

Supplemental data

Antibodies used for Flow Cytometry

BL = Biolegend (San Diego, CA),

BD = BD Biosciences (San Jose, CA)

PD-1 Panel

Brilliant Stain Buffer (BD Cat# 563794)

CD3-BUV395 (BD Cat# 563548)

CD4-BV650 (BL Cat# 317435)

CD8-BV711 (BL Cat# 301043)

CD45RO-BV421 (BL Cat# 304223)

CD197-FITC (BL Cat# 353215)

CD62L-PE-Cy7 (BL Cat# 304821)

CD95-APC (BL Cat# 305611)

CD279-PE (BL Cat# 329905)

HLA*DR-APC-Cy7 (BL Cat# 307617)

CD38-PerCP-Cy5.5 (BL Cat# 356613)

NK Panel

Brilliant Stain Buffer (BD Cat# 563794)

CD3-BUV395 (BD Cat# 563548)

CD45-FITC (BD Cat# 555482)

CD16-PE-Cy7 (BL Cat# 302016)

CD56-BV421 (BL Cat# 318328)

NKp44-APC (BL Cat# 325109)

NKp30-BV711 (BD Cat# 563383)

NKp46-PE (BD Cat# 557991)

Monocyte Panel

Brilliant Stain Buffer (BD Cat# 563794)

CD3-BUV395 (BD Cat# 563548)

CD19-BV650 (BL Cat# 302237)

CD14-BV711 (BL Cat# 301837)

CD16- PE-Cy7 (BL Cat# 302016)

CD163-PE (Trillium Cat# CD163-158P)

CD56-BV421 (BL Cat# 318328)

CD312-FITC (SeroTech Cat# MCA2330F)

CD97-APC (eBiosciences Cat # 17-6979-41)

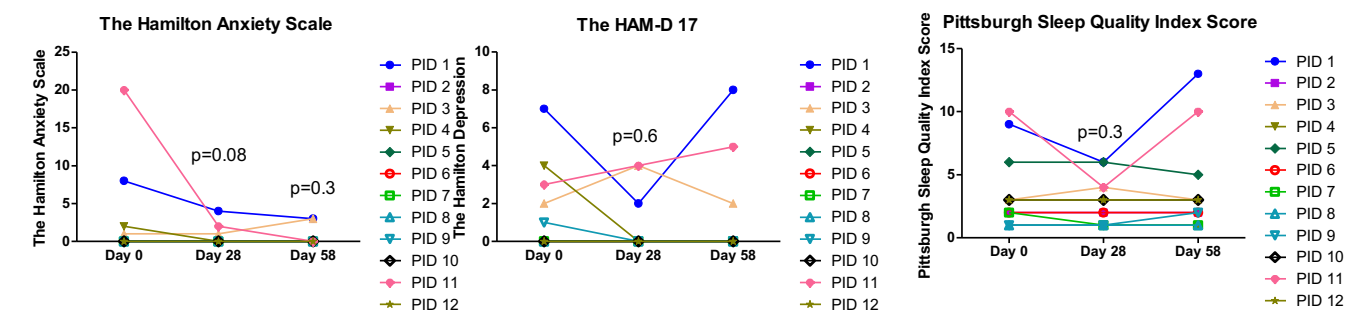
CD206-APC-Cy7 (BL Cat# 321120)

CD38- PerCP-Cy5.5 (BL Cat# 356613)

HLA*DR-APC-Cy7 (BL Cat# 307617)

Supplemental Figure 1. Hamilton Anxiety and Depression and Pittsburgh Sleep Quality Index Scores in HIV positive patients receiving aprepitant

The Wilcoxon signed-rank test was used to determine whether within subject median change from day 0 is significantly different than 0. P values are indicated on the graphs.



Supplemental Table 1A. Adverse events by subject (Number of adverse events), n (% of total individuals with adverse event)

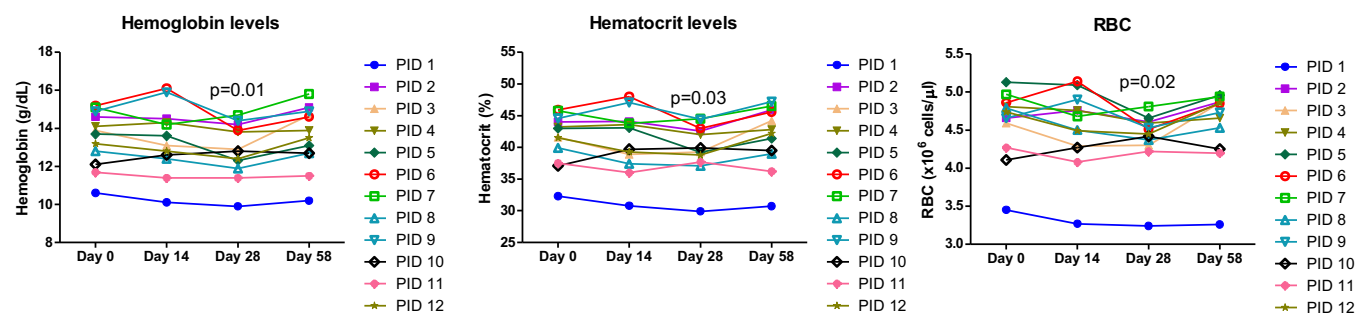
	Subject 1	Subject 3	Subject 4	Subject 6	Subject 7	Subject 11	Subject 12	Total
Any Serious Adverse Events								
Yes	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
No	3 (100)	9 (100)	1 (100)	4 (100)	1 (100)	3 (100)	1 (100)	22 (100)
Total	3 (100)	9 (100)	1 (100)	4 (100)	1 (100)	3 (100)	1 (100)	22 (100)
Severity								
Mild	0 (0)	6 (66.7)	1 (100)	1 (25.0)	1 (100)	2 (66.7)	1 (100)	12 (54.5)
Moderate	3 (100)	3 (33.3)	0 (0)	3 (75.0)	0 (0)	1 (33.3)	0 (0)	10 (45.5)
Severe	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Total	3 (100)	9 (100)	1 (100)	4 (100)	1 (100)	3 (100)	1 (100)	22 (100)

Supplemental Table 1B. Adverse events details by subject, n (%)

	Subject 1	Subject 3	Subject 4	Subject 6	Total
Relationship to Medication					
Not related	0 (0)	0 (0)	0 (0)	1 (25.0)	1 (5.9)
Possible	3 (100)	9 (100)	1 (100)	2 (50.0)	15 (88.2)
Unlikely	0 (0)	0 (0)	0 (0)	1 (25.0)	1 (5.9)
Action Taken					
None	3 (100)	9 (100)	1 (100)	4 (100)	17 (100)
Outcome					
Improved	0 (0)	2 (22.2)	0 (0)	0 (0)	2 (11.8)
Recovered/resolved	3 (100)	6 (66.7)	1 (100)	3 (75.0)	13 (76.5)
Unchanged	0 (0)	1 (11.1)	0 (0)	1 (25.0)	2 (11.8)
Ongoing					
No	3 (100)	8 (88.9)	1 (100)	3 (75.0)	15 (88.2)
Yes	0 (0)	1 (11.1)	0 (0)	1 (25.0)	2 (11.8)

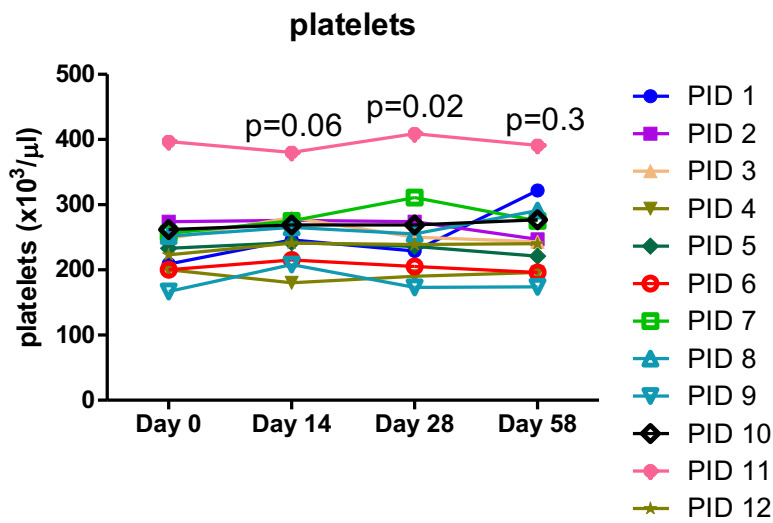
Supplemental Figure 2. Hemoglobin, hematocrit and RBC count in HIV positive patients receiving aprepitant

Wilcoxon signed-rank test was used to determine whether within subject median change from day 0 is significantly different than 0. Significant p values (<0.05) are indicated on the graphs.



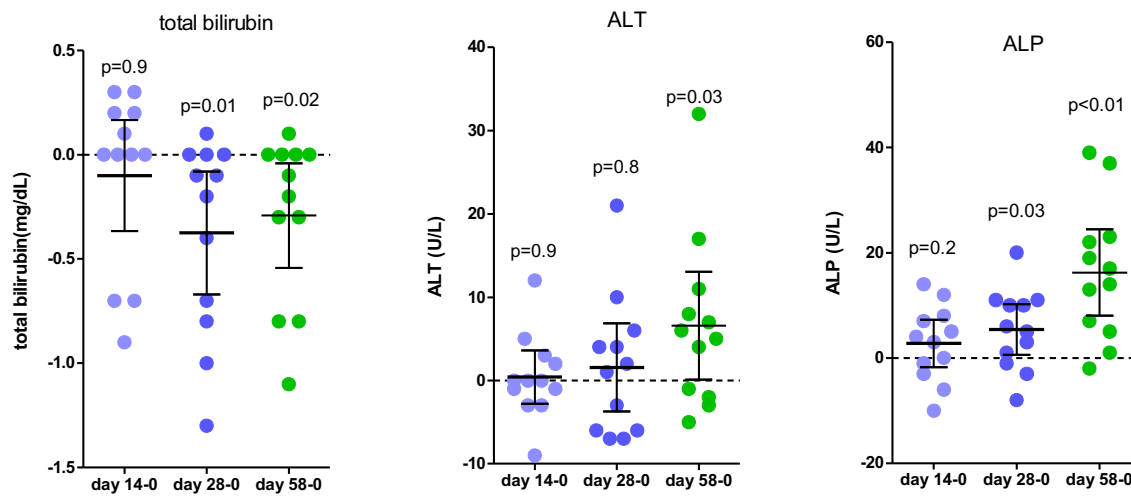
Supplemental Figure 3. Platelets in HIV positive patients receiving aprepitant

Wilcoxon signed-rank test was used to determine whether within subject median change from day 0 is significantly different than 0. P values are indicated on the graph.



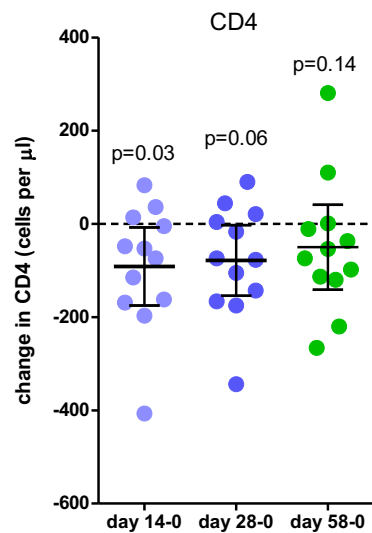
Supplemental Figure 4. Changes in total bilirubin, alanine aminotransferase (ALT) and alkaline phosphatase (ALP) in HIV positive patients receiving aprepitant

Results are presented as changes in marker levels between day 0 and 14, day 0 and 28 or day 0 and 58 as indicated. Vertical bars are the widths of the 95% confidence intervals. P values by Wilcoxon signed-rank test are indicated on the plots.



Supplemental Figure 5. Changes in CD4+ T-cell count in HIV positive patients receiving aprepitant

Results are presented as changes in absolute CD4+ T-cell numbers between day 0 and 14, day 0 and 28 or day 0 and 58 as indicated. Vertical bars are the widths of the 95% confidence intervals. P values by Wilcoxon signed-rank test are indicated on the plot.

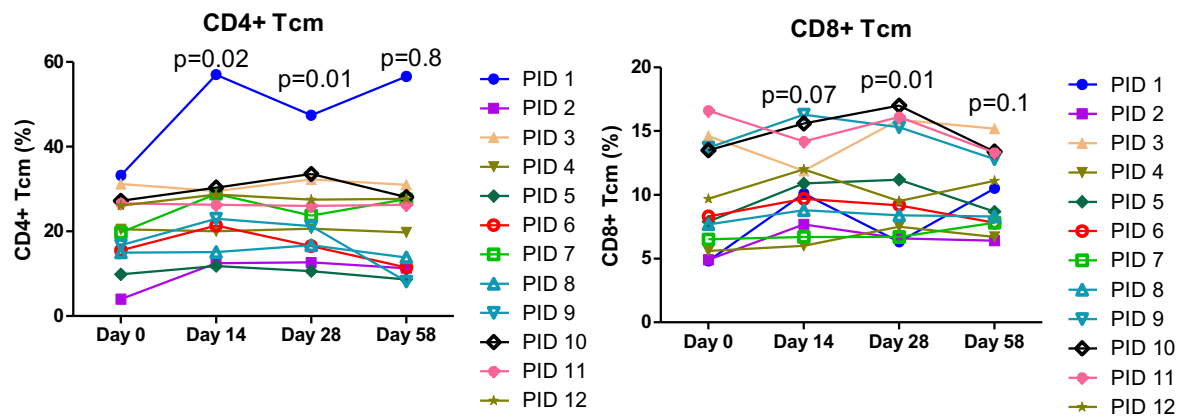


Supplemental Table 2. Viral loads by ultrasensitive HIV viral load assay in HIV positive patients receiving aprepitant

	HMMCgag (RNA copies/mL)	
PID	Day 0	Day 28
1	<0.75	0.75
2	<0.75	<0.73
3	0.91	<0.77
4	<0.84	<0.78
5	<0.79	<1.0
6	5.8	14
7	0.84	<0.84
8	0.79 *	2.9 *
9	5.1	4.3
10	2.5	3.6 *
11	<0.93	<0.75
12	1.6	<0.75
* HIV-1 DNA detected in controls without RT; values likely do not represent the true viral load.		

Supplemental Figure 6. CD4+ Tcm and CD8+ Tcm in HIV positive patients receiving aprepitant

Wilcoxon signed-rank test was used to determine whether within subject median change from day 0 is significantly different than 0. P values are indicated on the graphs.



Supplemental Table 3. Complete list of proteins affected by Aprepitant treatment.

Likelihood ratio tests were performed using the ANOVA function of the car R package to calculate proteins that showed significant changes in their expression levels after treatment with Aprepitant. The regression coefficient demonstrates both the direction and the magnitude of the change. False discovery rate (FDR) adjusted p-values that account for multiple comparisons are included in the table.

Protein Name	p-value	regression coefficient	FDR adjusted p-value
Proteins with higher expression after Aprepitant treatment			
Cathepsin.Z	0.0000001	1124.24	0.00019
Complement.C5	0.0000007	333.18	0.00033
Thioredoxin.domain.containing.protein.12	0.0000007	136.45	0.00033
Lysosomal.protective.protein	0.0000054	5066.01	0.00107
Asialoglycoprotein.receptor.1	0.0000063	563.37	0.00107
Interleukin.1.receptor.like.1	0.000007	360.3	0.00107
Leptin.receptor	0.000007	208.47	0.00107
Vitamin.K.dependent.protein.C	0.0000073	126.67	0.00107
Vascular.endothelial.growth.factor.A	0.0000105	614.31	0.00118
Thyroid.Stimulating.Hormone	0.0000108	106.16	0.00118
Alpha.1.antitrypsin	0.0000101	51.14	0.00118
Cathepsin.F	0.0000192	671.07	0.00168
SPARC.like.protein.1	0.0000261	972.5	0.00214
CD209.antigen	0.0000448	215.04	0.00345
Protein.Z.dependent.protease.inhibitor	0.0000655	676.02	0.00477
Low.density.lipoprotein.receptor.related.protein.1.soluble	0.0000945	190.75	0.0059
Ectonucleoside.triphosphate.diphosphohydrolase.5	0.0001118	312.56	0.00666
Tenascin	0.0001182	754.37	0.00673
Hemojuvelin	0.0001448	188.67	0.00775
Dipeptidyl.peptidase.2	0.0001478	83.43	0.00775
Apolipoprotein.L1	0.0001663	2536.24	0.00778
Neutral.ceramidase	0.0001639	842.07	0.00778
Importin.subunit.alpha.1	0.0002651	15.81	0.01085
Carboxypeptidase.B2	0.0003413	771.38	0.01315
Receptor.tyrosine.protein.kinase.erbB.3	0.0003373	16.98	0.01315
Arylsulfatase.B	0.0003595	54.83	0.01345
N.acylethanolamine.hydrolyzing.acid.amidase	0.000442	14283.52	0.01565
Complement.C5b.C6.complex	0.0004405	53.67	0.01565
Apolipoprotein.M	0.0004957	1020.63	0.01709
Mannose.binding.protein.C	0.0005168	4744.67	0.01736
Netrin.4	0.0005469	52.05	0.01791
Myeloperoxidase	0.0006469	868.43	0.02067

Afamin	0.000909	2474.82	0.02706
Leucine.rich.repeats.and.immunoglobulin.like.domains.protein.3	0.0009027	371.17	0.02706
Coagulation.Factor.XI	0.0010709	99.34	0.03027
Ectonucleotide.pyrophosphatase.phosphodiesterase.family.member.7	0.0015461	1456.99	0.03895
Trefoil.factor.2	0.0015002	905.11	0.03895
Carbohydrate.sulfotransferase.15	0.0014862	230.99	0.03895
Alpha.L.iduronidase	0.0015351	227.07	0.03895
X14.3.3.protein.sigma	0.0016442	657.89	0.04064
Coagulation.factor.VII	0.001769	32.23	0.04291
Tyrosine.protein.kinase.receptor.TYRO3	0.0022148	32.48	0.0509
Sex.hormone.binding.globulin	0.0025452	415.88	0.05738
Annexin.A5	0.002978	42.74	0.06395
Endoglin	0.0032778	142.54	0.06926
Cation.independent.mannose.6.phosphate.receptor	0.0034334	1745.8	0.07139
Interleukin.1.receptor.type.2	0.0036332	828.22	0.07322
Antileukoproteinase	0.003985	1191.68	0.07792
Hepatocyte.growth.factor.receptor	0.0042657	381.01	0.08151
Apolipoprotein.E.isoform.E4.	0.0043579	10324.45	0.08156
Tumor.necrosis.factor.receptor.superfamily.member.17	0.0051153	285.84	0.09018
X.ray.repair.cross.complementing.protein.6	0.0052317	19.12	0.09018
Fetuin.B	0.0053305	411	0.09069
Antithrombin.III	0.0058503	5302.97	0.09417
Coagulation.Factor.V	0.0059664	2603.88	0.09417
Serum.amyloid.P.component	0.0059186	2017.48	0.09417
Repulsive.guidance.molecule.A	0.0059114	901.57	0.09417
Low.affinity.immunoglobulin.gamma.Fc.region.receptor.II.b	0.0065189	143.19	0.10144
Proprotein.convertase.subtilisin.kexin.type.7	0.0065823	94.27	0.10144
Apolipoprotein.B	0.007017	531.23	0.10689
Dynactin.subunit.2	0.0072794	51.37	0.10961
Vesicular.integral.membrane.protein.VIP36	0.0092095	1035.22	0.13293
Prolactin	0.0097931	150.02	0.13795
Platelet.activating.factor.acetylhydrolase	0.0099422	30.57	0.13856
Low.density.lipoprotein.receptor.related.protein.1B	0.0102701	2711.67	0.13887
Kallikrein.8	0.0103155	323.48	0.13887
Hepatocyte.growth.factor.like.protein	0.0101436	190.66	0.13887
Ficolin.2	0.0103887	87.57	0.13887
Histone.lysine.N.methyltransferase.EHMT2	0.0109072	41.24	0.14433
Acid.sphingomyelinase.like.phosphodiesterase.3a	0.0119748	579.79	0.15479
Polymeric.immunoglobulin.receptor	0.0120526	527.47	0.15479
Tumor.necrosis.factor.ligand.superfamily.member.13B	0.013382	67.54	0.16696
Troponin.I.cardiac.muscle	0.0138724	11.36	0.16984
Tumor.necrosis.factor.ligand.superfamily.member.18	0.0146045	18.4	0.17715
gp41.C34.peptide.HIV	0.0151481	53.99	0.17933
SLAM.family.member.6	0.0168835	13.52	0.19573
Prothrombin	0.0177929	7511.12	0.20121
Tyrosine.protein.kinase.JAK2	0.0175136	520.17	0.20121
GDNF.family.receptor.alpha.2	0.0210211	153.56	0.22509
Heparan.sulfate.6.O.sulfotransferase.1	0.020985	77.62	0.22509

Bone.morphogenetic.protein.10	0.022183	67.14	0.23063
Superoxide.dismutase.Mn.mitochondrial	0.0231	1214.72	0.23641
Vascular.endothelial.growth.factor.receptor.2	0.0256144	260.73	0.2546
Lactadherin	0.0261737	33.55	0.2546
Dipeptidyl.peptidase.1	0.0276894	17.15	0.25909
C.C.motif.chemokine.25	0.0292203	1372.75	0.26582
Thrombin	0.029538	58.83	0.26589
C.type.lectin.domain.family.4.member.K	0.0296335	5.52	0.26589
Inter.alpha.trypsin.inhibitor.heavy.chain.H4	0.0304957	998.97	0.26942
Serum.albumin	0.0306954	938.38	0.26942
Plasma.protease.C1.inhibitor	0.0308496	456.21	0.26942
Osteopontin	0.0310604	689.7	0.26946
Leucine.rich.repeat.transmembrane.protein.FLRT3	0.0338482	648.63	0.28981
Complement.factor.H.related.protein.5	0.0352502	163.9	0.29986
Interleukin.1.alpha	0.0360755	21.32	0.3049
Small.nuclear.ribonucleoprotein.F	0.0369421	96.48	0.31022
Interleukin.13.receptor.subunit.alpha.1	0.0442405	140.83	0.35555
Cadherin.1	0.0450888	4115.38	0.35798
Lymphatic.vessel.endothelial.hyaluronic.acid.receptor.1	0.0448173	5.08	0.35798
Endoplasmic.reticulum.resident.protein.29	0.0455619	347.66	0.35922
Toll.like.receptor.2	0.0457937	32.1	0.35922
Apolipoprotein.E.isoform.E3.	0.0463321	7597.34	0.36128
Interleukin.1.receptor.type.1	0.0472266	628.78	0.36335
Iduronate.2.sulfatase	0.0477439	215.09	0.36363
Complement.component.C7	0.0496138	32.02	0.36944

Proteins with lower expression after aprepitant treatment

RNA.binding.protein.39	0.0000019	-24.31	0.00062
Lymphocyte.activation.gene.3.protein	0.0000141	-805.78	0.00142
Fibroblast.growth.factor.10	0.0000171	-22.03	0.0016
Thrombospondin.4	0.0000925	-34.93	0.0059
Prolyl.endopeptidase.FAP	0.0000889	-62.54	0.0059
Complement.component.C1q.receptor	0.0001627	-1059.77	0.00778
Proto.oncogene.tyrosine.protein.kinase.receptor.Ret	0.0001768	-197.88	0.00799
Angiogenin	0.0002119	-244.91	0.00925
Contactin.1	0.0002632	-21.92	0.01085
Casein.kinase.II.subunit.alpha	0.0006857	-49.23	0.02139
C.type.mannose.receptor.2	0.0009396	-390.06	0.02735
Complement.C3d.fragment	0.0010861	-993.46	0.03027
B.cell.receptor.CD22	0.0015167	-49.02	0.03895
Transforming.growth.factor.beta.1	0.0019026	-105.38	0.04532
Dermatopontin	0.0020388	-356.27	0.04769
Insulin.like.growth.factor.I	0.0025845	-64.15	0.05738
Alpha.2.HS.glycoprotein	0.0028688	-126.74	0.06264
Cadherin.5	0.0036132	-510.22	0.07322
Mitochondrial.import.inner.membrane.translocase.subunit.TIM14	0.0039548	-62.9	0.07792
Bcl.2.like.protein.2	0.0042933	-49.82	0.08151
Interleukin.2.receptor.subunit.alpha	0.0047577	-20.12	0.08778

Collectin.12	0.0049055	-56.77	0.08925
Matrix.extracellular.phosphoglycoprotein	0.0051149	-6.93	0.09018
Caspase.2	0.0052082	-27.9	0.09018
Tyrosine.protein.kinase.Lck	0.0057966	-17.67	0.09417
Ephrin.type.B.receptor.2	0.0057257	-668.89	0.09417
A.disintegrin.and.metalloproteinase.with.thrombospondin.motifs.15	0.0088473	-19.46	0.1317
C.C.motif.chemokine.22	0.0090311	-120.17	0.13293
Dickkopf.related.protein.4	0.0092344	-727.14	0.13293
Killer.cell.lectin.like.receptor.subfamily.F.member.1	0.0097481	-8.33	0.13795
X3.hydroxyacyl.CoA.dehydrogenase.type.2	0.0114884	-1923.43	0.1505
Kin.of.IRRE.like.protein.3	0.0125014	-12.38	0.159
Brain.natriuretic.peptide.32	0.0130641	-16.3	0.16456
Resistin	0.0135274	-73.7	0.16718
Interleukin.17.receptor.A	0.0149428	-12.78	0.17933
Fibroblast.growth.factor.receptor.1	0.0151954	-31.12	0.17933
Macrophage.metalloelastase	0.0166674	-107.25	0.19495
Protein.SET	0.0178168	-24.39	0.20121
Fibroblast.growth.factor.4	0.0182924	-21.82	0.20481
Complement.factor.B	0.0194922	-1483.65	0.2164
DnaJ.homolog.subfamily.B.member.1	0.0201203	-148.01	0.22149
Collagen.alpha.1.XXIII..chain	0.0203047	-146.39	0.22166
Cyclin.dependent.kinase.1.G2.mitotic.specific.cyclin.B1.complex	0.0214777	-60	0.22509
Serine.threonine.protein.kinase.17B	0.021154	-391.15	0.22509
Cell.adhesion.molecule.related.down.regulated.by.oncogenes	0.0213899	-512.65	0.22509
Transforming.growth.factor.beta.2	0.0229862	-15.1	0.23641
SLIT.and.NTRK.like.protein.5	0.023771	-71.77	0.2414
Interleukin.6	0.0251052	-84.91	0.25298
Serum.paraoxonase.arylesterase.1	0.0265226	-6.78	0.2546
Hexokinase.2	0.0266258	-62.83	0.2546
High.affinity.nerve.growth.factor.receptor	0.0262084	-92.38	0.2546
Junctional.adhesion.molecule.B	0.0262935	-403.71	0.2546
Integrin.alpha.IIb.beta.3.complex	0.0262954	-603.76	0.2546
Growth.differentiation.factor.11.8	0.0268917	-81.97	0.25528
Stem.cell.growth.factor.alpha	0.0272723	-169.29	0.25703
Brevican.core.protein	0.0288439	-58.38	0.26582
Complement.C3b.inactivated	0.0287461	-473.67	0.26582
Platelet.derived.growth.factor.subunit.A	0.0291544	-1366.45	0.26582
Estrogen.receptor	0.0299204	-30.41	0.26664
Angiopoietin.4	0.0330986	-36.9	0.28526
Serine.threonine.protein.kinase.PAK.7	0.0394663	-96.77	0.32931
Protein.tyrosine.kinase.6	0.0409221	-52.08	0.33861
Dual.specificity.mitogen.activated.protein.kinase.kinase.3	0.0410979	-337.57	0.33861
Reticulon.4.receptor	0.041536	-114.38	0.34008
Galectin.4	0.0422867	-33.84	0.34407
Interleukin.23.receptor	0.0428074	-357.32	0.34616
Fibroblast.growth.factor.2	0.0467248	-293.11	0.36219
Interleukin.22	0.0474299	-198.68	0.36335
Peptidyl.prolyl.cis.trans.isomerase.F.mitochondrial	0.0484853	-5449.62	0.36714

Advanced.glycosylation.end.product.specific.receptor.soluble	0.0492815	-12.29	0.36944
Matrix.metalloproteinase.17	0.0496341	-21.57	0.36944