

Supplemental materials

Figure S1a Pathway network analysis of the top 100 genes regulated by Klotho in MO3.13 cells

Figure S1b Pathway network analysis of the top 100 genes genes regulated by Klotho in MO3.13 cells

Table S1: qPCR confirmation of the 91 regulated genes using RNA from cultured MO3.13 cells treated with Klotho for 1, 2.5 and 3.5 hrs.

Table S2: Signal Transduction Pathway Reporters.

Table S3. Up-regulated genes of Klotho treated MO3.3 cells vs. CGP database

Table S4. Down-regulated genes of Klotho treated MO3.3 cells vs. CGP database

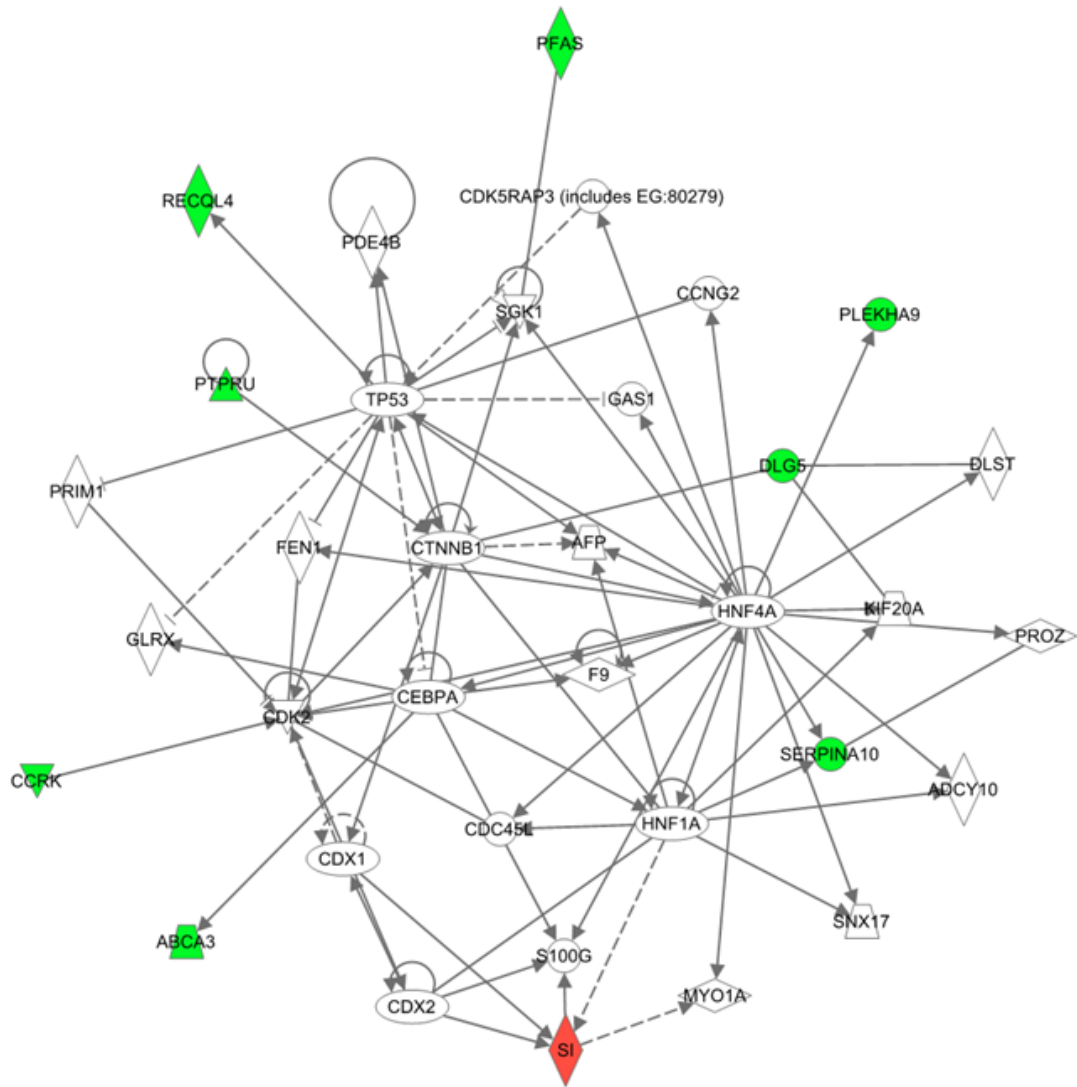


Figure S1b

Table S1: qPCR confirmation of the 91 regulated genes using RNA from cultured MO3.13 cells treated with Klotho for 1, 2.5 and 3 hrs.

	Symbol	Accession	1 hr		2.5 hr		3.5 hr	
			T-TEST p	Fold change	T-TEST p value	Fold change	T-TEST p	Fold change
Upregulated genes in microarray	EFNA1	NM_004428	0.161265172	59.10500237	0.120140584	3.285812142	0.066557075	-6.744680017
	SLC5A8	NM_145913	0.058682932	125243.3953	0.037845128	3.832547513	0.903803812	1.17249627
	TGIF2LX	NM_138960	0.048905691	7010.046668	0.650856242	23.02246403	0.009382928	11770.734
	GRAP2	NM_004810	0.000308192	3.645836843	0.168020537	3.645836843	0.412034139	-2.922257548
	CCDC68	NM_025214	0.016717437	68.56379217	0.264388058	2.408135659	0.69509389	3.449171824
	KLHL34	NM_153270	0.136752737	64.3057126	0.011906026	3.308666772	0.649535219	4.290809944
	MAOA	NM_000240	0.854426924	1.155519548	0.59091956	1.367224353	0.4852378	9.621421112
	LGR6	NM_001017403	0.02086637	216430.1055	0.233625846	28.01841962	0.250623278	-4.580219271
	GRIA3	NM_007325	0.041391395	7565.440303	0.022064942	4.187966784	0.099600274	-5.658488249
	TFCP2L1	NM_014553	0.03788333	2.693300118	0.457965401	1.706747927	0.680885323	3.916549883
	DKFzP451A211	BX647655	0.481440261	-11.27293805	0.149731692	-39.91198148	0.063332655	-348.1945955
	SERPINA10	NM_016186	0.847621387	-1.33464711	0.21522808	2.259886004	0.050130694	-9.772651195
	MGAM	NM_004668	0.191380288	26.38918701	0.160939215	-85.25721358	0.504860167	-27.54560032
	IL28A	NM_172138	0.551332298	-2.022219593	0.178558388	-1.739909902	0.013850091	-21.06948774
	GPR112	NM_153834	0.661096047	69362.82321	0.021583644	14.8079875	0.398177848	42.80131846
	CHRFAM7A	NM_139320	0.280662103	12.31099105	0.982474495	1.018361653	0.071233849	-9.213504422
	KRT14	NM_000526	0.457221637	3.088432928	0.710552035	1.162038725	0.611528688	23.96599058
	NRXN3	NM_004796	0.072158492	33461.357	0.095986602	178.6819383	0.831281944	-2.040255738
	DCN	NM_001920	0.198235271	687.0993938	0.280765163	-1.587502785	0.267514773	-3.87380142
	Downregulated genes in microarray	HSPG2	NM_005529	0.554416856	1.624739397	0.026173244	-2.004294625	0.512144638
C10orf125		NM_198472	0.351367867	2.153786133	0.980456404	1.007804236	0.204814309	138.5807763
PKHD1L1		NM_177531	0.078761264	41915.85198	0.285975298	-2.392241417	0.510812122	18.37386633
GIMAP6		NM_024711	0.018566545	155.0806632	0.724134093	-2.005205366	0.482628728	-13.07509932
ACSM2B		NM_182617	0.379755745	-27.24887948	0.229180716	-261.7568231	0.232487448	-399.5087617
WDR63		NM_145172	0.276861743	2.515842603	0.425622731	-1.782312114	0.17397345	-7.623305363
IGF2		NM_000612	0.154427173	-91.97213973	0.026436015	-3.292107419	0.000929036	-21.5370687
MYO18B		NM_032608	0.405047949	4.253179274	0.000692931	6.850693308	0.013211593	-7.623305363
DCTN1		NM_004082	0.050887813	-11.06648383	0.049498314	-2.918494287	0.000364798	-36.93926699
RPL35		NM_007209	0.984561327	-1.090350269	0.853566585	-1.134353562	0.408621181	-2.423485303
CENTG1		NM_014770	0.822063138	-1.806409527	0.024528155	-2.461625547	0.036142694	-132.3991454
MNS1		NM_018365	0.046662955	2.901652996	0.080234408	-2.25023032	0.040416703	-5.261290342
USP9Y		NM_004654	0.434089666	2.945559441	0.857831631	-1.089582943	0.496263637	12.87276442
NID2		NM_007361	0.247068629	2.085232619	0.839561969	1.176193902	0.008247724	-3.81605862
GLI3		NM_000168	0.974710259	1.017626633	0.977270247	-1.014119988	0.021284751	-5.658488249
LOC151534		AK125271	0.46479509	1.674280984	0.457636988	-1.391636975	0.041709327	-4.454972934
C9orf25		NM_147202	0.211793166	406.4333563	0.480518823	-1.290252859	0.083465842	-2.290109635
CBWD5		NM_001024916	0.525389188	-6.772984371	0.069779499	-2.521833282	0.081799304	-6.477408211
UNC13B		NM_006377	0.066892608	4.464633242	0.455327421	3.997060569	0.007006012	-8.419590107
TCTN2		NM_024809	0.187518586	17.37019045	0.181876754	-1.938003094	0.084603571	-4.725335179
PPIG		NM_004792	0.446975706	159.0726134	0.394148292	-1.89779674	0.255160805	-49.02401255
DLG5		NM_004747	0.143842361	-627.3492433	0.198902335	-226.5601005	0.100216213	-2065.225116
LRP1		NM_002332	0.803040683	1.331951607	0.014278106	-1.634029413	0.3017484	-22.60782033
ZFH3		NM_006885	0.099063823	-383.954532	0.04303407	-1.724667361	0.07303407	-4717.314264
AFAP1		NM_198595	0.084297753	3.010928259	0.119272069	-2.15317848	0.622013418	2.635207684
PFAS		NM_012393	0.092480741	-308.2858794	0.018420638	-2.891400474	0.135394378	-1102.897753
POLR2A		NM_000937	0.401410104	3.630600863	0.27314673	-1.330672444	0.015404594	-7.321216223
PPP2R1A		NM_014225	0.011088177	3.306278684	0.391087582	-1.933654928	0.57904073	9.688343388
FASN		NM_004104	0.160737298	192.0327192	0.305797886	-1.647102934	0.032996448	-10.51043154
TNS1		NM_022648	0.309044145	2.921835588	0.417079553	-1.368201955	0.00583758	-6.974468766
HGFAC		NM_001528	0.113706852	10.74213113	0.369845716	-2.063868573	0.141474084	-3.58941815
AMT		NM_000481	0.646220085	-1.931593705	0.273010681	-1.428810763	0.538852156	42.16332294
FZD5		NM_003468	0.080894736	-3.196422984	0.016745923	-1.559837057	0.168461781	479.2329628
PLEKHA9		NM_015899	0.206271033	-3.958055019	0.293024028	-1.308657589	0.008393467	-7.245490368
WIPF1		NM_003387	0.786542414	4.218923711	0.26795869	-778.9660634	0.753833201	-13.72514989
DISC1		NM_018662	0.331706315	22.37074918	0.012553647	-1.698640399	0.144209896	-15.98614306
GNAS		NM_001077490	0.970104107	-1.100473954	0.314189142	-12.36979769	0.084669003	-160.9441877
PTPRU		NM_005704	0.729642764	-1.821076674	0.43682763	-1.157496094	0.243805011	-2.561667686
DENND3		NM_014957	0.199436129	724.1819124	0.983024767	1.011430706	0.036397393	-6.736892756
ABCA3		NM_001089	0.430884828	-1.671864972	0.018736518	-1.862767058	0.06491135	-4.278435477
ZBTB4		NM_020899	0.714701213	1.380516693	0.744670647	-1.212100349	0.010659642	-17.75823959
RECQL4		NM_004260	0.699024193	-4.404439185	0.003368955	-2.119538247	0.231730261	-57.69669066
LPXN		NM_004811	0.043187002	42.13289081	0.248177719	-39.78547383	0.0271134	-4.886325598
C9orf58		NM_031426	0.55770638	-1.470654478	0.146677168	-1.732612076	0.011559539	-11.35626619
ZNF528		NM_032423	0.13481532	129.2071114	0.203671997	-2.261946492	0.039867733	-8.085946548
UGDH		NM_003359	0.026786705	19.20675203	0.004399933	-1.542719324	0.131601407	-60.49525154
CCDC40		NM_017950	0.798168735	-1.591302744	0.344855013	-1.611938871	0.014196535	-6.149276449
MED25		NM_030973	0.293633209	48.73461695	0.021544297	-1.521784116	0.988099931	1.036162301
SARM1		NM_015077	0.04781428	2.861705081	0.084253425	-2.101991917	0.952622821	1.195750726
NCLN		NM_020170	0.163503289	9.936297251	0.377378868	1.198823975	0.018184723	-3.656381653
B4GALNT3		NM_173593	0.294222132	155.7989464	0.025438911	-2.82905817	0.002763255	-8.586578257
ERBB3		NM_001982	0.007961409	5.959570386	0.113013827	-2.037882284	0.744785431	3.980408963
ITSN2		NM_006277	0.145462795	365.4528987	0.258121582	-28.36222005	0.518493882	10.51650436
SI		NM_001041	0.08991093	2668.614134	0.031000563	4.844171694	0.427179973	33.42641357
DOCK5		NM_024940	0.121871285	5.592687294	0.739658698	-1.212865668	0.233295948	199.6390315
FLNB		NM_001457	0.336654714	1.674280984	0.549972929	-1.416173634	0.156828162	-3.186744453
MAP3K5		NM_005923	0.170903129	-114.4144136	0.024558563	-2.798796191	0.258920103	-324.1272862
CCDC136		NM_022742	0.054402028	-304.744914	0.022811735	-3.098502335	0.676337097	-12.41274252
MBOAT1		NM_001080480	0.078818954	6.861584024	0.114637753	-1.988414068	0.220659828	-3.63112518
KIF1A		NM_004321	0.3260589	147.9065022	0.064730553	-1.911527472	0.23085106	-4.532844489
TCF7		NM_003202	0.177260069	2.966047427	0.056031879	1.763446763	0.120209567	-3.750501017
RTP1		NM_153708	0.221440729	10.26888996	0.638291	-1.174214781	0.843468906	2.029676779
THTPA		NM_024328	0.509161658	-2.623437342	0.040872913	-1.797599419	0.004072953	-8.858628356

Table S2: Signal Transduction Pathway Reporters.

Reporter	Pathway	Transcription Factor
C/EBP Reporter	C/EBP	C/EBP
E2F Reporter	Cell Cycle	E2F/DP1
p53 Reporter	p53/DNA Damage	p53
GATA Reporter	GATA	GATA
LXR Reporter	Liver X Receptor	LXRa
SRE Reporter	MAPK/ERK	Elk-1/SRF
AP1 Reporter	MAPK/JNK	AP-1
NF B Reporter	NF B	NF B
Pax3 Reporter	Pax3	Pax3
Pax6 Reporter	Pax6	Pax6
FOXO Reporter	PI3K/AKT	FOXO
PPAR Reporter	PPAR	PPAR
SP1 Reporter	SP1	SP1
VDR Reporter	Vitamin D Receptor	Vitamin D Receptor
TCF/LEF Reporter	Wnt	TCF/LEF
YY1 Reporter	YY1	YY1

Table S3. Up-regulated genes of Klotho treated MO3.3 cells vs. CGP database

Database	Description	Category
UVB_NHEK3_C2	Regulated by UV-B light in normal human epidermal keratinocytes, cluster 2	Cancer; Stress
HUMAN_TISSUE_TESTIS	Genes expressed specifically in human testis tissue	hormone
BECKER_TAMOXIFEN_RESISTANT_UP	Genes that are reproducibly up-regulated in untreated or permanently tamoxifen-treated MaCa 3366/TAM	Cancer
LEE_E2F1_UP	Genes up-regulated in hepatoma tissue of E2f1 transgenic mice	Cancer
ZHAN_MULTIPLE_MYELOMA_VS_NORMAL_DN	158 genes commonly dysregulated in CD-1 and CD-2 groups upregulated	Cancer
KANNAN_P53_DN	Target genes down regulated by p53	Cancer
GH_GHRHR_KO_24HRS_UP	Up-regulated at least 2-fold 24 hours following injection of human growth hormone (GH) into mice lacking functional GHRHR (lit/lit), and with no detectable hormone	Cancer
BRENTANI_IMMUNE_FUNCTION	Cancer related genes involved in immune function	Cancer
BRCA1_OVEREXP_UP	Upregulated by induction of exogenous BRCA1 in EcR-293 cells	Cancer
YAGI_AML_PROG_FAB	French-American-British (FAB) type-specific probe sets of acute myeloid leukemia (AML)	Cancer
BRCA1_OVEREXP_PROSTATE_UP	Up-regulated with stable, ectopic overexpression of BRCA1 in DU-145 human prostate cancer cell lines, compared to neo-only controls	Cancer
GH_GHRHR_KO_24HRS_DN	Up-regulated at least 2-fold 6 hours following injection of human growth hormone	hormone
ROSS_AML1_ETO	Genes that distinguish pediatric acute myeloid leukemia (AML) subtype t	Cancer
VENTRICLES_UP	Upregulated in the ventricles of healthy hearts, compared to atria	Cardiovascular
CHIARETTI_T_ALL	Genes overexpressed in leukemia cells.	Cancer
CHIARETTI_T_ALL_DIFF	Genes expressed in T-cell acute lymphocytic leukemia	Cancer
SCHURINGA_STAT5A_UP	Differential Gene Expression in CB CD34 Cells Expressing STAT5A(1*6) Up-regulated	Cell proliferation differentiation and cell su
DIAB_NEPH_DN	Downregulated in the glomeruli of cadaver kidneys from patients with diabetic nephropathy, compared to normal controls	Diabetes; insulin/IGF-1
MARTINELLI_IFNS_DIFF	Relative expression levels of neutrophil-specific genes in immature versus mature neutrophils	immunoregulatory activities
GOLDRATH_CYTOLYTIC	Genes associated with cytolytic effector function induced during antigen activation of CD8+ T cells.	immunoregulatory activities
UVB_NHEK3_ALL	Regulated by UV-B light in normal human epidermal keratinocytes, cluster 5	Cancer; Stress
MATSUDA_VALPHAINKT_DIFF	Differential gene expression between developmental stages of Va14i NKT cells	immunoregulatory activities
HSC_LATEPROGENITORS_FETAL	Up-regulated in mouse hematopoietic late progenitors from fetal liver (Late Progenitors Shared + Fetal)	cell fate decisions
TARTE_MATURE_PC	Genes overexpressed in polyclonal plasmablastic cells (PPCs) as compared to mature plasma cells isolated from tonsils (TPCs) and mature plasma cell	immunoregulatory activities
WELCH_GATA1	We performed transcriptome analysis of G1E-ER4 cells a GATA-1-null erythroblast line that undergoes synchronous erythroid maturation when GATA-1 cell fate decisions	cell fate decisions; bone differentiation
YANG_OSTECLASTS_SIG	Relative gene expression for osteoclast-associated genes, chemokines, and chemokine receptors	cell fate decisions; bone differentiation
HSC_LATEPROGENITORS_ADULT	Up-regulated in mouse hematopoietic late progenitors from adult bone marrow (Late Progenitors Shared + Adult)	cell fate decisions; bone differentiation
DAC_IFN_BLADDER_UP	Interferon-regulated genes upregulated by DAC (DNA methylation inhibitors 5-aza-2'-deoxycytidine (5-Aza-CdR)) treatment in T24 bladder carcinoma cells	Cancer
HSC_LATEPROGENITORS_SHARED	Up-regulated in mouse hematopoietic late progenitors from both adult bone marrow and fetal liver	cell fate decisions; bone differentiation
ASTON_OLIGODENDROGLIA_MYELINATION_SUF	Genes upregulated in major depressive disorder	Depression; Myelin
VEGF_HUVEC_30MIN_UP	Up-regulated 30 minutes after VEGF treatment in human umbilical vein endothelial cells	Cardiovascular
NAKAJIMA_MCSMBP_EOS	Top 30 increased eosinophil specific transcripts	cell fate decisions; inflammation
VEGF_HUVEC_2HRS_UP	Up-regulated 2 hours after VEGF treatment in human umbilical vein endothelial cells	Cardiovascular
CPR_NULL-LOW_LIVER_UP	Up-regulated in mouse liver tissue from mice in which NADPH-cytochrome P450 reductase (CPR) was specifically deleted in the liver by cre-lox recomb	Stress
RORIE_ES_PNET_DN	The 30 genes showing the greatest decrease in expression in NBa Ews/Fli-1 (Neuroblastoma (NB) and the Ewing sarcoma (ES)/peripheral primitive neu	Cancer
HUMAN_TISSUE_PLACENTA	Genes expressed specifically in human placental tissue	hormone
LIAN_MYELOID_DIFF_GRANULE	Granule constituents expressed during mouse promyelocytic cell line cell differentiation	cell fate decisions; bone differentiation
AGEING_LYMPH_DN	Downregulated in human lymphocytes from old individuals, compared to young	Stress; aging
DAC_BLADDER_UP	Upregulated by DAC (DNA methylation inhibitors 5-aza-2'-deoxycytidine (5-Aza-CdR)) treatment in T24 bladder carcinoma cells	Cancer
CROONQUIST_IL6_RAS_UP	Genes upregulated in multiple myeloma cells exposed to the pro-proliferative cytokine IL-6 versus those with N-ras-activating mutations.	Cancer
HIPPOCAMPUS_DEVELOPMENT_PRENATAL	Highly expressed in prenatal mouse hippocampus (cluster 1)	Brain development
GH_EXOGENOUS_EARLY_UP	Up-regulated at early time points (1-4 hours) following treatment of mammary carcinoma cells (MCF-7) with exogenous human growth hormone	hormone; Cancer
PENG_RAPAMYCIN_UP	Genes upregulated in response to rapamycin starvation, an immunosuppressive and anticancer drug	Cancer
DAC_PANC_UP	Upregulated by DAC treatment in at least one of four pancreatic cancer cell lines, but not in normal (HPDE) cells	Cancer
ZHAN_MULTIPLE_MYELOMA_VS_NORMAL_UP	The 70 most significantly up-regulated genes in multiple myeloma (MM) in comparison with normal bone marrow PCs	Cancer
UVB_NHEK1_C2	Upregulated by UV-B light in normal human epidermal keratinocytes, cluster 2	Cancer; Stress
CPR_LOW_LIVER_UP	Up-regulated in mouse liver tissue from mice with reduced liver expression of NADPH-cytochrome P450 reductase (CPR), versus normal controls	Stress
LVAD_HEARTFAILURE_DN	Downregulated in the left ventricle myocardium of patients with heart failure following implantation of a left ventricular assist device	Cardiovascular
TSA_CD4_DN	Down-regulated in mouse CD4+ T-cells following 4 hour treatment with 100 nM trichostatin A (a potent, reversible inhibitor of histone deacetylase (HDAC))	Cancer
HOGERKORP_CD44_DN	Genes up-regulated in dendritic cells (DC) stimulated for 8 and 48 h	immunoregulatory activities
AGUIRRE_PANCREAS_CHR6	Genes on chromosome 6 with copy-number-driven expression in pancreatic adenocarcinoma.	Cancer
NAKAJIMA_MCS_UP	Most increased transcripts in activated human and mouse Mast Cells (MCs)	immunoregulatory activities
CREB_BRAIN_2WKS_UP	Up-regulated in the nucleus accumbens of mice after 2 weeks of induction of transgenic CREB (cAMP response element binding protein), transcription f	Brain; cAMP
BRCA1_SW480_UP	Up-regulated by infection of human colon adenocarcinoma cells (SW480) with Ad-BRCA1, versus Ad-LacZ control	Cancer
CARIES_PULP_HIGH_UP	Highly up-regulated (>4-fold) in pulpal tissue from extracted carious teeth (cavities), compared to tissue from extracted healthy teeth	hormone
AGED_MOUSE_RETINA_ANY_UP	Up-regulated in the retina of 16-month aged mice from any of four strains (S8, S10, SR1, B6J), versus 3-month young controls	Aging
STAEGE_EFTS_UP	Summary of genes up-regulated in Ewing family tumors EFTs compared with normal body atlas	Cancer
BLEO_MOUSE_LYMPH_LOW_24HRS_DN	Down-regulated at 24 hours following treatment of mouse lymphocytes (TK 3.7.2C) with a low dose of bleomycin (DNA-damaging agent)	Stress
CPR_NULL_LIVER_UP	Up-regulated in mouse liver tissue from mice in which NADPH-cytochrome P450 reductase (CPR) was specifically deleted in the liver by cre-lox recomb	Stress
FLECHNER_KIDNEY_TRANSPLANT_WELL_PBL_	Genes downregulated in peripheral blood lymphocytes (PBLs) of immunosuppressed patients with a well functioning kidney transplant relative to PBLs of	immunoregulatory activities
GRANDVAUX_IRF3_DN	Genes down-regulated by interferon regulatory factor 3 (IRF3) in Jurkat (T-cell)	immunoregulatory activities
TAKEDA_NUP8_HOXA9_3D_DN	Effect of NUP98-HOXA9 on gene transcription at 3 d after transduction Down (myelodysplastic syndromes and acute myeloid leukemia)	immunoregulatory activities; Cancer
CPR_NULL_LIVER_DN	Down-regulated in mouse liver tissue from mice in which NADPH-cytochrome P450 reductase (CPR) was specifically deleted in the liver by cre-lox reco	Stress
YU_CMYC_DN	Myc-repressed genes in neoplastic transformation	Cancer
CROONQUIST_RAS_STROMA_UP	Genes upregulated in multiple myeloma cells with N-ras-activating mutations versus those co-cultured with bone marrow stromal cells.	Cancer
TF2_KO_UP	Up-regulated in pyloric atrium tissue from gastrointestinal trefoil factor family Trefoil Factor 2 (Tf2) knockout mice, compared to wild-type controls	immunoregulatory activities
TNFALPHA_TGZ_ADIP_DN	Downregulated in mature, differentiated adipocytes following treatment with TNFalpha (anti-Diabetes)	Diabetes
HYPERME_COLONCA_SW48	Gene identified by chromatin IP and CpG island microarray as being hypermethylated in SW48 colon cancer cells, versus normal colon mucosa or WI3	Cancer
CMV_HCMV_TIMECOURSE_16HRS_DN	Down-regulated in fibroblasts following infection with human cytomegalovirus	Stress; immunoregulatory activities
UV_UNIQUE_FIBRO_UP	Up-regulated at any timepoint by treatment of human fibroblasts with UV light, but not by gamma radiation or 4-NQO	Stress
XPB_TTD-CS_DN	Down-regulated in XPB/TTD fibroblasts (expressing XPB-A355C), compared to XPB/CS fibroblasts (expressing XPB-T296C)	DNA repair; skin cancer
UV_UNIQUE_FIBRO_DN	Down-regulated at any timepoint by treatment of human fibroblasts with UV light, but not by gamma radiation or 4-NQO	Cancer; Stress
TSADAC_RKOSILENT_UP	Genes basally silent, with hypermethylated promoters, upregulated by the combination of TSA and DAC in RKO cells	Cancer
CHESLER_BRAIN_NEURAL_HIGH_GENES	Genes with high expression of transcripts in brain and other neural tissues (from the GNF Expression Atlas)	Brain development
HADDAD_CD45CD7_PLUS_VS_MINUS_UP	Genes enriched in CD45RAhiCD7hi vs CD45RAintCD7- HPCs	immunoregulatory activities
TSADAC_PANC50_UP	50 most interesting genes upregulated by the combination of TSA and DAC in at least one of four pancreatic cancer cell lines, but not in normal (HPDE) cells	Cancer
UVC_HIGH_ALL_UP	Up-regulated at any timepoint following treatment of WS1 human skin fibroblasts with UVC at a high dose (50 J/m^2) (clusters b1-b4)	DNA repair; Stress
HOUSTIS_ROS	Genes known to modulate ROS or whose expression changes in response to ROS	Stress
ZHAN_MULTIPLE_MYELOMA_SUBCLASSES_DIFF	The 30 most differentially expressed genes in a comparison of MM1 and MM4 subgroups (multiple Myeloma)	Cancer; Bone differentiation
WANG_HOXA9_VS_MEIS1_DN	Genomic signature of progenitors immortalized by Hoxa9 versus Hoxa9 plus Meis1 Increased expression in Hoxa9 plus Meis1-immortalized progenitors	Cancer
MARSHALL_SPLEEN_BAL	Genes downregulated in influenza-specific CD8+ T cells isolated from spleen as compared to those from bronchoalveolar lavage (BAL) during influenza	immunoregulatory activities
HANSON_NFKAPPB_IND	Ras-inducible, NF-kB-regulated genes	Cancer
TSA_CD4_UP	Up-regulated in mouse CD4+ T-cells following 4 hour treatment with 100 nM trichostatin A (a potent, reversible inhibitor of histone deacetylase (HDAC))	Cancer
FERRANDO_T_CELL_DIFFERENTIATION_PATHW	Genes involved with T cell differentiation which are upregulated in samples positive for HOX11, TAL1, or LYL1 by RT-PCR	immunoregulatory activities
IFNALPHA_NL_UP	Upregulated by interferon alpha treatment in normal primary hepatocytes	immunoregulatory activities
HADDAD_HSC_CD7_UP	Genes upregulated in human hematopoietic stem cells of the line CD45RA(hi) CD7+, which are biased toward developing into T lymphocytes or natural	immunoregulatory activities
GAMMA_UNIQUE_FIBRO_DN	Down-regulated at any timepoint by treatment of human fibroblasts with gamma radiation, but not by UV light or 4-NQO	Stress; DNA repair
LIZUKA_G2_GR_G3	Genes highly expressed in moderately differentiated vs. poorly differentiated hepatocellular carcinoma	Cancer
RESISTANCE_XENOGRAPTS_UP	Up-regulation is correlated with resistance of human cancer xenografts to at least six of seven anticancer drugs tested	Cancer
YAGI_AML_PROGNOSIS	French-American-British (FAB) type-specific probe sets of acute myeloid leukemia (AML)	Cancer
PARP_KO_UP	Downregulated in MEF cells from PARP knockout mice; PARP deficiency also up-regulates genes that encode extracellular matrix or cytoskeletal protei	Cancer; Aging
LEE_ACOX1_UP	Genes up-regulated in hepatoma tissue in Acox1 KO mice	Cancer
IFNALPHA_NL_HCC_UP	Upregulated by interferon alpha treatment in both normal primary hepatocytes and Hep3B hepatocellular carcinoma cells	Cancer
DAC_PANC50_UP	50 most interesting genes upregulated by DAC treatment in at least one of four pancreatic cancer cell lines, but not in normal (HPDE) cells	Cancer
BRG1_ALAB_DN	Down-regulated at 18 and 24 hours following adenovirus-mediated expression of BRG1 in ALAB breast cancer cells with mutant, inactive BRG1	Cancer
LEE_MYC_TGFA_UP	Genes up-regulated in hepatoma tissue of Myc+Tgfa transgenic mice	Cancer
HOHENKIRK_MONOCYTE_DEND_DN	Down-regulated mRNAs in monocyte-derived DCs	cell fate decisions; immunoregulatory acti
HUMAN_TISSUE_THYMUS	Genes expressed specifically in human thymus tissue	cell fate decisions
TPA_RESIST_MIDDLE_UP	Upregulated by TPA at two consecutive timepoints between 2-24hrs in resistant HL-525 cells. The tumor promoter 12-O-tetradecanoylphorbol-13-acetat	Cancer
MMS_MOUSE_LYMPH_HIGH_4HRS_UP	Up-regulated at 4 hours following treatment of mouse lymphocytes (TK 3.7.2C) with a high dose of methyl methanesulfonate (MMS) (DNA damage agent)	DNA repair; Stress

Table S4. Down-regulated genes of Klotho treated MO3.3 cells vs. CGP database

Database	Description	Category
HEARTFAILURE_ATRIA_DN	Downregulated in the atria of failing hearts (DCM and ICM) compared to healthy controls	Cardiovascular
IFN_BETA_GLIOMA_UP	Up-regulated in human glioma cells (T98) at 48 hours following treatment with interferon-beta	Cancer
HEARTFAILURE_VENTRICLE_DN	Downregulated in the ventricles of failing hearts (DCM and ICM) compared to healthy controls	Cardiovascular
GUO_HEX_DN	Down-regulated genes in day-6 Hex/ embryoid bodies	Cell fate decisions
JECHLINGER_EMT_UP	Genes upregulated for epithelial plasticity in tumor progression	Cancer
NING_COPD_DN	Downregulated genes in lung tissue of smokers with chronic obstructive pulmonary disease (COPD) vs smokers without disease (GOLD-2 vs GOLD-0)	Stress
ET743_SARCOMA_UP	Up-regulated following treatment with Et-743 at any timepoint in at least 8 of 11 sarcoma cell line	Cancer
EMT_UP	Up-regulated during the TGFbeta-induced epithelial-to-mesenchymal transition (EMT) of Ras-transformed mouse mammary epithelial (EpH4) cells (EMT is representative of late-stage tumor progression)	Cancer
ET743_SARCOMA_72HRS_UP	Up-regulated at 48 hours following treatment with Et-743 in at least 6 of 8 sarcoma cell lines	Cancer
RADAEVA_IFNA_UP	Upregulated by interferon alpha treatment in Hep3B hepatocellular carcinoma cells	Cancer
ZUCCHI_EPITHELIAL_UP	The 50 most upregulated genes in primary invasive breast ductal carcinoma or metastatic breast carcinoma isolated from lymph nodes, as compared to normal mammary epithelium.	Cancer
ELONGINA_KO_DN	Downregulated in MES cells from elongin-A knockout mice	Cell fate decisions
IDX_TSA_DN_CLUSTER1	Down-regulated at 48-96 hours during differentiation of 3T3-L1 fibroblasts into adipocytes with IDX (insulin, dexamethasone and isobutylxanthine), vs. fibroblasts treated with IDX + TSA	Cancer
TSA_HEPATOMA_UP	Up-regulated in more than one of several human hepatoma cell lines by 24-hour treatment with trichostatin A	Cancer
REOVIRUS_HEK293_UP	Up-regulated at any timepoint up to 24 hours following infection of HEK293 cells with reovirus strain T3Abney	Stress; Viral infection
IFNALPHA_HCC_UP	Upregulated by interferon alpha treatment in Hep3B hepatocellular carcinoma cells	Cancer
BENNETT_SLE_UP	Genes Significantly up-regulated in SLE patient Blood Mononuclear Cells	Immunoregulatory activities
ET743_SARCOMA_6HRS_UP	Up-regulated at 6 hours following treatment with Et-743 in at least 8 of 11 sarcoma cell lines	Cancer
RIBAVIRIN_RSV_UP	Up-regulation by infection of human pulmonary epithelial cells (A549) with respiratory syncytial virus (RSV) is enhanced by the anti-viral drug ribavirin	Stress; Viral infection
DNMT1_KO_UP	Upregulated following conditional knock-out of DNMT1 in MEFs	Cell fate decisions
REOVIRUS_HEK293_DN	Down-regulated at any timepoint up to 24 hours following infection of HEK293 cells with reovirus strain T3Abney	Stress; Viral infection
HDACI_COLON_TSA48HRS_UP	Upregulated by TSA at 48 hrs in SW260 colon carcinoma cells	Cancer
AGUIRRE_PANCREAS_CHR9	Genes on chromosome 9 with copy-number-driven expression in pancreatic adenocarcinoma.	Cancer
FALT_BCLL_UP	Genes up-regulated in VH3-21+ B-CLL	Immunoregulatory activities
CMV_ALL_DN	Downregulated at any timepoint following infection of primary human foreskin fibroblasts with CMV	Stress; Viral infection
AGUIRRE_PANCREAS_CHR17	Genes on chromosome 17 with copy-number-driven expression in pancreatic adenocarcinoma.	Cancer
CMV_24HRS_DN	Down-regulated in fibroblasts following infection with human cytomegalovirus	Stress; Viral infection
NF90_DN	Downregulated by ectopic expression of NF90 in GHOST(3)CXCR4 cells	Stress; Viral infection
VHL_RCC_UP	Upregulated in VHL-null renal carcinoma cells vs. VHL-rescued (Fig. 1a+b)	Cancer
HDACI_COLON_CLUSTER10	Regulated by TSA, butyrate and/or curcumin in SW260 colon carcinoma cells	Cancer
TGFBETA_LATE_UP	Upregulated by TGF-beta treatment of skin fibroblasts	Cancer
NOUZOVA_CPG_H4_UP	CpG islands with greatly increased H4 acetylation in ATRA-treated NB4 cells	Cancer
SRC_ONCOGENIC_SIGNATURE	Genes selected in supervised analyses to discriminate cells expressing activated H-Ras oncogene from control cells expressing GFP.	Cancer
HEARTFAILURE_ATRIA_UP	Upregulated in atria of failing hearts (DCM and ICM) compared to healthy controls	Cardiovascular
HDACI_COLON_TSBUT_UP	Upregulated by both butyrate and TSA at any timepoint up to 48 hrs in SW260 colon carcinoma cells	Cancer
ROTH_HTERT_DIFF	Expression of selected genes involved in DNA repair and cell-cycle control in hTERT-transduced T cells	Stress; Cell fate decisions
MANALO_HYPOXIA_DN	Genes downregulated in human pulmonary endothelial cells under hypoxic conditions or after exposure to AdCA5, an adenovirus carrying constitutively active hypoxia-inducible factor 1	Cardiovascular
FSH_OVARY_MCV152_DN	Down-regulated in ovarian epithelial cells (MCV152) 72 hours following FSH treatment, compared to untreated	hormone
HDACI_COLON_TSA_UP	Upregulated by TSA at any timepoint up to 48 hrs in SW260 colon carcinoma cells	Cancer
BRCA2_BRCA1_UP	Genes up-regulated in BRCA2-linked breast tumors, relative to BRCA1-linked tumors	Cancer
LI_FETAL_VS_WT_KIDNEY_DN	These are genes identified by simple statistical criteria as differing in their mRNA expression between WTs and fetal kidneys HIGH	Cell fate decisions
GH_GHRHR_KO_6HRS_DN	Down-regulated at least 2-fold 6 hours following injection of human growth hormone	hormone
HDACI_COLON_BUT30MIN_DN	Downregulated by butyrate at 30 min in SW260 colon carcinoma cells	Cancer
TGFBETA_C5_UP	Upregulated by TGF-beta treatment of skin fibroblasts, cluster 5	Cancer
UVC_TTD-XPCS_COMMON_DN	Down-regulated at any timepoint following treatment of both XPB/CS and XPB/TTD fibroblasts with 3 J/m ² UVC	Stress
JNK_UP	Upregulated by expression of constitutively active JNK in 3T3 cells	Cancer
H2O2_CSBRESCUED_C1_UP	Upregulated by H2O2 in CSB-rescued fibroblasts (Table 1, cluster 1)	Stress
BRENTANI_REPAIR	Cancer related genes involved in DNA repair	Cancer; DNA repair
UVB_NHEK1_DN	Downregulated by UV-B light in normal human epidermal keratinocytes	Stress
BRENTANI_PROTEIN_MODIFICATION	Cancer related genes involved in protein modification	Cancer
P53_BRCA1_UP	Upregulated by expression of p53 in p53-null, brca1-null MEFs; most genes are further upregulated by simultaneous expression of BRCA1	Cancer
AGUIRRE_PANCREAS_CHR19	Genes on chromosome 19 with copy-number-driven expression in pancreatic adenocarcinoma.	Cancer
TGFBETA_ALL_UP	Upregulated by TGF-beta treatment of skin fibroblasts	Cancer
UVB_NHEK2_DN	Downregulated by UV-B light in normal human epidermal keratinocytes	Stress
AGUIRRE_PANCREAS_CHR8	Genes on chromosome 8 with copy-number-driven expression in pancreatic adenocarcinoma.	Cancer
CROMER_HYPOPHARYNGEAL_MET_VS_NON_UP	Genes increased in metastatic hypopharyngeal cancer tumours	Cancer
ET743_RESIST_DN	Down-regulated in two Et-743-resistant cell lines	Cancer
CTNNB1_ONCOGENIC_SIGNATURE	Genes selected in supervised analyses to discriminate cells expressing activated beta-catenin (CTNNB1) oncogene from control cells expressing GFP.	Cancer
CORTEX_ENRICHMENT_LATE_UP	Up-regulated in the cortex of mice that are exposed to an enriched environmental habitat for 2 or 14 days	Brain
MAGRANGEAS_MULTIPLE_MYELOMA_IGL_VS_IGK	Genes downregulated in multiple myeloma plasma cells that secrete the light chain immunoglobulin Igi-lambda versus those that secrete Igi-kappa.	Cancer
BRCA1_OVEXEXP_DN	Downregulated by induction of exogenous BRCA1 in EcR-293 cells	Cancer
CROONQUIST_RAS_STROMA_DN	Genes upregulated in multiple myeloma cells with N-ras-activating mutations.	Cancer
NAB_LUNG_DN	Down-regulated in human non-small cell lung carcinoma cell line H460 following 24-hour treatment with sodium butyrate	Cancer
CMV_8HRS_DN	Downregulated at 8hrs following infection of primary human foreskin fibroblasts with CMV	Stress; Viral infection
CHANG_SERUM_RESPONSE_UP	CSR (Serum Response) signature for activated genes (Stanford)	Immunoregulatory activities
CMV_HCMV_TIMECOURSE_20HRS_UP	Up-regulated in fibroblasts following infection with human cytomegalovirus	Stress; Viral infection
H2O2_CSBDIFF_C2	Deficient induction by H2O2 in CSB-null fibroblasts, compared to CSB-rescued	Stress
GH_EXOGENOUS_ALL_UP	Up-regulated consistently at all time points (1-24 hours) following treatment of mammary carcinoma cells (MCF-7) with exogenous human growth hormone	Cancer
WERNERONLY_FIBRO_DN	Downregulated in fibroblasts from Werner (but not old) individuals, compared to young	Aging
CROONQUIST_IL6_STROMA_UP	Genes upregulated in multiple myeloma cells exposed to the pro-proliferative cytokine IL-6 versus those with N-ras-activating mutations.	Cancer
HDACI_COLON_TSA2HRS_UP	Upregulated by TSA at 2 hrs in SW260 colon carcinoma cells	Cancer
GOLUB_ALL_VS_AML_UP	Genes highly correlated with acute lymphoblastic leukemia (correlation P(g,c) > 0.30)	Cancer
OXSTRESS_RPE_HNETBH_DN	Downregulated by HNE and t-BH in retinal pigment epithelium cells (Tables 3)	Stress
HDACI_COLON_CLUSTER9	Regulated by TSA, butyrate and/or curcumin in SW260 colon carcinoma cells	Cancer
SMITH_HCV_INDUCED_HCC_UP	Genes highly expressed in hepatitis C-related hepatocellular carcinoma	Cancer
YE_INTRAMETASTATIC_HCC_UP	Genes highly expressed in hepatocellular carcinoma with intra-hepatic metastasis.	Cancer
HDACI_COLON_TSA12HRS_UP	Upregulated by TSA at 12 hrs in SW260 colon carcinoma cells	Cancer
NADLER_OBESITY_UP	Genes with increased expression with obesity	Cell fate decisions; Obesity
ET743_HELA_DN	Downregulated by Et-743 in HeLa cells	Cancer
HBX_HCC_DN	Downregulated by expression of Hepatitis B virus HBx protein in SK-Hep-1 hepatocellular carcinoma cells	Cancer
DORSAM_HOXA9_DN	Genes upregulated by HOXA9	Cancer
LIAN_MYELOID_DIFF_RECEPTORS	Transcription modulators presented during myeloid differentiation	Cell fate decisions
HUMAN_TISSUE_LIVER	Genes expressed specifically in human liver tissue	Cell fate decisions
IDX_TSA_UP_CLUSTER2	Strongly up-regulated at 8 hours during differentiation of 3T3-L1 fibroblasts into adipocytes with IDX (insulin, dexamethasone and isobutylxanthine), vs. fibroblasts treated with IDX + TSA	Cell fate decisions
HASLINGER_B_CLL_13Q14	Top 25 Genes Differentially Expressed in the Respective B-Cell Lymphocytic Leukemia	Cancer
MYOD_NIH3T3_UP	Up-regulated at 24 hours in NIH 3T3 murine fibroblasts following transduction with MyoD and incubation in differentiation medium	Cell fate decisions
MYOD_BRG1_UP	Genes up-regulated following transduction of MyoD in NIH 3T3 cells that fail to achieve full induction with expression of a dominant-negative BRG1 allele; induction thought to require full induction	Cell fate decisions
HDACI_COLON_BUT24HRS_DN	Downregulated by butyrate at 24 hrs in SW260 colon carcinoma cells	Cancer
IGF_VS_PDGF_UP	Up-regulated in mouse C2AS12 myoblasts by treatment with IGF1, compared to treatment with PDGF	Cancer
SERUM_FIBROBLAST_CORE_UP	Core group of genes consistently up-regulated following exposure to serum in a variety of human fibroblast cell lines	Cell fate decisions
UVC_XPCS_8HR_DN	Down-regulated at 8 hours following treatment of XPB/CS fibroblasts with 3 J/m ² UVC	Stress
PENG_GLUTAMINE_UP	Genes upregulated in response to glutamine starvation	Stress
ADIP_VS_FIBRO_UP	Upregulated following 7-day differentiation of murine 3T3-L1 fibroblasts into adipocytes	Cell fate decisions
UVC_XPCS_4HR_DN	Down-regulated at 4 hours following treatment of XPB/CS fibroblasts with 3 J/m ² UVC	Stress
WALLACE_JAK2_DIFF	JAK2-dependent genes with a 7-fold change in both experiments 1 and 2	Cell fate decisions
UV-CMV_UNIQUE_HCMV_6HRS_DN	Down-regulated in fibroblasts at 6 hours following infection with UV-inactivated CMV, but not untreated CMV	Stress; Viral infection
VANASSE_BCL2_TARGETS	Differential Gene Expression Analysis of Murine CD19+ B Cells Overexpressing Bcl-2	Cancer
ET743PT650_COLONCA_DN	Downregulated by both Et-743 and Pt-650 in HCT116 cells	Cancer
MOREAUX_TACI_HI_IN_PPC_UP	PPC genes overexpressed in TACI low patients. B-cell activating factor (BAFF) and a proliferation-inducing ligand (APRIL) have been shown to promote multiple myeloma (MM) cell growth	Cancer
GAY_YY1_DN	List of YY1 target genes identified in MEFs expressing ~25% of YY1 Down	Cell fate decisions