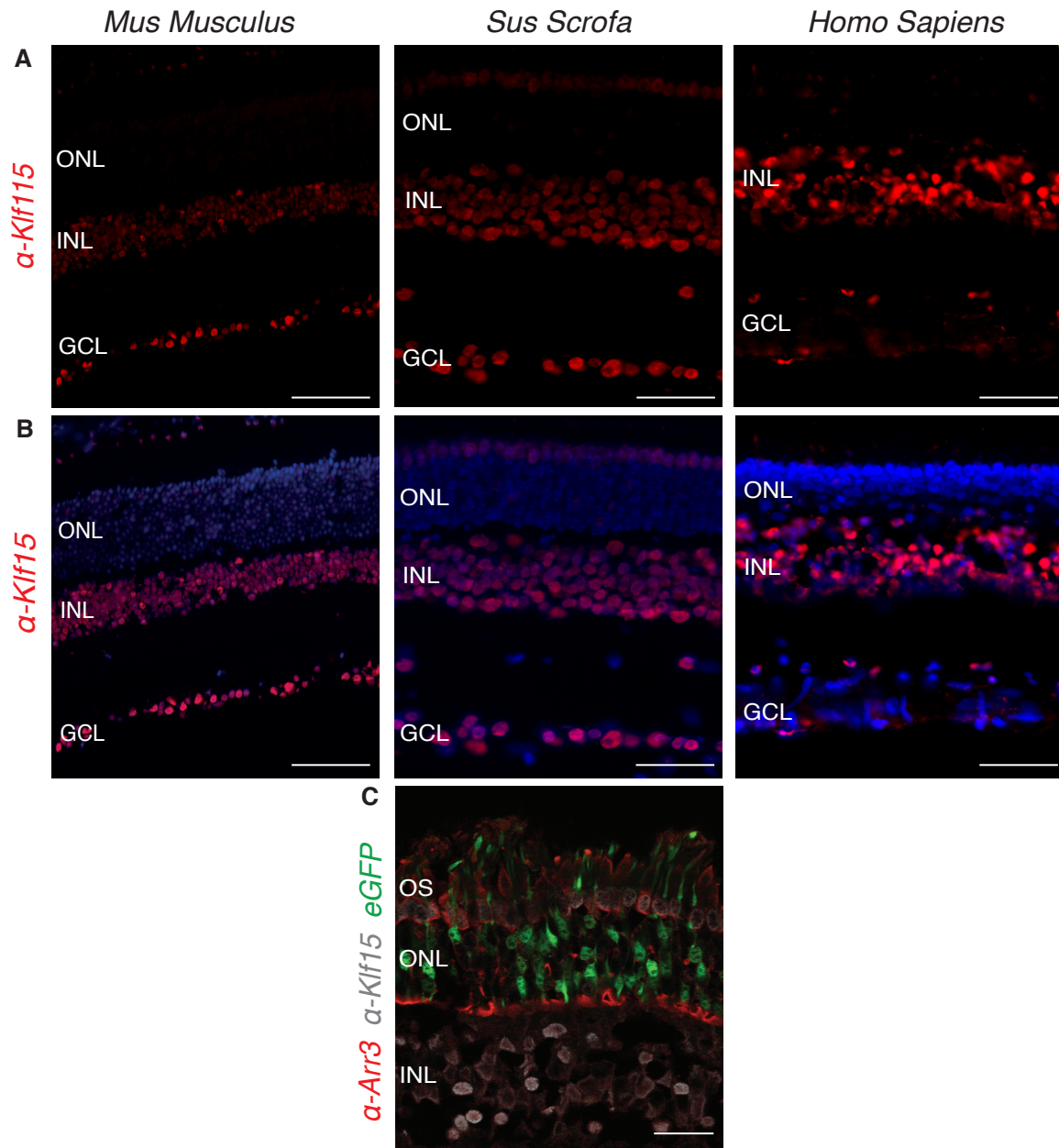
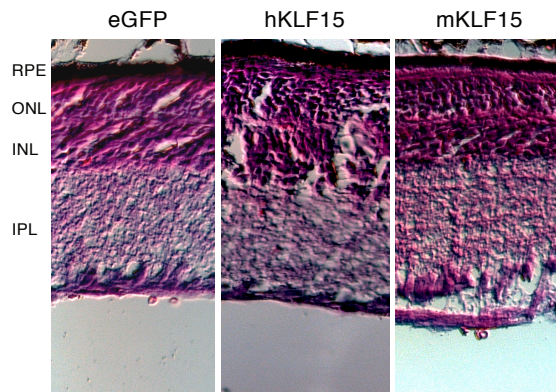


Supplemental Figure 1



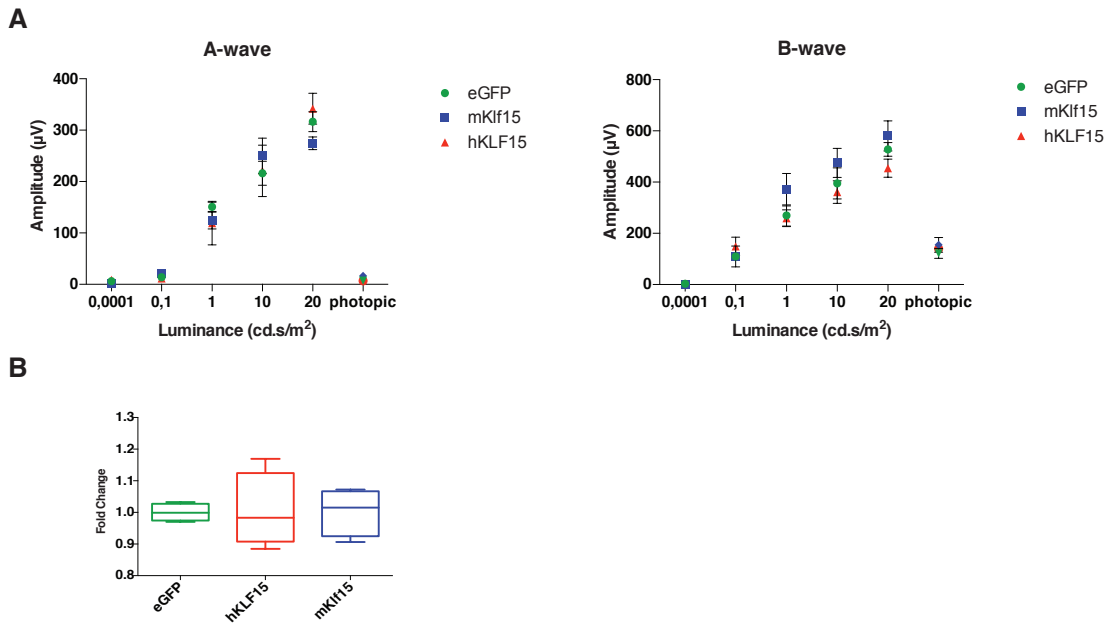
Supplemental Figure 1. Klf15 is not expressed in rods. (A-B) Immunofluorescences of Klf15 in murine, porcine and human retina show the absence of endogenous Klf15 in rods. Scale bar 50 μ m. (C) Co-immunofluorescence confocal analysis of porcine retina injected with AAV8-hGNAT1-eGFP to mark rods (green), shows the presence of Klf15 expression, in grey, in the inner nuclear layer, INL, in ganglion cells layer, GCL and in cones, as revealed by co-expression with arrestin 3, Arr3 in red, whereas eGFP shows no co-localization with Klf15 staining. OS, outer segment; ONL, outer nuclear layer; INL, inner nuclear layer. Scale bar 25 μ m.

Supplemental Figure 2



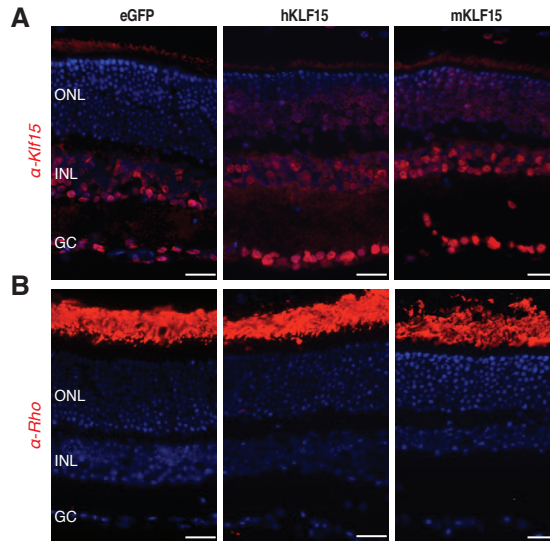
Supplemental Figure 2. hKLF15 and mKlf15 preserve retinal morphology in adRP transgenic RHO-P347S mice. Haematoxylin and eosin (H&E) staining of P347S mouse retinæ shows the preservation of Outer Nuclear Layer (ONL) morphology in the eyes injected with AAV8 driving hKLF15 or mKlf15 compared with eGFP treated eyes. RPE, retinal pigment epithelium; ONL, outer nuclear layer; INL, inner nuclear layer; IPL, inner plexiform layer.

Supplemental Figure 3



Supplemental Figure 3. Human hKLF15 and murine mKlf15 ectopic expression in wild type mouse retina do not exert detrimental effects. (A) Electretinography (ERG) analysis on wild-type C57Bl6/J mice subretinally injected at postnatal day 60 (PD60) with AAV8-CMV-hKLF15 (n=5) AAV8-CMV-mKlf15 (n=5) or AAV8-hGNAT1-eGFP (n=5) and analysed after 80 days. Retinal responses in both scotopic (dim light) and photopic (bright light) show no differences in A-, left panel, and B-waves, right panel, amplitudes, evoked by increasing light intensities. **(B)** qReal Time PCR of murine Rho expression mRNA levels ($2^{-\Delta\Delta C_t}$) show no differences upon injection of AAV8-CMV-hKLF15, AAV8-CMV-mKlf15 or AAV8-CMV-eGFP. Error bars, means \pm s.e.m. * $p < 0.05$, *** $p < 0.001$; two-tailed Student's t test.

Supplemental Figure 4



Supplemental Figure 4. Immunofluorescence analysis of C57Bl6/J wild-type mice subretinally injected with KLF15. (A) Klf15 staining of retina following administration at postnatal day 60 (P60) of AAV8-hGNAT1-eGFP (n=5), AAV8-CMV-hKLF15 (n=5) or AAV8-CMV-mKlf15 (n=5) and analysed after 80 days post injection (P140). Transduced retinæ show expression and maintenance of ONL integrity upon human and murine KLF15 expression (red) in the ONL; (B) rhodopsin localization and expression in the correspondent transduced areas is unaltered upon human and murine Klf15 expression in rods (A). Outer nuclear layer, ONL, inner nuclear layer, INL, and ganglion cells, GC.

Supplemental Table 1. Transcription factor Position Weight Matrix (PWM, Transfac) recognizing the *RHODOPSIN* proximal promoter.

Matrix	Factor name	Position (strand)	Core score	Matrix score	Sequence
V\$ZFP281_05	ZFP281 secondary motif	(+)	1.000	0.983	tgaacaCCCCCaatctc
V\$TIEG1_Q6	TIEG1	(-)	1.000	0.998	gaacaCCCCC
V\$LRF_Q3	LRF	(-)	0.992	0.962	gaacaCCCCCa
V\$KLF15_Q2	KLF15	(-)	0.996	0.956	gaacACCCCcaatc
V\$KLF8_Q5_01	KLF8	(-)	1.000	0.970	gaaCACCCcc
V\$ZIC3_01	Zic3	(-)	1.000	0.961	gaaCACCCc
V\$TBX5_Q2	Tbx5	(-)	1.000	0.967	gaACACCccc
V\$LRF_Q2	LRF	(-)	1.000	0.969	aacaCCCCC
V\$KLF8_Q5	KLF8	(-)	1.000	0.971	aCACCCccea
V\$KLF_Q3	KLF	(-)	0.994	0.955	acaCCCCC
V\$ZXDB_Q1	ZXDB	(-)	1.000	0.955	cACCCc
V\$ZXL_Q2	ZXL	(-)	0.993	0.958	cACCCc
V\$CHCH_Q1	Churchill	(-)	0.983	0.983	cACCCc
V\$CPBP_Q6	CPBP	(+)	0.997	0.994	CACCCc
V\$CPBP_Q6	CPBP	(+)	0.966	0.959	ACCCc
V\$CHCH_Q1	Churchill	(-)	0.986	0.975	aCCCCC
V\$YB1_Q4	YB-1	(+)	1.000	0.978	accCCAATct
V\$CHCH_Q1	Churchill	(-)	0.986	0.986	cCCCCA
V\$CPBP_Q6	CPBP	(+)	1.000	0.996	CCCCAa
V\$MOVOB_Q1	MOVOB	(-)	1.000	0.962	CCCCAa
V\$GEN_INI2_B	GEN_INI	(+)	0.995	0.976	cccCAATC
V\$GEN_INI3_B	GEN_INI	(+)	0.993	0.979	cccCAATC
V\$GEN_INI_B	GEN_INI	(+)	0.995	0.973	cccCAATC
V\$GFI1B_Q6	Gfi1b	(+)	0.995	0.972	cccAATCTcc
V\$GATA6_Q1	GATA-6	(-)	0.975	0.973	ccCAATCtcc
V\$GATA3_Q1	GATA-3	(-)	0.977	0.977	ccCAATCt
V\$GATA2_Q1	GATA-2	(-)	0.979	0.976	ccCAATCtcc
V\$GATA1_Q1	GATA-1	(-)	0.997	0.994	ccCAATCtcc
V\$HOXA7_Q1	HOXA7	(+)	1.000	1.000	cCAATct
V\$IK2_Q1	Ik-2	(-)	1.000	0.953	aatcTCCCAGat
V\$RELA_Q3	RelA-p65	(-)	1.000	0.952	aatctCCCAGa
V\$IK_Q5	Ikars	(-)	1.000	0.965	atCTCCcaga
V\$NGN2_Q3	Ngn-2	(+)	1.000	0.953	atctccCAGATgctga
V\$IK_Q5_01	Ikars	(-)	1.000	0.995	tcTCCCA
V\$CPBP_Q6	CPBP	(+)	0.995	0.995	CTCCcag
V\$CHCH_Q1	Churchill	(-)	0.984	0.984	cTCCCA
V\$E2A_Q6_01	E2A	(-)	0.990	0.962	ctcccAGATGctg
V\$HEN2_Q2	HEN2	(-)	1.000	0.997	tcccAGATG
V\$E2A_Q6	E2A	(-)	0.976	0.962	cccAGATG
V\$GATA6_Q1	GATA-6	(+)	0.955	0.953	ccaGATGctg
V\$GATA2_Q1	GATA-2	(+)	0.982	0.978	ccaGATGctg
V\$GATA1_Q1	GATA-1	(+)	0.993	0.990	ccaGATGctg
V\$TALLIKE_Q6	Tal like	(-)	0.995	0.955	ccAGATGctgat
V\$HTF4_Q2	HTF4	(-)	0.968	0.969	ccAGATG
V\$NRL_Q1	NRL	(+)	1.000	0.970	cagatGCTGat
V\$NMYC_Q2	NMYC	(-)	1.000	1.000	cAGATG
V\$E2A_Q6_02	E2A	(+)	0.990	0.988	CAGATgct
V\$TAL1_Q6_01	Tal-1	(+)	1.000	0.953	CAGATgc
V\$NMYC_Q2	NMYC	(+)	0.954	0.965	CAGATg
V\$MAFA_Q4	MAFA	(-)	1.000	0.998	atGCTGA
V\$MAFK_Q3	MafK	(-)	1.000	0.955	atGCTGAttca

V\$MAFB_Q4_01	MAFB	(-)	1.000	1.000	tGCTGAt
V\$FRA2_Q4_01	Fra-2	(-)	0.983	0.979	tgCTGATTca

Supplemental Table 2. List of differentially expressed genes (DEGs) in porcine retina upon hKLF15 ectopic expression.

Ensembl gene ID	Gene Name	Log₂(FoldChange)	FDR
ENSSSCG00000011796	CRYGS	1,96	3,06E-08
ENSSSCG00000015595	ATF3	1,63	3,06E-08
ENSSSCG00000022111		1,47	3,04E-06
ENSSSCG00000028038		1,75	3,04E-06
ENSSSCG00000000492	LYZ	1,67	6,80E-06
ENSSSCG00000006472	CRABP2	1,59	6,80E-06
ENSSSCG00000006979	MSR1	1,6	1,86E-05
ENSSSCG00000013612	ACP5	1,6	3,59E-05
ENSSSCG00000027130	TNFRSF12A	1,45	3,59E-05
ENSSSCG00000000660	A2M	1,36	6,48E-05
ENSSSCG00000005638	LCN2	1,51	9,51E-05
ENSSSCG00000007208	TRIB3	1,45	0,000172977
ENSSSCG00000005267	ANXA1	1,21	0,000206727
ENSSSCG00000004195	ARG1	1,07	0,000526059
ENSSSCG00000012880	CPT1A	-0,9	0,000674971
ENSSSCG00000030344	CLDN19	-1,38	0,000692567
ENSSSCG00000011590	RHO	-0,84	0,001711068
ENSSSCG00000025390		1,1	0,001718333
ENSSSCG00000010210	SLC16A9	1,27	0,0017615
ENSSSCG00000010613	ITPRIP	1,14	0,0017615
ENSSSCG00000003524	C1QA	1,11	0,002267724
ENSSSCG00000025698	SERPINE1	1,32	0,002267724
ENSSSCG00000010647	ADRB1	1,2	0,00284353
ENSSSCG00000024059	VAT1	0,59	0,003155809
ENSSSCG00000009644	ADAM28	1,17	0,00324015
ENSSSCG00000013586	LRRC8E	-0,96	0,005732384
ENSSSCG00000017956	CD68	1,17	0,005732384
ENSSSCG00000009216	SPP1	1,06	0,00620305
ENSSSCG00000024246		-0,86	0,006214199
ENSSSCG00000026526	CATSPER4	-1,2	0,006817098
ENSSSCG00000022309	GPR34	1,06	0,008883936
ENSSSCG00000029371	C5AR1	0,96	0,009231119
ENSSSCG00000023033	PARP3	0,66	0,012830289
ENSSSCG00000000734		1,16	0,012985203
ENSSSCG00000010224	EGR2	1,16	0,012985203
ENSSSCG00000017920	CXCL16	1,11	0,013156332
ENSSSCG00000003369	ICMT	-0,66	0,015022376
ENSSSCG00000008786		1,14	0,015022376
ENSSSCG00000010705	GMFG	1,15	0,015022376

ENSSSCG00000011322	CCR1	1,11	0,015022376
ENSSSCG00000027550	PLCD1	0,72	0,015881265
ENSSSCG00000016286	PRSS56	1,12	0,016454742
ENSSSCG00000003135	KCNJ14	-0,7	0,017845183
ENSSSCG00000017343	GFAP	1	0,017845183
ENSSSCG00000000368	MMP19	1,02	0,018011387
ENSSSCG00000012881	CPT1A	-0,89	0,018011387
ENSSSCG00000024609	GNAT1	-0,6	0,018011387
ENSSSCG00000012364	VSIG4	1,11	0,018520249
ENSSSCG00000003170	SLC17A7	-0,61	0,018637969
ENSSSCG00000010277	SLC29A3	0,76	0,020219438
ENSSSCG00000024495	SELPLG	0,96	0,020219438
ENSSSCG00000006620	TUFT1	0,59	0,022946535
ENSSSCG00000009437	KBTBD7	-0,44	0,024024029
ENSSSCG00000006243	PENK	-1	0,027072384
ENSSSCG00000006634	TNFAIP8L2	1,08	0,029542591
ENSSSCG00000010732	FAM53B	-0,65	0,030276515
ENSSSCG00000007115	THBD	0,95	0,031539432
ENSSSCG00000010684	RGS10	0,96	0,031539432
ENSSSCG00000000136	CSF2RB	1,08	0,032019368
ENSSSCG00000001025	DSP	-1,05	0,032019368
ENSSSCG00000002720	CLEC18A	0,78	0,032019368
ENSSSCG00000008239	CAPG	0,9	0,032019368
ENSSSCG000000025899		-0,83	0,032019368
ENSSSCG00000011397	SLC38A3	-0,63	0,032019964
ENSSSCG00000030638	CH242-168I5.2	1,03	0,032019964
ENSSSCG00000006610	S100A11	1,04	0,033960107
ENSSSCG00000000648	CLEC7A	1,06	0,037120112
ENSSSCG00000003124	CRX	-0,48	0,037120112
ENSSSCG00000005465	SUSD1	0,9	0,037120112
ENSSSCG00000013909	CRLF1	-1,01	0,040720279
ENSSSCG00000003601	HCRTR1	-0,84	0,040858391
ENSSSCG00000011713	P2Y12R	0,9	0,040858391
ENSSSCG00000011808	SST	-1,05	0,040858391
ENSSSCG00000012018	CHODL	0,88	0,040858391
ENSSSCG00000005229	VLDLR	-0,49	0,042531039
ENSSSCG00000000195	PRPH	0,99	0,043790204
ENSSSCG00000004024		0,91	0,043790204
ENSSSCG00000004578	ANXA2	0,79	0,043790204
ENSSSCG00000005339		0,89	0,043790204
ENSSSCG00000004789	THBS1	0,98	0,04498596
ENSSSCG00000023374	SRGN	0,99	0,04498596
ENSSSCG00000014920	FZD4	-0,62	0,045862814

ENSSSCG00000002297	RDH12	-0,56	0,047239854
ENSSSCG00000015405	CD36	1,03	0,047239854
ENSSSCG00000006183	SBSPON	0,72	0,04831452
ENSSSCG00000028363	TMPRSS9	1,02	0,05122971
ENSSSCG00000014921	PRSS23	0,79	0,051623438
ENSSSCG00000002883	DMKN	0,89	0,052970778
ENSSSCG00000015336	SLC25A13	-0,37	0,052970778
ENSSSCG00000030485	ELFN1	-0,7	0,053472411
ENSSSCG00000003465	FBLIM1	0,47	0,055856973
ENSSSCG00000003526	C1QB	0,88	0,055856973
ENSSSCG00000009002	TLR2	0,96	0,055856973
ENSSSCG00000011470	ABHD6	-0,43	0,055856973
ENSSSCG00000026302	MKI67	1,01	0,055856973
ENSSSCG00000026592	TLR6	0,94	0,055856973
ENSSSCG00000028579		0,91	0,055856973
ENSSSCG00000012941	SLC29A2	-0,86	0,058398102
ENSSSCG00000026710	CARHSP1	0,62	0,058398102
ENSSSCG00000015353	SCIN	0,97	0,058409179
ENSSSCG00000002533	WDR20	-0,42	0,059119358
ENSSSCG00000015320	CALCR	0,89	0,060084418
ENSSSCG00000021084	S100A6	1	0,060084418
ENSSSCG00000024816	CEBPB	0,96	0,060084418
ENSSSCG00000005591	GPR144	-0,99	0,060095154
ENSSSCG00000001930	PKM	-0,45	0,062094944
ENSSSCG00000006862	VCAM1	0,83	0,062094944
ENSSSCG00000010581	PSD	-0,53	0,062094944
ENSSSCG00000023557	CCRL2	0,88	0,062094944
ENSSSCG00000008937	AMBN	0,98	0,065516749
ENSSSCG00000003275		0,94	0,066152027
ENSSSCG00000007625	ARPC1B	0,87	0,066152027
ENSSSCG00000004291	NT5E	-0,62	0,066476444
ENSSSCG00000006379	CD48	0,98	0,068197428
ENSSSCG00000026184	MPP4	-0,48	0,068290441
ENSSSCG00000017439	KRT32	0,94	0,070614513
ENSSSCG00000021557		0,88	0,070614513
ENSSSCG00000027046	USP9Y	0,89	0,070614513
ENSSSCG00000022236	FOLR1	0,85	0,071210433
ENSSSCG00000005503	TLR4	0,95	0,077548044
ENSSSCG00000008123	ARID5A	0,84	0,077548044
ENSSSCG00000024725	C2orf71	-0,65	0,077548044
ENSSSCG00000025741	SNX20	0,97	0,077548044
ENSSSCG00000000223		0,88	0,08061489
ENSSSCG00000000958	DYRK2	-0,62	0,08061489

ENSSSCG00000001469	SLA-DMB	0,77	0,08061489
ENSSSCG000000015258	GLB1L2	-0,75	0,08061489
ENSSSCG000000026084	MFSD7	0,71	0,08061489
ENSSSCG000000028103		-0,66	0,08061489
ENSSSCG000000028711	CASP1	0,84	0,08061489
ENSSSCG000000010603	NEURL1	-0,55	0,081874872
ENSSSCG000000030921	APOA1	0,79	0,081874872
ENSSSCG00000004554		0,89	0,083812341
ENSSSCG00000005587	NEK6	0,85	0,084781746
ENSSSCG00000003651	RHBDL2	0,8	0,08506656
ENSSSCG000000029852	WNT5A	-0,81	0,08506656
ENSSSCG000000017473	TOP2A	0,91	0,088275952
ENSSSCG000000016851	OSMR	0,71	0,089873226
ENSSSCG00000009445	PCDH8	-0,64	0,092169462
ENSSSCG00000008624		-0,55	0,092945279
ENSSSCG00000008664	FAM84A	0,82	0,092945279
ENSSSCG000000017087	GM2A	0,74	0,092945279
ENSSSCG00000003525	C1QC	0,86	0,093207956
ENSSSCG000000015706	LYPD1	0,44	0,093207956
ENSSSCG000000022056	GPR37L1	0,62	0,093207956
ENSSSCG000000026583	TLR1	0,85	0,093207956
ENSSSCG000000027196	GIMAP6	0,86	0,093207956
ENSSSCG000000010347	LRIT2	-0,7	0,093618926
ENSSSCG00000007240		0,94	0,094933926
ENSSSCG000000015395		-0,52	0,096757612
ENSSSCG00000007831	CACNG3	-0,51	0,097636479
ENSSSCG000000011398	SEMA3F	-0,61	0,097636479
ENSSSCG000000015113	ABCG4	-0,52	0,097636479
ENSSSCG000000010683	GRK5	-0,5	0,098219952
ENSSSCG00000001887	SCAMP5	-0,43	0,099643731
ENSSSCG000000015907	GALNT3	0,73	0,099928158