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Fig. 1. Principal Component Analysis. The PCA of raw expression data. The colored dots represent groups of examined samples' deficiencies.



Fig. 2. Principal Component Analysis. The PCA of gene expression data in comparison between healthy and RBCK1 disease samples. Only down-regulated genes were presented in this data. Colors show groups of examined samples' deficiencies.



Fig. 3. Heatmap of expression data after normalization. Each column represents the expression levels of all genes from one of the examined samples (healthy, RBCK1, CINCA, MWS, MVK). Each row represents the expression levels of a gene across all samples.



RBCK1 deficiency versus healthy samples

total = 48803 variables

Fig. 4. Volcano Plot. Volcano plots showing differential expression between healthy and diseased samples. X axis represents Fold Change value, while Y axis represents P value. Red dots represent differentially expressed genes.



Fig. 5. Volcano Plot. Volcano plots showing differential expression between all diseased samples. X-axis represents Fold Change value, while Y-axis represents P value. Red dots represent differentially expressed genes.

	Gene name	P-value	logFC	
1	HBBP1	1.141737e-06	0.4786540	
2	C20orf127	6.579816e-06	0.4264092	
3	MAOA	2.440151e-06	0.6300522	
4	RFFL	3.421255e-06	0.5362195	
5	EPB41	2.627018e-07	0.4556318	
6	FAM83A	2.497823e-08	0.6278024	
7	NSUN3	5.924530e-08	0.4098833	
8	PPM1A	4.976705e-06	0.5563138	
9	HES6	6.051238e-05	0.4230913	
10	STOM	5.554047e-05	0.4090811	

Table 1. Top 10 most differentially expressed downregulated genes from comparison between healthy and RBCK1 samples

Table 2	. Top 10 m	ost differential	ly expressed	upregulated	genes in	comparison	between
RBCK1	deficiency	and MWS					

	Gene name	P-value	logFC	
1	RHD	4.681915e-05	0.5447136	
2	CA1	2.060478e-08	0.6516630	
3 UBL7		4.361623e-06	0.4322227	
4	HBBP1	1.284623e-08	0.4898661	
5	LOC647958	3.833628e-04	0.4407032	
6 PRR5		2.400870e-05	0.5007257	
7	LOC649604	3.972521e-07	0.4215989	
8	C20orf127	6.046749e-09	0.4938760	
9	RNF123	1.022530e-06	0.4021701	
10 MAOA		1.650408e-08	0.6626294	

Table 3. Dif	fferentially	expressed	genes,	involved	into	several	significant	pathways,	obtained
from KEGG									

	Signaling pathway	Leishmaniasis	Hematopoietic cell lineage	Dilated cardio- myopathy	Pantothenate and CoA biosynthesis	Vibrio cholerae infection	Primary immune- deficiency
1	TIAM1	FCGR2A	MME	TPM3	VNN1	TCIRG1	CD79A
2	FOXO3	PTGS2	HLA-DRB5	ACTG1	UPB1	ACTG1	CD8B
3	STAT1	HLA-DRB5	CD8B	ITGB1	VNN2	PRKACB	CD8A
4	GNB4	FCGR3B	IL1R2	ITGA4	ZNF586		
5	GRB2	NCF4	CSF3R	PRKACB	VNN3		
6	CXCL5	TLR2	CD8A				
7	PIK3CG	IL1B	IL1B				
8	ROCK1	NCF2					
9	PIK3R1						
10	VAV3						

Table 4. Groups of genes involved in several significant pathways obtained from KEGG

	Natural killer cell mediated cytotoxicity	Antigen processing and presentation	Staphylococcus aureus infection	RIG-I-like receptor signalling pathway
1	KIR2DL3	KIR2DL3	FCGR2A	CXCL8
2	KIR2DL1	KIR2DL1	KRT23	MAPK13
3	KIR2DS5	KIR2DS5	FCGR1A	CXCL10
4	KIR3DL1	KIR2DL4	FCAR	ISG15
5	KLRC1	KIR3DL1	FPR2	
6	SH2D1B	KLRC1		
7	PRF1	KLRD1		
8	FASLG	KLRC2		
9	KLRD1	KIR3DL3		
10	KLRC2	KIR2DS3		
11	KIR3DL3	KIR3DL2		
12	GZMB	IFNG		
13	KIR2DS3			
14	KIR3DL2			



Fig. 6. Over representation analysis (ORA). Barplots showing groups of pathways found in the three clusters of highly expressed genes. X-axis represents the ratio of the group of genes from the input cluster found in the pathway to the total number of genes presented in it.



Fig. 7. Over representation analysis (ORA). Barplots showing groups of pathways found in the three clusters of highly expressed genes. X-axis represents the ratio of the group of genes from the input cluster found in the pathway to the total number of genes presented in it.



Fig. 8. Over representation analysis (ORA). Barplots showing groups of pathways found in the two clusters of highly expressed genes. X-axis represents the ratio of the group of genes from the input cluster found in the pathway to the total number of genes presented in it.



Fig. 9. Gene Ontology (GO). Barplots showing groups of GO pathways found in the co-expression genes clusters (1, 2). X-axis represents the number of genes presented in a pathway. The presented category is a Biological Process (BP).



Fig. 10. Gene Ontology (GO). Barplots showing groups of GO pathways found in the co-expression genes clusters (3, 4) (Biological Process category).







Fig. 12. Gene Ontology (GO). Barplots showing groups of GO pathways found in the co-expression genes clusters (1, 2) (Cellular Component category).





Fig. 13. Gene Ontology (GO). Barplots showing groups of GO pathways found in the co-expression genes clusters (3, 4) (Cellular Component category).



Fig. 14. Gene Ontology (GO). Barplots showing groups of GO pathways found in the co-expression genes clusters (5, 6) (Cellular Component category).



Fig. 15. Gene Ontology (GO). Barplots showing groups of GO pathways found in the co-expression genes clusters (7, 8) (Cellular Component category).



Fig. 16. Gene Ontology (GO). Barplots showing groups of GO pathways found in the co-expression genes clusters (9, 10) (Cellular Component category).



Fig. 17. Gene Ontology (GO). Barplots showing groups of GO pathways found in the co-expression genes clusters (1, 2) (Molecular Function category).



Fig. 18. Gene Ontology (GO). Barplots showing groups of GO pathways found in the co-expression genes clusters (3, 4) (Molecular Function category).



Fig. 19. Gene Ontology (GO). Barplots showing groups of GO pathways found in the co-expression genes clusters (5, 6) (Molecular Function category).

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Fig. 20. KEGG graph. Barplots showing groups of pathways found in the two clusters of highly expressed genes. X-axis represents the ratio of the group of genes from the input cluster found in the pathway to the total number of genes presented in it.

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	ID	Pathway name	Genes
1	WP5115	Network map of SARS-CoV-2 signaling pathway	FAM83A HP IFI27
2	WP5039	SARS-CoV-2 innate immunity evasion and cell-specific immune response	NUP98
3	WP5098	T-cell activation SARS-CoV-2	TSC1



Fig. 21. STRING graph. Protein-protein interactions graph from STRING. Contains genes from one of the co-expression modules, created with CemiTool.

Gene ID	P-value	Log FC
KIR2DL4	0.00209788651071389	-0.205005232102024
KIR3DL3	0.00814053762563458	-0.216763412869406
KLRD1	0.000135183376061967	-0.249270886125981
KLRC1	0.000207571425358897	-0.259263386490044
KIR2DL1	0.0354069148029456	-0.168799854782198
KIR2DL3	0.000139918664310681	-0.260887263850761
KIR3DL2	0.365968629026214	-0.0719313216278259

 Table 6. DEGs from STRING graph

Gene ID	P-value	Log FC	
Do	wn-regulated genes (Healthy	vs CINCA)	
IFIT3	1.74609331700504e-05	-0.448294716210724	
LOC441763	1.47233982896637e-05	-0.609014232620713	
SOD2	2.78149438373382e-07	-0.58012265425286	
IKZF3	1.31806278781658e-05	-0.423217419210266	
Down-r	egulated genes (Healthy vs RE	BCK1 deficiency)	
RHD	3.06377501094136e-07	-0.611200490393251	
CA1	7.79560593336739e-10	-0.576206913434433	
GLUL	8.6252507011449e-08	-0.433818845743858	
HBBP1	2.21004809448002e-10	-0.493952695553687	
LOC730996	5.4158206826892e-07	-0.429182308276256	
PRR5	6.15756364362851e-06	-0.466970969137613	
C200RF127	4.29196932508036e-11	-0.503823086693028	
MAOA	3.45635687661528e-11	-0.71149687967469	
EPB41	1.05073344811606e-06	-0.524086955692296	
RFFL	1.7787876243623e-07	-0.463262474363137	
SRRD	3.69305686343315e-08	-0.435308561743468	
EPB41	4.10834311666971e-16	-0.625604788043923	
BZRPL1	2.57994400142045e-06	-0.471173744671184	
FAM83A	5.44854038181488e-12	-0.599507727918373	
C180RF10	1.09048508902326e-07	-0.428416420839521	
ISCA1L	1.52691122702879e-10	-0.501956290642989	
UBE2H	5.90301268371945e-08	-0.474685055389697	
LOC389293	9.7265992847629e-07	-0.444237498423597	
MARCH8	1.56620224759829e-05	-0.415145328541088	
ABCC13	2.51980754979099e-11	-0.606438102500972	
YOD1	2.61445184502943e-07	-0.429200889815241	
MAP2K3	3.2094776830514e-07	-0.535762246169115	
ICAM4	8.13314317075278e-06	-0.440589759357464	
GYPB	5.35537151818344e-06	-0.535621231895341	
GPR146	1.01136419337272e-08	-0.567645214457263	
USP12	2.99253437362475e-09	-0.605356436449592	
PPM1A	2.03539778781035e-09	-0.528857796785936	
LOC643008	1.73442878109425e-05	-0.485040439363551	
NFIX	5.22268953523978e-06	-0.4724728396363	
HMBS	1.4693732690123e-05	-0.424183404232344	
STOM	1.24284526630849e-10	-0.531310670851352	
TSTA3	1.34938350092169e-10	-0.477282328432734	
KLC3	2.05774537169341e-05	-0.405164523068791	
LOC441763	0.000181082483566001	-0.667692304622325	
ARL4A	7.26925152801753e-08	-0.489367144774149	
KLF1	0.000135750708139281	-0.404669273020196	
ALAS2	2.35459034179256e-06	-0.502284988409139	
ABCC13	1.90891282700382e-11	-0.547661149453971	
CMBL	0.000251673924439325	-0.531786088886633	
ENDOGL1	1.42332012702017e-09	-0.431639051878824	
TTC25	9.73324861047136e-07	-0.443481768944991	
SLC6A9	1.26902867532115e-07	-0.491538129593716	
MT1G	1.361860014615e-09	-0.537206194645534	
KANK2	1.97993569285184e-05	-0.468624785292866	
C5ORF4	2.35196973740107e-09	-0.561928828951184	
FBXO9	4.97135009981045e-06	-0.419062143443751	
APOBEC2	4.17733010579391e-09	-0.511778758016943	
CTNNAL1	2.0166448384343e-10	-0.596649699430933	
SFRP2	2.91591303469987e-07	-0.5367816022116	
DARC	2.23228930373954e-06	-0.506758228600563	

CDKL1	5.18558137141098e-11	-0.456240499526942
NR2C2	2.74471210362574e-07	-0.467063780892068
UBE2V1	4.22395050446097e-09	-0.414052200088762
NUP98	5.96598638237005e-13	-0.436454846129473
KRT1	0.000149381819429962	-0.472058867502659
PIP5K1B	1.61607968161147e-06	-0.40278495445915
TMOD1	8.08685868503521e-07	-0.457177922927007
ACSL6	1 6920257303265e-09	-0.482186233547585
BCL2L1	4 07848891215034e-06	-0.56278357895157
ARI 4A	2 44775976433304e-07	-0.498357318723835
TRIM10	0.000136589544130928	-0.406188853239464
DDB1	2 1990/3119130896-06	-0.411424516867145
HK1	1.0612/2799/9703e-05	-0.4/169750081173
TSC1	1.778/771/750638- 05	0.468256438090652
NEK7	0.000170340220630802	0.433066810325831
	2.005023100725542.06	0.480141040758087
AK NDID2	2.003923199723346-00	0.421844525724224
I OC441010	0.06644866645005 a 11	-0.421844555724224
LUC441019 MDNI 2	2.00044800043903e-11	-0.301163032184118
	2.93/0////0193936-00	-0.3001298340/2088
ULUL TCD11L2	2.74870382034478e-09	-0.340312230012823
TCPTIL2	1.20/09391/9518/e-06	-0.4/1494396335578
FECH	5.41086882496622e-06	-0.51141422/9/8014
TBCEL	3.94419209473046e-06	-0.478551678063247
RAPIGAP	1.33890086146641e-11	-0.988635102618676
OSBP2	7.3910625318555e-08	-0.600874698724962
TMEM56	6.12390440720877e-05	-0.483039958948652
RHOT1	1.10308558627238e-05	-0.446354148644388
GSTA5	0.000209202795444071	-0.506344731509343
BPGM	3.35779076418107e-07	-0.539997871952786
TMEM158	2.72463341738246e-06	-0.407924550530202
CISD2	7.53793555390848e-18	-0.596995403396861
MAP2K3	6.33459801757628e-07	-0.607553874348244
SIAH2	1.38346158335195e-07	-0.410553400629246
LOC253012	1.4820449345248e-14	-0.714106701309741
DPM2	1.31973076649606e-06	-0.444373234792454
SLC14A1	3.61407330577942e-06	-0.472533746138953
C14ORF45	1.06861423592279e-05	-0.406521505707906
TSPAN7	9.74035130571459e-06	-0.582083373265941
RHAG	8.55144551318859e-07	-0.438406584483529
OR2W3	3.35702401663645e-05	-0.478425163113573
GYPE	0.000108299870959704	-0.419783780145331
MAP2K3	2.62556504967366e-08	-0.533593365911246
HS.568705	1.19878618554507e-06	-0.401117514638576
HS.563750	1.53991608195374e-11	-0.562247486891869
BNIP3L	8.67977553186154e-07	-0.437108330372131
IFI27	3.07621715357289e-05	-0.522310561539633
FAM10A7	3.06701055612153e-10	-0.431638059297229
TSPAN7	1.79002824480927e-08	-0.597581551791717
CTNNAL1	1.20238873602371e-09	-0.591752492581158
ITLN1	3.35065885877735e-06	-0.470439194740778
C18ORF10	1.43867425110084e-06	-0.444342452561307
TCP11L2	2.2293531169601e-05	-0.444685661263156
FAM83A	1.70381102055525e-13	-0.733775779774681
HPS1	5 38685063353283e-07	-0 441403240291118
ALAS?	6 87503728242588e-09	-0 668295016947645
MGC13057	1 55986789814511e-07	-0 456397469333022
LOC253012	7 08472253869593e_06	-0.4814632803348
FPR41	9.43861898867066= 1/	-0 68160625/77078/
	2.7483001020585202 00	0.40065020402267
TDIM22	4 82250402492450c 07	0.445110561057617
	4.033304724834376-07	-0.44311030103/01/
CHD2	0.2/99392/01495e-12	-0.430443690611727

MARCH8	2.56157544228178e-06	-0.474205738912535
BPGM	1.45034368022173e-10	-0.542350150009864
BPGM	6.20859756105282e-05	-0.423679510669356
FECH	1.15231264764613e-06	-0.561792657767508
LOC253012	5.73998378461065e-16	-0.681069526086712
SOX6	4.1110047227485e-05	-0.444872082134934
RHCE	2.39065579240491e-10	-0.576783549807026
PPM1A	6.58118313415536e-08	-0.486525770111466
l	Down-regulated genes (Healthy	v vs MVK)
OR7D2	7.04254590259349e-07	-0.445190246204898
CTAG2	1.37293178849356e-08	-0.425508982145102
	Down-regulated genes (Healthy	v vs MWS)
MAPK8IP1	3.23183843676115e-08	-0.426087995959029
GPR128	3.21031089903406e-09	-0.404337799088839
HP	4.72312538568793e-08	-0.410948832911504
	Un-regulated gene (Healthy ve	
HS 332360	1 35896745487404e-06	1 61321965741775
II5.552500	aulated games (Healthy vs DB(W1 deficiency)
DI AOD 1	guiateu genes (neanny vs KDC	0 802420400426565
PLA2KI EL 100212	0.000199207127737016	0.892439400430505
FLJ00512	5.04011541/0/01e-0/	0.01(7070(422(20)
HIST IH2BI	0.0002/8443535449/58	0.916/2/064236308
ANKMY2	6.51/12549381586-06	0.418964835449505
HS.551123	6.458/9094685694e-13	3.168/0105950953
HS.19339	6.03473284790242e-07	0.464301646441145
HS.542923	0.000384929864622159	1.15592770980196
HS.531457	7.58513792049983e-05	0.419426602559435
HS.552143	1.58377723350902e-07	1.29376182615501
RPS29	1.97801903881016e-05	0.412319477580699
	Up-regulated genes (Healthy v	vs MWS)
SNORD101	2.98981619650048e-06	1.59871466324165
GPM6B	2.67626160499603e-06	1.50880585329478
	Up-regulated genes (Healthy	vs MVK)
HBBP1	1.14173704941383e-06	0.478653983440068
C200RF127	6.5798157203638e-06	0.426409184547074
MAOA	2.44015082103226e-06	0.630052228582019
RFFL	3.4212549477718e-06	0.536219474675563
EPB41	2.62701820835691e-07	0.455631839848625
FAM83A	2.49782329060035e-08	0.627802381539782
NSUN3	5.92453035266978e-08	0.409883315641316
PPM1A	4.9767051917542e-06	0.556313765226818
HES6	6.05123772618859e-05	0.423091284342303
STOM	5.5540472638423e-05	0.409081086031493
TSTA3	3.08936535341488e-06	0.446142229778541
SNORD101	4.65225998118568e-06	1.73120617955731
ABCC13	4.26519783082112e-05	0.401252510049555
CDKL1	2.74858844333723e-07	0.466255440087856
NUP98		
1.77.4.1	4.30772014356358e-08	0.414001599570805
ARL4A	4.30772014356358e-08 2.77034252417117e-05	0.414001599570805 0.571251272351404
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ARL4A NRIP3 LOC441019 RAP1GAP TMEM158	4.30772014356358e-08 2.77034252417117e-05 6.49414101845174e-06 1.03497404016182e-05 1.04200655288737e-06 1.78835519450909e-05	0.414001599570805 0.571251272351404 0.459589541823844 0.490979582676609 1.37706133345479 0.559385168815898
ARL4A NRIP3 LOC441019 RAP1GAP TMEM158 CISD2	4.30772014356358e-08 2.77034252417117e-05 6.49414101845174e-06 1.03497404016182e-05 1.04200655288737e-06 1.78835519450909e-05 1.23869398791649e-08	0.414001599570805 0.571251272351404 0.459589541823844 0.490979582676609 1.37706133345479 0.559385168815898 0.451745023155612
ARL4A NRIP3 LOC441019 RAP1GAP TMEM158 CISD2 LOC253012	4.30772014356358e-08 2.77034252417117e-05 6.49414101845174e-06 1.03497404016182e-05 1.04200655288737e-06 1.78835519450909e-05 1.23869398791649e-08 4.14821610170912e-06	0.414001599570805 0.571251272351404 0.459589541823844 0.490979582676609 1.37706133345479 0.559385168815898 0.451745023155612 0.509662208073758
ARL4A NRIP3 LOC441019 RAP1GAP TMEM158 CISD2 LOC253012 HS.563750	4.30772014356358e-08 2.77034252417117e-05 6.49414101845174e-06 1.03497404016182e-05 1.04200655288737e-06 1.78835519450909e-05 1.23869398791649e-08 4.14821610170912e-06 9.33931440883221e-09	0.414001599570805 0.571251272351404 0.459589541823844 0.490979582676609 1.37706133345479 0.559385168815898 0.451745023155612 0.509662208073758 0.694052147312873
ARL4A NRIP3 LOC441019 RAP1GAP TMEM158 CISD2 LOC253012 HS.563750 DLEU1	4.30772014356358e-08 2.77034252417117e-05 6.49414101845174e-06 1.03497404016182e-05 1.04200655288737e-06 1.78835519450909e-05 1.23869398791649e-08 4.14821610170912e-06 9.33931440883221e-09 1.02150679853994e-05	0.414001599570805 0.571251272351404 0.459589541823844 0.490979582676609 1.37706133345479 0.559385168815898 0.451745023155612 0.509662208073758 0.694052147312873 0.407460618680324
ARL4A NRIP3 LOC441019 RAP1GAP TMEM158 CISD2 LOC253012 HS.563750 DLEU1 TSPAN7	4.30772014356358e-08 2.77034252417117e-05 6.49414101845174e-06 1.03497404016182e-05 1.04200655288737e-06 1.78835519450909e-05 1.23869398791649e-08 4.14821610170912e-06 9.33931440883221e-09 1.02150679853994e-05 4.46178512125141e-05	0.414001599570805 0.571251272351404 0.459589541823844 0.490979582676609 1.37706133345479 0.559385168815898 0.451745023155612 0.509662208073758 0.694052147312873 0.407460618680324 0.583825631997659
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ARL4A NRIP3 LOC441019 RAP1GAP TMEM158 CISD2 LOC253012 HS.563750 DLEU1 TSPAN7 FAM83A MGC13057	4.30772014356358e-08 2.77034252417117e-05 6.49414101845174e-06 1.03497404016182e-05 1.04200655288737e-06 1.78835519450909e-05 1.23869398791649e-08 4.14821610170912e-06 9.33931440883221e-09 1.02150679853994e-05 4.46178512125141e-05 5.82403503434797e-08 1.0208393292274e-06	0.414001599570805 0.571251272351404 0.459589541823844 0.490979582676609 1.37706133345479 0.559385168815898 0.451745023155612 0.509662208073758 0.694052147312873 0.407460618680324 0.583825631997659 0.716128748862842 0.562824585588067

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MAQA	1.65040803323732e-08	0.662629399111838
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REFL	4 36928552031925e-07	0.50126076803325
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STOM TETA2	1.929704283967486-07	0.470839892557033
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FBXO7	1./3488026848113e-05	0.481788633054943
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FBXO9	2.96510615876494e-07	0.58757516476698
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SFRP2	3.34359368888017e-05	0.463411053916889

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HPS1	1 51749795631051e-06	0.536099902719691
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GSTA5	0.0003/82/0612556844	0.559254146538072
BPGM C20ODE175	4.391599536832876-07	0.629161726961319
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MAP2K3	8.82066030756384e-05	0.550400306445956
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DPM2	4.94692074399743e-07	0.56194631281929
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CTNNAL1	5.66791939967482e-06	0.478277555850092
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MGC13057	1.63797088915475e-07	0.517491538633812
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MBNL3	4.11697885109786e-05	0.405879635475871
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TRIM23	8.00947566589959e-06	0.447847245538033
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BPGM	7.31919750054256e-09	0.57663903012379
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HAGH	8.25879624009117e-05	0.410057922274795
LOC253012	1.29770172634334e-10	0.567851589068332
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HPS1	3.58586332548645e-07	0.550024732917581