	**1.02	Acox3	acyl-CoA oxidase 3, pristanoyl
36.93	163.18	**2.14	Acsm5	acyl-CoA synthetase medium-chain family member 5
0.03	0.13	*2.00	Adcy10	adenylate cyclase 10
0.37	0.80	**1.11	Adcy5	adenylate cyclase 5
0.77	1.59	**1.04	Adcy9	adenylate cyclase 9
5.11	11.48	**1.17	Adipor2	adiponectin receptor 2
36.68	110.91	**1.60	Aldh1a1	aldehyde dehydrogenase 1 family, member A1
13.88	54.7	**1.98	Cpt1a	carnitine palmitoyltransferase 1A
0.08	0.27	*1.75	Cpt1b	carnitine palmitoyltransferase 1B
102.21	209.6	**1.04	Ech1	enoyl-CoA hydratase 1
25.08	73.7	**1.55	Fads6	fatty acid desaturase 6
0.39	1.67	**2.09	Foxo1	forkhead box O1
2.45	7.69	**1.65	Igf2bp3	insulin-like growth factor 2 mRNA binding protein 3
1.56	3.9	**1.30	Igf2r	insulin-like growth factor 2 receptor
12.63	43.8	**1.79	Igfbp1	insulin-like growth factor binding protein 1
4.82	29.0	**2.59	Igfbp2	insulin-like growth factor binding protein 2
0.00	0.12	*6.95	Igfbp1l	insulin-like growth factor binding protein-like 1
0.00	0.35	**8.46	Lpar2	lysophosphatidic acid receptor 2
6.26	13.5	**1.10	Lpgat1	lysophosphatidylglycerol acyltransferase 1
4.81	11.83	**1.30	Lrp11	LDL receptor related protein 11
0.63	1.50	**1.26	Lrp6	LDL receptor related protein 6
1.08	2.37	*1.14	Mapk8	mitogen-activated protein kinase 8
440.80	891.4	**1.02	Pck1	phosphoenolpyruvate carboxykinase 1
98.30	205.90	**1.07	Por	cytochrome p450 oxidoreductase
0.94	2.92	**1.64	Prkaa2	protein kinase AMP-activated catalytic subunit alpha 2
0.23	2.08	**3.16	Prkacb	protein kinase cAMP-activated catalytic subunit beta
0.62	5.5	**3.14	Prkar2a	protein kinase cAMP-dependent type 2 regulatory subunit alpha
10.72	35.9	**1.74	Rxra	retinoid X receptor alpha
0.16	0.59	*1.90	Sgk3	serum/glucocorticoid regulated kinase family, member 3
3.76	7.66	**1.03	Slc4a2	solute carrier family 4 member 2
0.12	0.67	**2.45	Slc4a4	solute carrier family 4 member 4
5.88	13.44	**1.19	Tsc22d3	TSC22 domain family, member 3
3.33	2.23	-0.58	Acot5	acyl-CoA thioesterase 5
180.32	85.5	**1.08	Angptl8	angiopoietin-like 8

1409.77	931.13	-0.60	Apoa4	apolipoprotein A4
25.49	9.8	** -1.38	Fabp5	fatty acid binding protein 5
14.10	6.2	** -1.18	Fasn	fatty acid synthase
79.90	37.4	** -1.10	Pklr	pyruvate kinase L/R
692.36	249.8	** -1.47	Scd	stearoyl-CoA desaturase
88.91	41.54	** -1.10	Srebf1	sterol regulatory element binding transcription factor 1

Appendix Table 3 Feces metabolite statistics of significant differences of GKf-vs-GK-TBf

index	GKf_ mean	GK-TBf _mean	log2_ FC	Pvalue	vip	MS2 name	MS2 score	CAS	C_ID
POS	543533	30124227	5.79	0.000	4.21	(R)-5-Phosphomevalonate	0.645	-	C01107
POS	2184484	30105966	3.78	0.027	3.32	Caffeine	0.991	-	C07481
POS	534449	6299661	3.56	0.000	1.89	4-Amino-2,6-dinitrotoluene	0.520	-	C16394
POS	19738354	127236313	2.69	0.000	7.85	1,3,7-Trimethyluric acid	1.000	-	C16361
POS	5498003	28544453	2.38	0.000	3.52	1,7-Dimethyluric acid	0.994	-	C16356
POS	7449206	34600043	2.22	0.030	3.20	Theophylline	0.999	58-55-9	C07130
POS	2453952	9369814	1.93	0.001	1.91	Westcort	0.918	-	C00762
POS	1754898	6537842	1.90	0.000	1.72	25-Hydroxycholecalciferol	0.859	-	C01561
POS	6580470	24501977	1.90	0.000	3.33	Cholic Acid	0.890	81-25-4	C00695
POS	1219085	4190425	1.78	0.001	1.24	theobromine	0.982	-	C07480
POS	10461231	34762920	1.73	0.000	3.87	4a-Carboxy-4b-methyl-5a-cholesta-8,24-dien-3b-ol	0.610	-	C15808
POS	1982688	5847171	1.56	0.000	1.52	cis-9,10-Epoxystearic acid	0.996	-	C19418
POS	25929082	70933157	1.45	0.000	5.08	Adenine	0.998	73-24-5	C00147
POS	1770616	4197239	1.25	0.000	1.20	Xanthurenic acid	0.941	59-00-7	C02470
POS	7253017	15188313	1.07	0.005	1.91	Glycocholic Acid	0.892	475-31-0	C01921
POS	29519634	55469025	0.91	0.021	3.25	Deamino-alpha-keto-demethylphosphinothricin	0.784	-	C17948
POS	22887387	36602140	0.68	0.017	2.48	Citrulline	0.997	-	C00327
POS	18905776	27867076	0.56	0.037	1.91	5-Hydroxyectoine	0.566	-	C16432
POS	28563479	41835182	0.55	0.004	2.49	Glycochenodeoxycholic acid	0.609	640-79-9	C05466
POS	14112248	20433803	0.53	0.000	1.91	Testosterone	0.997	58-22-0	C00535
POS	9278726	13047089	0.49	0.009	1.32	Dihydropteroic acid	0.680	-	C00921
POS	17904252	24197821	0.43	0.000	1.89	4-Pyridoxic acid	0.594	82-82-6	C00847

POS	138995219	165781179	0.25	0.040	3.26	Choline	1.000	62-49-7	C00114
POS	17587629	19557974	0.15	0.000	1.03	9-Hydroxyfluorene	0.828	-	C06711
POS	7363823	5205374	-0.50	0.001	1.05	Anhalamine	0.997	-	C12231
POS	32680444	21368127	-0.61	0.003	2.33	Sphingosine	0.909	-	C00319
POS	9744273	6167947	-0.66	0.044	1.15	Phenylacetaldehyde	0.958	122-78-1	C00601
POS	11737640	6726318	-0.80	0.035	1.34	Uracil	0.965	66-22-8	C00106
POS	337355375	188668115	-0.84	0.000	8.85	5-Aminopentanoate	1.000	-	C00431
POS	6057903	3343178	-0.86	0.001	1.19	3-Oxo-3-phenylpropanoate	0.910	-	C07114
POS	5183266	2540111	-1.03	0.020	1.02	Indoleacetic acid	0.994	-	C00954
POS	107966974	50332260	-1.10	0.000	5.51	Allopurinol	0.994	315-30-0	-
POS	51763885	23929467	-1.11	0.000	4.01	Leu	0.888	-	C00123
POS	8409325	3775029	-1.16	0.000	1.65	9-HpODE	0.988	-	C14827
POS	11979498	4906848	-1.29	0.000	2.04	D-Serine	0.676	-	C00740
POS	87051023	34168786	-1.35	0.000	5.56	Indoline	0.989	496-15-1	-
POS	34759789	13511227	-1.36	0.002	3.27	Pyrrolidine	0.999	123-75-1	-
POS	44847539	17184849	-1.38	0.029	3.23	L-Pipecolic acid	0.978	3105-95-1	C00408
POS	36492795	13136653	-1.47	0.001	3.43	Xanthine	0.644	69-89-6	C00385
POS	21794362	7610864	-1.52	0.000	2.82	2-Aminoisobutyric acid	0.974	62-57-7	-
POS	3881228	1353814	-1.52	0.005	1.09	Betulinic acid	0.807	472-15-1	-
POS	29372168	9277598	-1.66	0.000	3.49	Furfural	0.996	-	C14279
POS	3050542	934864	-1.71	0.000	1.13	Chlormadinone acetate	0.971	302-22-7	-
POS	32814407	9668474	-1.76	0.001	3.43	L-Threonine	0.880	-	C00188
POS	27009391	7879500	-1.78	0.006	2.94	L-Glutamine	0.658	56-85-9	C00064
POS	7662506	2223969	-1.78	0.018	1.48	Larixinic acid	0.999	-	C11918
POS	38891011	10609294	-1.87	0.004	3.66	Nicotinamide	0.656	98-92-0	C00153
POS	55498649	15104402	-1.88	0.013	4.09	Kynurenic acid	0.995	492-27-3	C01717

POS	5177093	1396157	-1.89	0.011	1.28	Stearidonic Acid	0.844	20290-75-9	C16300
POS	7437530	1951770	-1.93	0.001	1.64	13-OxoODE	0.994	-	C14765
POS	25841660	6539222	-1.98	0.000	3.31	9-OxoODE	0.987	54232-59-6	C14766
POS	9883976	2432991	-2.02	0.008	1.79	Prostaglandin I2	0.997	35121-78-9	C01312
POS	115274629	27113155	-2.09	0.003	6.49	5-Hydroxyindole-3-acetic acid	0.952	54-16-0	C05635
POS	23345493	5396704	-2.11	0.000	3.34	Maltose	0.999	-	C00208
POS	49826960	11352618	-2.13	0.000	4.87	Adenosine	1.000	-	C00212
POS	518191274	117779702	-2.14	0.019	12.74	1-Naphthylamine	0.997	-	C14790
POS	10924235	2444643	-2.16	0.000	2.13	N-Acetylneuraminate	0.912	-	C00270
POS	33897966	6505393	-2.38	0.000	3.82	Niacinamide	0.952	-	C00153
POS	4122851	739867	-2.48	0.013	1.20	Serotonin	0.944	50-67-9	C00780
POS	21429496	3734835	-2.52	0.006	2.90	Creatinine	0.842	60-27-5	C00791
POS	2660347	457001	-2.54	0.000	1.10	Methyl oleate	0.771	112-62-9	-
POS	20821548	3496480	-2.57	0.011	2.70	13-HpODE	0.992	-	C04717
POS	4205544	686802	-2.61	0.018	1.19	Styrene	0.988	-	C07083
POS	30416965	4496233	-2.76	0.018	3.26	Phytosphingosine	0.979	554-62-1	C12144
POS	2209168	318118	-2.80	0.000	1.07	Xanthosine	0.908	146-80-5	C01762
POS	4705746	621108	-2.92	0.048	1.27	Galangin	0.989	-	C10044
POS	25630527	2857860	-3.16	0.001	3.47	Genistein	0.994	446-72-0	C09126
POS	24485286	2536441	-3.27	0.007	3.12	16-Methoxy-2,3-dihydro-3-hydroxytabersonine	0.983	-	C04578
POS	4506677	432968	-3.38	0.013	1.37	Morphine	0.796	-	C01516
POS	70282489	4985577	-3.82	0.008	5.35	4-Hydroxyquinoline	0.999	611-36-9	-
POS	6992924	478162	-3.87	0.001	1.86	Guanosine	0.994	118-00-3	C00387
POS	36395716	2337986	-3.96	0.001	4.26	Glycitein	0.988	-	C14536

POS	47392536	1824287	-4.70	0.000	5.11	4',7-dihydroxyisoflavone	0.996	-	C10208
NEG	6369703	86138	-6.21	0.001	1.66	Inosine	0.971	58-63-9	C00294
NEG	12957284	417874	-4.95	0.000	2.38	Chrysin	0.872	480-40-0	C10028
NEG	9726871	912731	-3.41	0.000	2.01	L-Ascorbic acid	0.838	-	C00072
NEG	13213018	1461413	-3.18	0.001	2.22	4',5,7-trihydroxyflavone	0.852	-	C01477
NEG	7263692	825389	-3.14	0.000	1.71	3-Hydroxybutyric acid	0.919	-	C01089
NEG	23851391	3059208	-2.96	0.000	3.13	Ferulate	0.930	-	C01494
NEG	3301279	444260	-2.89	0.000	1.15	2,5-Dihydroxybenzoate	0.937	-	C00628
NEG	6270188	954490	-2.72	0.000	1.58	Uridine	0.968	58-96-8	C00299
NEG	4268723	718860	-2.57	0.000	1.29	Raffinose	0.558	-	C00492
NEG	18103699	3390872	-2.42	0.034	2.00	Tropic acid	0.871	-	C01456
NEG	7609838	1453137	-2.39	0.008	1.53	Taurocholic acid	0.979	81-24-3	C05122
NEG	147830650	28818378	-2.36	0.042	5.51	3-(3-Hydroxyphenyl) propionic acid	0.975	-	C11457
NEG	15444188	3085022	-2.32	0.000	2.37	Melibiose	0.891	-	C05402
NEG	83383965	17690555	-2.24	0.000	5.52	D-Lactic acid	0.999	-	C00256
NEG	12239313	3036431	-2.01	0.000	2.07	Pyruvic acid	0.929	127-17-3	C00022
NEG	19783517	5573153	-1.83	0.000	2.55	D-(+)-Xylose	0.965	-	C00181
NEG	3088958	889787	-1.80	0.000	1.00	PGJ2	0.861	-	C05957
NEG	34129614	9895624	-1.79	0.001	3.03	13-HODE	0.928	-	C14762
NEG	22683496	7529365	-1.59	0.003	2.31	9-OxoODE	0.981	54232-59-6	C14766
NEG	788492021	282653771	-1.48	0.000	15.20	Dihomo-gamma-Linolenic Acid	0.629	-	C03242
NEG	28085719	10659340	-1.40	0.001	2.49	Xanthine	0.993	69-89-6	C00385
NEG	29244612	11137800	-1.39	0.000	2.84	L-Valine	0.911	72-18-4	C00183
NEG	10561464	4400274	-1.26	0.000	1.54	Allopurinol	0.995	315-30-0	-
NEG	179430752	76005889	-1.24	0.011	5.49	Cortisone	0.992	-	C00762

NEG	31255915	14203126	-1.14	0.000	2.68	Propionic acid	0.998	-	C00163
NEG	655427246	324779982	-1.01	0.000	11.83	Palmitoleic acid	0.997	373-49-9	C08362
NEG	722041308	380118466	-0.93	0.001	12.10	Arachidonic Acid	0.994	506-32-1	C00219
NEG	18543317	13899236	-0.42	0.013	1.15	Nicotinate	0.748	-	C00253
NEG	44768261	54762046	0.29	0.000	2.10	PGD2	0.993	-	C00696
NEG	626870807	1098840569	0.81	0.000	14.62	Deoxycholic acid	0.995	83-44-3	C04483
NEG	1649139523	3511276563	1.09	0.000	29.79	Lithocholic acid	0.998	434-13-9	C03990
NEG	34496734	77557276	1.17	0.000	4.41	Heptadecanoic acid	0.708	506-12-7	-
NEG	18648117	46747798	1.33	0.000	3.54	Adenine	0.970	73-24-5	C00147
NEG	1155911610	3624019076	1.65	0.000	34.36	Cholic acid	0.991	81-25-4	C00695
NEG	28393834	99014111	1.80	0.001	4.93	1,7-Dimethyluric acid	0.735	-	C16356
NEG	3002037	10670053	1.83	0.045	1.39	Theophylline	0.976	-	C07130
NEG	35256806	192117391	2.45	0.000	7.97	1,3,7-Trimethyluric acid	0.929	-	C16361
NEG	1497835	10333130	2.79	0.000	1.87	Butylparaben	0.784	94-26-8	-

Note: \log_2_FC is a logarithmic value of GK-TBf/GKf