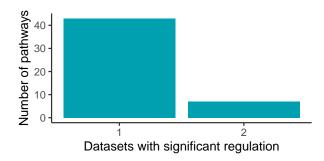
Reactome Analysis Result

17 August, 2022

Introduction

This report summarizes the pathway analysis result created by the **Reactome Analysis Service**. For more information, visit https://www.reactome.org.

In this reports, pathways found differentially expressed at an adjusted p-value <=0.05 are considered to be significantly regulated.



Analysis Overview

- Number of datasets analysed: 3
- Reactome version: 81
- Disease pathways were included

Dataset summaries

RNASEQ_NORM_1:

- 2399 pathways
- 9635 fold changes for genes / proteins

PROTEOMICS_INT_2:

- 2096 pathways
- 4553 fold changes for genes / proteins

PROTEOMICS_INT_3:

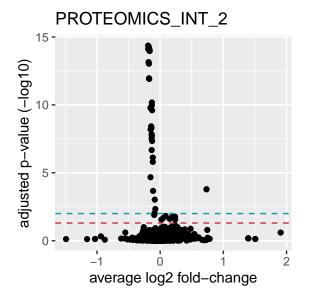
- 1683 pathways
- 1987 fold changes for genes / proteins

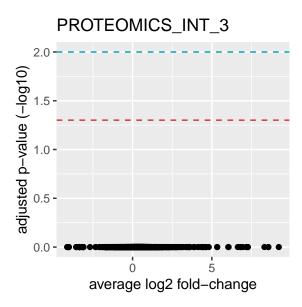
Number of datasets the different pathways were found to be significantly regulated in:

Pathway analysis

RNASEQ_NORM_1 (01b0l-) aninted period perio

average log2 fold-change



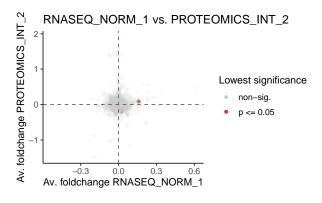


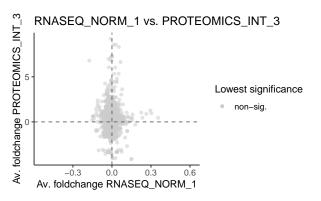
These volcano plots summarize the pathway results for every dataset. Every point is one pathway. The x-axis represents the average fold-change of all genes / proteins within that pathway. The y-axis represents the p-value where "higher" values are more significant (-log10 transformation). The red line represents p = 0.05, and the blue line p = 0.01.

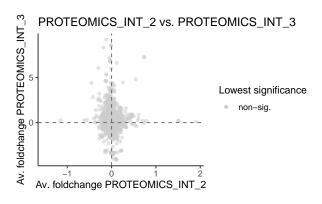
Pathway correlation

Correlation between all datasets (if more than one). Every point represents one pathway, with the x-axis showing the average fold-change of one dataset and the y-axis the average fold-change of the other dataset. Only pathways that were observed in both

datasets are shown. Points are colored based on the lowest observed significance.







Similar regulated pathways

Pathways that show the same direction on all of the datasets. The direction of regulation is only assessed for significantly regulated pathways.

Gluconeogenesis (R-HSA-70263)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	Up	Up
FDR	0.001	0.015	1
Av. FC	0.159	0.087	0.826
N Genes	27	18	7

Pyruvate metabolism (R-HSA-70268)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	Up	Down
FDR	0.002	0.439	1
Av. FC	0.13	0.123	0.01
N Genes	25	20	4

Cholesterol biosynthesis (R-HSA-191273)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	Down	Down
FDR	0.004	0.976	1
Av. FC	0.105	-0.067	-0.286
N Genes	26	21	6

Glycolysis (R-HSA-70171)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	Up	Up
FDR	0.019	0.251	1
Av. FC	0.122	0.043	0.499
N Genes	62	57	26

Glucose metabolism (R-HSA-70326)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	$\mathbf{U}\mathbf{p}$	Up	Up
FDR	0.024	0.251	1
Av. FC	0.101	0.035	0.517
N Genes	79	66	28

The citric acid (TCA) cycle and respiratory electron transport (R-HSA-1428517)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	Up	Up
FDR	0.035	0.476	1
Av. FC	0.041	0.013	0.528
N Genes	169	118	9

Pyruvate metabolism and Citric Acid (TCA) cycle (R-HSA-71406)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	$\mathbf{U}\mathbf{p}$	Up	Up
FDR	0.035	0.37	1
Av. FC	0.071	0.061	0.339
N Genes	47	38	6

Effects of PIP2 hydrolysis (R-HSA-114508)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Down	Up	Up
FDR	0.035	0.409	1
Av. FC	-0.119	0.097	1.033
N Genes	19	10	7

${\bf Keratinization}~({\bf R\text{-}HSA\text{-}}6805567)$

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	Up	Up
FDR	0.971	< 0.001	1
Av. FC	0.002	0.733	7.267
N Genes	13	15	2

Formation of the cornified envelope (R-HSA-6809371)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	Up	Up
FDR	0.971	< 0.001	1
Av. FC	0.002	0.733	7.267
N Genes	13	15	2

Collagen formation (R-HSA-1474290)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	$_{ m Up}$	Up
FDR	0.971	0.016	1
Av. FC	0.02	0.197	0.863
N Genes	33	9	2

Collagen biosynthesis and modifying enzymes (R-HSA-1650814)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	Up	Up
FDR	0.879	0.017	1
Av. FC	0.037	0.236	0.863
N Genes	24	7	2

Metabolism of carbohydrates (R-HSA-71387)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	Up	Up
FDR	0.366	0.021	1
Av. FC	0.039	0.047	0.582
N Genes	210	110	39

HDMs demethylate histones (R-HSA-3214842)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	Up	Up
FDR	0.918	0.024	1
Av. FC	0.06	0.15	1.452
N Genes	22	16	10

Diseases of carbohydrate metabolism (R-HSA-5663084)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	Up	Down
FDR	0.79	0.028	1
Av. FC	0.02	0.238	-0.142
N Genes	26	11	2

Diseases of metabolism (R-HSA-5668914)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	Up	Down
FDR	0.945	0.028	1
Av. FC	-0.002	0.02	0.11
N Genes	146	59	8

L13a-mediated translational silencing of Ceruloplasmin expression (R-HSA-156827)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	Down	Up
FDR	0.076	< 0.001	1
Av. FC	0.014	-0.172	0.861
N Genes	98	92	33

GTP hydrolysis and joining of the 60S ribosomal subunit (R-HSA-72706)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	Down	Down
FDR	0.076	< 0.001	1
Av. FC	0.014	-0.169	0.75
N Genes	99	93	34

Eukaryotic Translation Initiation (R-HSA-72613)

TUTTOE &_	NORM_1 PROTEOMICS	_INT_2 PROTEOMICS_INT_3
Regulation U	Down	Down
FDR 0.1	69 < 0.00 1	1
Av. FC 0.0	-0.166	0.641
N Genes 10	6 99	37

Cap-dependent Translation Initiation (R-HSA-72737)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	Down	Down
FDR	0.169	< 0.001	1
Av. FC	0.011	-0.166	0.641
N Genes	106	99	37

Eukaryotic Translation Termination (R-HSA-72764)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	Down	Up
FDR	0.106	< 0.001	1
Av. FC	0.012	-0.183	0.929
N Genes	79	72	22

Nonsense Mediated Decay (NMD) independent of the Exon Junction Complex (EJC) (R-HSA-975956)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	Down	Down
FDR	0.108	< 0.001	1
Av. FC	0.014	-0.178	0.795
N Genes	81	75	25

Response of EIF2AK4 (GCN2) to amino acid deficiency (R-HSA-9633012)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	Down	Up
FDR	0.187	< 0.001	1
Av. FC	0.003	-0.177	1.474
N Genes	87	75	25

rRNA processing in the nucleus and cytosol (R-HSA-8868773)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Down	Down	Down
FDR	0.982	< 0.001	1
Av. FC	-0.018	-0.131	0.368
N Genes	179	164	53

Major pathway of rRNA processing in the nucleolus and cytosol (R-HSA-6791226)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Down	Down	Down
FDR	0.982	< 0.001	1
Av. FC	-0.019	-0.131	0.432
N Genes	169	156	48

Nonsense-Mediated Decay (NMD) (R-HSA-927802)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	Down	Down
FDR	0.48	< 0.001	1
Av. FC	0.004	-0.153	0.349
N Genes	100	93	31

Nonsense Mediated Decay (NMD) enhanced by the Exon Junction Complex (EJC) (R-HSA-975957)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	Down	Down
FDR	0.48	< 0.001	1
Av. FC	0.004	-0.153	0.349
N Genes	100	93	31

rRNA processing (R-HSA-72312)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	Down	Down
FDR	0.971	< 0.001	1
Av. FC	-0.003	-0.127	0.368
N Genes	210	177	53

Selenoamino acid metabolism (R-HSA-2408522)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	Down	Up
FDR	0.219	< 0.001	1
Av. FC	0.009	-0.142	0.882
N Genes	98	88	26

Activation of the mRNA upon binding of the cap-binding complex and eIFs, and subsequent binding to 43S (R-HSA-72662)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	Down	Down
FDR	0.442	< 0.001	1
Av. FC	0.009	-0.138	0.216
N Genes	56	54	22

Translation initiation complex formation (R-HSA-72649)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	Down	Down
FDR	0.469	< 0.001	1
Av. FC	0.008	-0.138	0.209
N Genes	55	54	21

Differently regulated pathways

Peptide chain elongation (R-HSA-156902)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	Down	Up
FDR	0.023	< 0.001	1
Av. FC	0.022	-0.19	1
N Genes	76	70	22

Eukaryotic Translation Elongation (R-HSA-156842)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	Down	Up
FDR	0.024	< 0.001	1
Av. FC	0.021	-0.191	0.844
N Genes	80	73	25

Viral mRNA Translation (R-HSA-192823)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	Down	Up
FDR	0.024	< 0.001	1
Av. FC	0.021	-0.183	1
N Genes	76	70	21

tRNA processing in the mitochondrion (R-HSA-6785470)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	Down	
FDR	0.035	0.876	
Av. FC	0.092	-0.045	
N Genes	30	10	

Selenocysteine synthesis (R-HSA-2408557)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	Down	Up
FDR	0.035	< 0.001	1
Av. FC	0.019	-0.173	0.957
N Genes	80	71	22

Formation of a pool of free 40S subunits (R-HSA-72689)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	$\mathbf{U}\mathbf{p}$	Down	Up
FDR	0.035	< 0.001	1
Av. FC	0.019	-0.179	0.889
N Genes	88	82	29

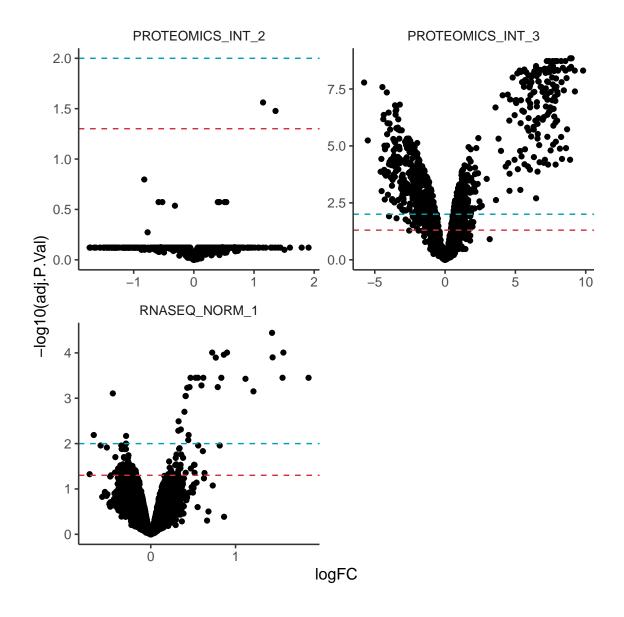
SRP-dependent cotranslational protein targeting to membrane (R-HSA-1799339)

	RNASEQ_NORM_1	PROTEOMICS_INT_2	PROTEOMICS_INT_3
Regulation	Up	Down	Down
FDR	0.049	< 0.001	1
Av. FC	0.023	-0.131	0.795
N Genes	99	90	24

Protein / Gene level results

Classical differential expression analysis performed on the genes / proteins of every dataset.

Note: Depending on the gene set analysis method used, the approach used to assess differential expression at the gene / protein level may vary to the approach used for the pathway level.



Top up-regulated protein/genes

 $RNASEQ_NORM_1$

Identifier	$\log FC$	AveExpr	t	P.Value	adj.P.Val	В
BNIP3	1.4304274	6.666911	22.19318	0e+00	0.0000361	10.171831
P4HA1	0.8992228	6.416131	17.77266	0e + 00	0.0000984	8.947316
HK2	0.7247112	8.063837	17.29776	0e + 00	0.0000984	8.783464
BNIP3L	1.5639788	6.314996	16.90878	0e + 00	0.0000984	8.643586

PDK1	0.8618324	5.701135	16.27642	1e-07	0.0001098	8.404620
ALDOC	1.4369878	4.734219	15.69334	1e-07	0.0001257	8.170745
LSP1	0.7670601	6.497991	15.39744	1e-07	0.0001271	8.046780
PGAM1	0.5563008	6.603261	13.33462	3e-07	0.0003536	7.070835
LRRC32	1.5541424	2.540811	13.28421	3e-07	0.0003536	7.044278
PFKFB3	0.6198045	6.859403	12.79536	5e-07	0.0003540	6.779263

PROTEOMICS_INT_2

Identifier	$\log FC$	AveExpr	t	P.Value	adj.P.Val	В
BNIP3	1.1501779	7.095424	10.290713	0.0000060	0.0274470	1.5116969
PFKFB1	1.3576658	4.237815	9.150372	0.0000146	0.0333264	1.2107273
ALDOC	0.5397200	9.790111	5.921890	0.0003301	0.2673182	-0.2253584
P4HA1	0.5114222	9.150517	5.762490	0.0003965	0.2673182	-0.3289791
ATP6V0A1	0.3979885	4.494340	5.552152	0.0005077	0.2673182	-0.4718919
HK2	0.4160983	11.404262	5.505908	0.0005364	0.2673182	-0.5042822
CYP51A1	0.4253395	8.613711	5.430676	0.0005871	0.2673182	-0.5577403
EGLN1	0.4750521	8.643898	4.350154	0.0023463	0.7490352	-1.4373729
PLOD1	0.6777617	7.513716	4.313148	0.0024677	0.7490352	-1.4714017
FAM162A	0.4865269	7.819647	4.160191	0.0030465	0.7570007	-1.6148894

PROTEOMICS_INT_3

Identifier	$\log FC$	AveExpr	t	P.Value	adj.P.Val	В
TULP4	8.902727	5.776730	64.16186	0	0	17.17166
PER1	8.996711	5.699838	61.07338	0	0	16.99892
KAT8	8.249013	5.268666	55.90728	0	0	16.66222
PQBP1	7.400367	4.693230	53.22149	0	0	16.45915
KIAA1328	7.647092	5.036851	52.31745	0	0	16.38584
RTEL1	7.838099	5.136767	50.61254	0	0	16.24018
RPL23A	8.548221	5.540185	50.59391	0	0	16.23853
COPA	7.233563	4.994465	49.72247	0	0	16.16006
MYBL2	7.959296	5.105207	49.51805	0	0	16.14125
MAPK8IP3	7.552670	4.904254	46.47470	0	0	15.84151

Top down-regulated protein/genes

 $RNASEQ_NORM_1$

Identifier	$\log FC$	AveExpr	t	P.Value	adj.P.Val	В
HBEGF	-0.4473824	5.0413632	-10.952011	1.70e-06	0.0007821	5.644067
TXNDC5	-0.6721486	1.4212203	-8.156577	1.92 e-05	0.0064612	3.400059
GPR18	-0.2911268	5.1606444	-8.062159	2.11e-05	0.0067810	3.310576
KMT2D	-0.2919845	7.5607475	-7.615446	3.32 e- 05	0.0099928	2.873055
LRMP	-0.3471323	9.3778792	-7.479229	3.82 e- 05	0.0110163	2.734843
ATAD3B	-0.5912630	5.2618181	-7.409564	4.12e-05	0.0110163	2.663264
HIVEP3	-0.5178978	3.2512681	-7.288022	4.68e-05	0.0121969	2.536915
VPS13B	-0.3428788	6.2821650	-7.127403	5.57e-05	0.0131986	2.367036
MDN1	-0.3080664	8.2231456	-7.107367	5.69 e-05	0.0131986	2.345609
GAB2	-0.2927246	0.6595078	-7.097583	5.75 e-05	0.0131986	2.335126

PROTEOMICS_INT_2

Identifier	$\log FC$	AveExpr	t	P.Value	adj.P.Val	В
HMGCR	-0.8236797	5.263031	-6.985115	0.0001052	0.1595978	0.3729681
CHKA	-0.5235475	6.852022	-5.974878	0.0003108	0.2673182	-0.1917794
BBS12	-0.5868384	4.274366	-5.609294	0.0004744	0.2673182	-0.4323561
RPL21	-0.3142277	9.640674	-5.283460	0.0007022	0.2906392	-0.6651349
JCHAIN	-0.7684119	8.702611	-4.734450	0.0014060	0.5334724	-1.0996475
APOB	-0.5510180	7.933287	-4.342573	0.0023706	0.7490352	-1.4443222
BCAR3	-0.5864598	3.663056	-4.167524	0.0030156	0.7570007	-1.6079058
EDRF1	-0.3756723	8.499256	-4.080263	0.0034057	0.7570007	-1.6916875
GNL3L	-0.2643112	8.268937	-3.970167	0.0039769	0.7570007	-1.7995111
KPNA2	-0.2565554	10.712666	-3.894432	0.0044291	0.7570007	-1.8750483

${\bf PROTEOMICS_INT_3}$

Identifier	$\log FC$	AveExpr	t	P.Value	adj.P.Val	В
SRPK1	-5.756722	8.311077	-30.32816	0	0e + 00	13.352490
PSMA3	-4.456275	9.685077	-28.33225	0	0e + 00	12.886711
DDX24	-4.143542	7.411492	-26.13666	0	0e + 00	12.314169
HSP90AB1	-3.221118	11.905779	-22.00105	0	2e-07	11.025990
SH2B2	-3.559877	6.618130	-21.77783	0	2e-07	10.947268

-3.484433	11.473918	-21.37344	0	2e-07	10.801931
-3.470225	8.214070	-20.45514	0	3e-07	10.458309
-3.512653	7.637680	-20.08188	0	3e-07	10.312974
-4.018100	11.033658	-19.66453	0	3e-07	10.146398
-3.518869	9.039439	-19.14459	0	4e-07	9.932611
	-3.470225 -3.512653 -4.018100	-3.470225 8.214070 -3.512653 7.637680 -4.018100 11.033658	-3.470225 8.214070 -20.45514 -3.512653 7.637680 -20.08188 -4.018100 11.033658 -19.66453	-3.470225 8.214070 -20.45514 0 -3.512653 7.637680 -20.08188 0 -4.018100 11.033658 -19.66453 0	-3.484433 11.473918 -21.37344 0 2e-07 -3.470225 8.214070 -20.45514 0 3e-07 -3.512653 7.637680 -20.08188 0 3e-07 -4.018100 11.033658 -19.66453 0 3e-07 -3.518869 9.039439 -19.14459 0 4e-07