

Table S3A: Reactome Pathways Upregulated 2.5h pi

| Description | STM | | T3SS-1 ^{mut} | | T3SS-2 ^{mut} | |
|--|------------|----------|-----------------------|----------|-----------------------|----------|
| | gene ratio | p-value | gene ratio | p-value | gene ratio | p-value |
| Cytokine Signaling in Immune system | 0.2194767 | 4.65E-28 | 0.199128 | 2.80E-21 | 0.2514535 | 7.85E-26 |
| Signaling by Interleukins | 0.2359307 | 7.40E-23 | 0.201299 | 6.70E-15 | 0.2662338 | 1.24E-20 |
| Toll Like Receptor 3 (TLR3) Cascade | 0.4141414 | 1.68E-18 | 0.272727 | 5.73E-08 | 0.3939394 | 5.08E-13 |
| MyD88-independent TLR4 cascade | 0.41 | 2.62E-18 | 0.28 | 1.74E-08 | 0.4 | 1.40E-13 |
| TRIF(TICAM1)-mediated TLR4 signaling | 0.41 | 2.62E-18 | 0.28 | 1.74E-08 | 0.4 | 1.40E-13 |
| Toll Like Receptor 4 (TLR4) Cascade | 0.3384615 | 7.70E-16 | 0.253846 | 1.38E-08 | 0.3461538 | 1.85E-12 |
| TRAF6 mediated induction of NFkB and MAP kinases upon TLR7/8 or 9 activation | 0.3870968 | 2.74E-15 | 0.247312 | 3.49E-06 | 0.3655914 | 1.77E-10 |
| Toll Like Receptor 7/8 (TLR7/8) Cascade | 0.3829787 | 4.08E-15 | 0.244681 | 4.24E-06 | 0.3617021 | 2.48E-10 |
| MyD88 dependent cascade initiated on endosome | 0.3829787 | 4.08E-15 | 0.244681 | 4.24E-06 | 0.3617021 | 2.48E-10 |
| Toll Like Receptor 9 (TLR9) Cascade | 0.3673469 | 1.87E-14 | 0.234694 | 8.98E-06 | 0.3469388 | 8.93E-10 |
| MyD88:MAL(TIRAP) cascade initiated on plasma membrane | 0.3684211 | 3.92E-14 | 0.242105 | 5.14E-06 | 0.3473684 | 1.52E-09 |
| Toll Like Receptor TLR6:TLR2 Cascade | 0.3684211 | 3.92E-14 | 0.242105 | 5.14E-06 | 0.3473684 | 1.52E-09 |
| Toll-like Receptor Cascades | 0.2967742 | 4.54E-14 | 0.232258 | 3.78E-08 | 0.3032258 | 1.19E-10 |
| Toll Like Receptor TLR1:TLR2 Cascade | 0.3571429 | 1.16E-13 | 0.234694 | 8.98E-06 | 0.3367347 | 3.77E-09 |
| Toll Like Receptor 2 (TLR2) Cascade | 0.3571429 | 1.16E-13 | 0.234694 | 8.98E-06 | 0.3367347 | 3.77E-09 |
| Toll Like Receptor 10 (TLR10) Cascade | 0.3764706 | 2.44E-13 | 0.247059 | 9.37E-06 | 0.3529412 | 5.49E-09 |
| Toll Like Receptor 5 (TLR5) Cascade | 0.3764706 | 2.44E-13 | 0.247059 | 9.37E-06 | 0.3529412 | 5.49E-09 |
| MyD88 cascade initiated on plasma membrane | 0.3764706 | 2.44E-13 | 0.247059 | 9.37E-06 | 0.3529412 | 5.49E-09 |
| Interleukin-17 signaling | 0.3888889 | 3.04E-12 | 0.236111 | 0.00012 | 0.3611111 | 3.32E-08 |
| MAP kinase activation | 0.40625 | 5.56E-12 | 0.234375 | 0.00032 | 0.375 | 4.82E-08 |
| RAF-independent MAPK1/3 activation | 0.6086957 | 5.61E-10 | 0.608696 | 5.45E-10 | 0.6956522 | 8.01E-11 |
| Interleukin-10 signaling | 0.4255319 | 5.90E-10 | 0.446809 | 6.80E-11 | 0.4680851 | 1.25E-09 |
| Death Receptor Signalling | 0.2624113 | 7.12E-10 | 0.198582 | 2.93E-05 | 0.2695035 | 2.30E-07 |
| TICAM1-dependent activation of IRF3/IRF7 | 0.8333333 | 1.45E-09 | 0.416667 | 0.00239 | 0.75 | 4.93E-07 |
| Interleukin-4 and Interleukin-13 signaling | 0.287037 | 1.62E-09 | 0.305556 | 7.24E-11 | 0.2962963 | 1.98E-07 |
| Interleukin-1 family signaling | 0.2446043 | 2.42E-08 | 0.165468 | 0.00211 | 0.2805755 | 4.91E-08 |
| DDX58/IFIH1-mediated induction of interferon-alpha/beta | 0.3076923 | 2.55E-08 | 0.24359 | 3.06E-05 | 0.2820513 | 3.68E-05 |
| TAK1 activates NFkB by phosphorylation and activation of IKKs complex | 0.4545455 | 2.88E-08 | 0.242424 | 0.00643 | 0.3636364 | 0.00016 |
| Interleukin-1 signaling | 0.2718447 | 3.69E-08 | 0.165049 | 0.00778 | 0.3106796 | 5.80E-08 |
| Signaling by the B Cell Receptor (BCR) | 0.2589286 | 6.83E-08 | 0.196429 | 0.00024 | 0.2946429 | 1.49E-07 |

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| MAPK family signaling cascades | 0.1843003 | 1.01E-07 | 0.139932 | 0.00173 | 0.1774744 | 0.00068 |
| Interferon Signaling | 0.2081218 | 1.24E-07 | 0.208122 | 1.17E-07 | 0.248731 | 6.92E-08 |
| p75NTR signals via NF-kB | 0.625 | 1.27E-07 | 0.375 | 0.00165 | 0.625 | 1.46E-06 |
| NF-kB is activated and signals survival | 0.6923077 | 1.54E-07 | 0.384615 | 0.0036 | 0.6923077 | 1.44E-06 |
| Ovarian tumor domain proteases | 0.3947368 | 2.82E-07 | 0.236842 | 0.00464 | 0.3421053 | 0.00018 |
| ZBP1(DAI) mediated induction of type I IFNs | 0.5238095 | 3.47E-07 | 0.428571 | 3.25E-05 | 0.5238095 | 4.69E-06 |
| Negative regulators of DDX58/IFIH1 signaling | 0.4117647 | 3.80E-07 | 0.294118 | 0.00047 | 0.4117647 | 8.63E-06 |
| Activation of IRF3/IRF7 mediated by TBK1/IKK epsilon | 0.5555556 | 5.87E-07 | 0.333333 | 0.00328 | 0.5555556 | 6.45E-06 |
| Negative regulation of MAPK pathway | 0.375 | 6.21E-07 | 0.225 | 0.00664 | 0.35 | 7.45E-05 |
| Downstream signaling events of B Cell Receptor (BCR) | 0.2650602 | 1.69E-06 | 0.180723 | 0.00517 | 0.3253012 | 2.20E-07 |
| TICAM1, RIP1-mediated IKK complex recruitment | 0.5 | 2.10E-06 | 0.25 | 0.02598 | 0.45 | 0.00016 |
| Nucleotide-binding domain, leucine rich repeat containing receptor (NLR) signaling pathways | 0.3090909 | 2.59E-06 | 0.218182 | 0.00242 | 0.3090909 | 7.95E-05 |
| Neutrophil degranulation | 0.1503132 | 3.26E-06 | 0.11691 | 0.01493 | 0.1899791 | 3.85E-07 |
| RIP-mediated NFkB activation via ZBP1 | 0.5294118 | 3.77E-06 | 0.470588 | 3.97E-05 | 0.5294118 | 3.20E-05 |
| TICAM1,TRAF6-dependent induction of TAK1 complex | 0.5294118 | 3.77E-06 | 0.117647 | 0.44587 | 0.4117647 | 0.00167 |
| IRAK2 mediated activation of TAK1 complex upon TLR7/8 or 9 stimulation | 0.5294118 | 3.77E-06 | 0.117647 | 0.44587 | 0.4117647 | 0.00167 |
| Adaptive Immune System | 0.1349206 | 4.86E-06 | 0.125661 | 0.00016 | 0.1746032 | 1.58E-07 |
| NOD1/2 Signaling Pathway | 0.3611111 | 5.73E-06 | 0.194444 | 0.03406 | 0.3333333 | 0.00041 |
| Regulation of necroptotic cell death | 0.5 | 6.96E-06 | 0.333333 | 0.00328 | 0.3888889 | 0.00247 |
| TRAF6-mediated induction of TAK1 complex within TLR4 complex | 0.5 | 6.96E-06 | 0.111111 | 0.47598 | 0.3888889 | 0.00247 |
| p75 NTR receptor-mediated signalling | 0.2371134 | 7.76E-06 | 0.14433 | 0.04243 | 0.2474227 | 0.00016 |
| SMAD2/SMAD3:SMAD4 heterotrimer regulates transcription | 0.375 | 8.37E-06 | 0.125 | 0.30608 | 0.3125 | 0.00214 |
| Interleukin-6 signaling | 0.6363636 | 9.43E-06 | 0.636364 | 9.29E-06 | 0.7272727 | 3.29E-06 |
| Regulated proteolysis of p75NTR | 0.6363636 | 9.43E-06 | 0.272727 | 0.06483 | 0.5454545 | 0.00059 |
| Transcriptional activity of SMAD2/SMAD3:SMAD4 heterotrimer | 0.3181818 | 1.36E-05 | 0.159091 | 0.08584 | 0.2954545 | 0.00088 |
| PIP3 activates AKT signaling | 0.1692308 | 1.54E-05 | 0.142308 | 0.00211 | 0.1538462 | 0.02829 |
| activated TAK1 mediates p38 MAPK activation | 0.4166667 | 1.61E-05 | 0.166667 | 0.15326 | 0.3333333 | 0.00377 |
| Diseases of Immune System | 0.4166667 | 1.61E-05 | 0.333333 | 0.00069 | 0.4166667 | 0.00015 |
| Diseases associated with the TLR signaling cascade | 0.4166667 | 1.61E-05 | 0.333333 | 0.00069 | 0.4166667 | 0.00015 |
| Interleukin-6 family signaling | 0.4166667 | 1.61E-05 | 0.375 | 0.00011 | 0.4583333 | 2.40E-05 |
| TRAF6 mediated NF-kB activation | 0.4166667 | 1.61E-05 | 0.375 | 0.00011 | 0.375 | 0.00082 |

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| Interferon alpha/beta signaling | 0.2608696 | 1.87E-05 | 0.188406 | 0.00624 | 0.2463768 | 0.00149 |
| Signaling by TGF-beta family members | 0.2254902 | 1.87E-05 | 0.147059 | 0.03159 | 0.245098 | 0.00014 |
| RIPK1-mediated regulated necrosis | 0.45 | 2.05E-05 | 0.3 | 0.00588 | 0.35 | 0.00491 |
| Regulated Necrosis | 0.45 | 2.05E-05 | 0.3 | 0.00588 | 0.35 | 0.00491 |
| NRIF signals cell death from the nucleus | 0.5 | 2.31E-05 | 0.125 | 0.41481 | 0.4375 | 0.00109 |
| MAP3K8 (TPL2)-dependent MAPK1/3 activation | 0.5 | 2.31E-05 | 0.3125 | 0.0098 | 0.5 | 0.00015 |
| IKK complex recruitment mediated by RIP1 | 0.4 | 2.48E-05 | 0.2 | 0.06209 | 0.36 | 0.00115 |
| Interleukin-12 family signaling | 0.2758621 | 2.54E-05 | 0.258621 | 9.96E-05 | 0.362069 | 6.58E-07 |
| TNFR1-induced NFkappaB signaling pathway | 0.3666667 | 2.56E-05 | 0.233333 | 0.01311 | 0.3333333 | 0.00123 |
| MAPK targets/ Nuclear events mediated by MAP kinases | 0.3548387 | 3.66E-05 | 0.225806 | 0.01568 | 0.3548387 | 0.00038 |
| ERKs are inactivated | 0.5384615 | 4.19E-05 | 0.307692 | 0.02197 | 0.3846154 | 0.01108 |
| p75NTR recruits signalling complexes | 0.5384615 | 4.19E-05 | 0.230769 | 0.0987 | 0.5384615 | 0.00022 |
| MAPK1/MAPK3 signaling | 0.1653543 | 4.20E-05 | 0.137795 | 0.00466 | 0.1692913 | 0.00472 |
| CLEC7A (Dectin-1) signaling | 0.2178218 | 4.98E-05 | 0.138614 | 0.05651 | 0.2574257 | 4.32E-05 |
| TNF signaling | 0.3023256 | 5.08E-05 | 0.209302 | 0.01081 | 0.3023256 | 0.00069 |
| IRAK2 mediated activation of TAK1 complex | 0.6 | 6.92E-05 | 0.1 | 0.60013 | 0.4 | 0.01988 |
| Regulation of TNFR1 signaling | 0.3333333 | 7.10E-05 | 0.272727 | 0.00163 | 0.3333333 | 0.00071 |
| Cytosolic sensors of pathogen-associated DNA | 0.2539683 | 7.66E-05 | 0.206349 | 0.00275 | 0.2857143 | 0.00015 |
| Membrane binding and targetting of GAG proteins | 0.5 | 7.74E-05 | 0.071429 | 0.72294 | 0.2857143 | 0.06563 |
| Synthesis And Processing Of GAG, GAGPOL Polyproteins | 0.5 | 7.74E-05 | 0.071429 | 0.72294 | 0.2857143 | 0.06563 |
| Downregulation of SMAD2/3:SMAD4 transcriptional activity | 0.3913043 | 7.81E-05 | 0.173913 | 0.13661 | 0.3478261 | 0.00279 |
| JNK (c-Jun kinases) phosphorylation and activation mediated by activated human TAK1 | 0.3913043 | 7.81E-05 | 0.086957 | 0.61044 | 0.2608696 | 0.0394 |
| Circadian Clock | 0.2428571 | 8.48E-05 | 0.142857 | 0.0827 | 0.2857143 | 6.73E-05 |
| Fc epsilon receptor (FCER1) signaling | 0.1940299 | 8.71E-05 | 0.119403 | 0.1252 | 0.2238806 | 0.00019 |
| Signaling by Receptor Tyrosine Kinases | 0.1406593 | 9.20E-05 | 0.116484 | 0.01872 | 0.1736264 | 6.71E-05 |
| Budding and maturation of HIV virion | 0.3448276 | 0.00011 | 0.137931 | 0.24578 | 0.4137931 | 3.60E-05 |
| Downstream signal transduction | 0.3448276 | 0.00011 | 0.275862 | 0.00272 | 0.3448276 | 0.00091 |
| Interferon gamma signaling | 0.2173913 | 0.00011 | 0.25 | 2.86E-06 | 0.2717391 | 2.25E-05 |
| Diseases of signal transduction | 0.1455026 | 0.00012 | 0.103175 | 0.15801 | 0.1560847 | 0.00681 |
| IRAK1 recruits IKK complex | 0.4666667 | 0.00013 | 0.133333 | 0.3829 | 0.4 | 0.00431 |
| IRAK1 recruits IKK complex upon TLR7/8 or 9 stimulation | 0.4666667 | 0.00013 | 0.133333 | 0.3829 | 0.4 | 0.00431 |
| Intracellular signaling by second messengers | 0.1535836 | 0.00014 | 0.129693 | 0.00895 | 0.1501706 | 0.03217 |
| Interleukin-27 signaling | 0.5454545 | 0.00014 | 0.454545 | 0.0015 | 0.5454545 | 0.00059 |

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| Signaling by TGF-beta Receptor Complex | 0.2328767 | 0.00015 | 0.136986 | 0.10281 | 0.2876712 | 3.99E-05 |
| Transcriptional Regulation by TP53 | 0.1452055 | 0.00016 | 0.117808 | 0.02703 | 0.1671233 | 0.0012 |
| Nuclear Events (kinase and transcription factor activation) | 0.36 | 0.00017 | 0.24 | 0.01845 | 0.36 | 0.00115 |
| Activation of NF-kappaB in B cells | 0.238806 | 0.00017 | 0.164179 | 0.02999 | 0.2835821 | 0.00011 |
| TNFR2 non-canonical NF-kB pathway | 0.2058824 | 0.00017 | 0.156863 | 0.01543 | 0.245098 | 0.00014 |
| Interleukin-3, Interleukin-5 and GM-CSF signaling | 0.2708333 | 0.00018 | 0.1875 | 0.02174 | 0.2708333 | 0.00211 |
| Programmed Cell Death | 0.1744186 | 0.0002 | 0.139535 | 0.01486 | 0.2151163 | 8.71E-05 |
| MAPK6/MAPK4 signaling | 0.2134831 | 0.00021 | 0.078652 | 0.67211 | 0.2134831 | 0.00471 |
| FCER1 mediated NF-kB activation | 0.2195122 | 0.00021 | 0.109756 | 0.28881 | 0.2439024 | 0.00068 |
| Assembly Of The HIV Virion | 0.4375 | 0.00022 | 0.0625 | 0.76939 | 0.3125 | 0.02818 |
| Regulation of TP53 Expression and Degradation | 0.2972973 | 0.00023 | 0.162162 | 0.10001 | 0.2432432 | 0.02017 |
| RAF/MAP kinase cascade | 0.1572581 | 0.00023 | 0.125 | 0.02719 | 0.1572581 | 0.02195 |
| TP53 Regulates Transcription of Death Receptors and Ligands | 0.5 | 0.00026 | 0.5 | 0.00026 | 0.4166667 | 0.00751 |
| Interleukin-35 Signalling | 0.5 | 0.00026 | 0.416667 | 0.00239 | 0.5 | 0.00107 |
| TGF-beta receptor signaling activates SMADs | 0.3125 | 0.00028 | 0.15625 | 0.14343 | 0.40625 | 2.16E-05 |
| TP53 Regulates Transcription of Cell Death Genes | 0.2727273 | 0.00029 | 0.272727 | 0.00029 | 0.2954545 | 0.00088 |
| Apoptosis | 0.1715976 | 0.00033 | 0.136095 | 0.02208 | 0.2130178 | 0.00013 |
| IL-6-type cytokine receptor ligand interactions | 0.4117647 | 0.00035 | 0.352941 | 0.00236 | 0.4117647 | 0.00167 |
| Signalizing by MET | 0.2151899 | 0.00041 | 0.151899 | 0.0412 | 0.2151899 | 0.0067 |
| Signalizing by Activin | 0.4615385 | 0.00045 | 0.153846 | 0.31706 | 0.3846154 | 0.01108 |
| Chemokine receptors bind chemokines | 0.25 | 0.00069 | 0.291667 | 4.00E-05 | 0.2708333 | 0.00211 |
| Interleukin-12 signaling | 0.25 | 0.00069 | 0.25 | 0.00068 | 0.3541667 | 1.07E-05 |
| Regulation of IFNG signaling | 0.4285714 | 0.00073 | 0.571429 | 6.23E-06 | 0.5714286 | 4.36E-05 |
| TRAF3-dependent IRF activation pathway | 0.4285714 | 0.00073 | 0.357143 | 0.00521 | 0.5 | 0.0004 |
| ER-Phagosome pathway | 0.2048193 | 0.00074 | 0.072289 | 0.74532 | 0.2168675 | 0.00492 |
| RHO GTPases activate IQGAPs | 0.3 | 0.00078 | 0.266667 | 0.00342 | 0.3 | 0.00479 |
| Regulation of TP53 Degradation | 0.2777778 | 0.00079 | 0.138889 | 0.20344 | 0.2222222 | 0.0456 |
| Cell junction organization | 0.1978022 | 0.00081 | 0.131868 | 0.09866 | 0.1868132 | 0.0263 |
| Transcriptional regulation of white adipocyte differentiation | 0.202381 | 0.00085 | 0.130952 | 0.11468 | 0.202381 | 0.01245 |
| Antigen processing-Cross presentation | 0.1919192 | 0.00086 | 0.080808 | 0.64637 | 0.2222222 | 0.00144 |
| MAPK3 (ERK1) activation | 0.5 | 0.00089 | 0.6 | 6.84E-05 | 0.7 | 2.12E-05 |
| Interleukin-20 family signaling | 0.32 | 0.00095 | 0.32 | 0.00094 | 0.4 | 0.00023 |
| Antiviral mechanism by IFN-stimulated genes | 0.2051282 | 0.00103 | 0.179487 | 0.00721 | 0.2692308 | 0.00012 |
| PTEN Regulation | 0.1714286 | 0.00106 | 0.107143 | 0.24279 | 0.1571429 | 0.07187 |

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| TRAF6 mediated IRF7 activation in TLR7/8 or 9 signaling | 0.4 | 0.00112 | 0.066667 | 0.74723 | 0.2666667 | 0.08174 |
| Intrinsic Pathway for Apoptosis | 0.25 | 0.00115 | 0.181818 | 0.03503 | 0.3409091 | 5.89E-05 |
| Downregulation of TGF-beta receptor signaling | 0.3076923 | 0.00127 | 0.153846 | 0.18863 | 0.4230769 | 5.98E-05 |
| Signaling by PDGF | 0.2241379 | 0.00127 | 0.206897 | 0.00386 | 0.2241379 | 0.01184 |
| C-type lectin receptors (CLRs) | 0.1690141 | 0.0013 | 0.119718 | 0.11471 | 0.2112676 | 0.00054 |
| Signaling by ERBB4 | 0.2444444 | 0.0014 | 0.088889 | 0.56361 | 0.2444444 | 0.01036 |
| Signaling by Leptin | 0.4545455 | 0.00152 | 0.454545 | 0.0015 | 0.4545455 | 0.00483 |
| NOTCH4 Activation and Transmission of Signal to the Nucleus | 0.4545455 | 0.00152 | 0.181818 | 0.24972 | 0.3636364 | 0.02847 |
| Spry regulation of FGF signaling | 0.375 | 0.00167 | 0.125 | 0.41481 | 0.25 | 0.09959 |
| ERK/MAPK targets | 0.3181818 | 0.00206 | 0.181818 | 0.12074 | 0.3181818 | 0.00882 |
| NOTCH2 Activation and Transmission of Signal to the Nucleus | 0.3181818 | 0.00206 | 0.090909 | 0.58579 | 0.2272727 | 0.09635 |
| Regulation of signaling by CBL | 0.3181818 | 0.00206 | 0.136364 | 0.30215 | 0.2727273 | 0.03211 |
| Signaling by PTK6 | 0.2222222 | 0.00209 | 0.12963 | 0.19044 | 0.2777778 | 0.00074 |
| Signaling by Non-Receptor Tyrosine Kinases | 0.2222222 | 0.00209 | 0.12963 | 0.19044 | 0.2777778 | 0.00074 |
| Membrane Trafficking | 0.1210191 | 0.00219 | 0.093949 | 0.29972 | 0.1544586 | 0.00087 |
| Cell death signalling via NRAGE, NRIF and NADE | 0.1973684 | 0.00219 | 0.105263 | 0.3471 | 0.2105263 | 0.01038 |
| Caspase activation via Death Receptors in the presence of ligand | 0.3529412 | 0.00238 | 0.294118 | 0.01291 | 0.2941176 | 0.03628 |
| ISG15 antiviral mechanism | 0.1971831 | 0.00306 | 0.183099 | 0.00798 | 0.2676056 | 0.00026 |
| TNF receptor superfamily (TNFSF) members mediating non-canonical NF-kB pathway | 0.3333333 | 0.00331 | 0.333333 | 0.00328 | 0.3888889 | 0.00247 |
| TCR signaling | 0.1680672 | 0.0034 | 0.092437 | 0.47175 | 0.1848739 | 0.01426 |
| Regulation of lipid metabolism by Peroxisome proliferator-activated receptor alpha (PPARalpha) | 0.1680672 | 0.0034 | 0.084034 | 0.60195 | 0.1764706 | 0.02655 |
| Activation of BH3-only proteins | 0.2666667 | 0.00347 | 0.2 | 0.04266 | 0.3333333 | 0.00123 |
| Cellular responses to stress | 0.1267606 | 0.00357 | 0.086854 | 0.54675 | 0.1690141 | 0.00032 |
| Signaling by Erythropoietin | 0.2916667 | 0.00358 | 0.25 | 0.01511 | 0.2083333 | 0.12914 |
| Growth hormone receptor signaling | 0.2916667 | 0.00358 | 0.25 | 0.01511 | 0.2916667 | 0.01463 |
| Dissolution of Fibrin Clot | 0.3846154 | 0.00364 | 0.384615 | 0.0036 | 0.4615385 | 0.0018 |
| Cell-Cell communication | 0.1627907 | 0.00403 | 0.131783 | 0.05745 | 0.1782946 | 0.01874 |
| Activated NOTCH1 Transmits Signal to the Nucleus | 0.2580645 | 0.00433 | 0.064516 | 0.76829 | 0.2258065 | 0.05527 |
| Negative regulation of FGFR4 signaling | 0.2580645 | 0.00433 | 0.096774 | 0.51804 | 0.1290323 | 0.4756 |
| NOTCH3 Activation and Transmission of Signal to the Nucleus | 0.28 | 0.0046 | 0.08 | 0.65634 | 0.24 | 0.05691 |

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| Antigen Presentation: Folding, assembly and peptide loading of class I MHC | 0.28 | 0.0046 | 0.16 | 0.17062 | 0.24 | 0.05691 |
| Vesicle-mediated transport | 0.1169415 | 0.00477 | 0.095952 | 0.2325 | 0.1484258 | 0.00283 |
| Downstream TCR signaling | 0.1734694 | 0.00478 | 0.081633 | 0.63489 | 0.2040816 | 0.00645 |
| Endosomal Sorting Complex Required For Transport (ESCRT) | 0.25 | 0.00533 | 0.0625 | 0.78352 | 0.28125 | 0.00763 |
| Gene and protein expression by JAK-STAT signaling after Interleukin-12 stimulation | 0.2307692 | 0.00565 | 0.205128 | 0.01787 | 0.3589744 | 5.40E-05 |
| PPARA activates gene expression | 0.1623932 | 0.00621 | 0.08547 | 0.57993 | 0.1794872 | 0.02235 |
| Regulation of TP53 Activity | 0.15 | 0.00642 | 0.125 | 0.06608 | 0.1375 | 0.20034 |
| Signaling by NOTCH2 | 0.2424242 | 0.00651 | 0.090909 | 0.56131 | 0.1818182 | 0.1657 |
| Oncogene Induced Senescence | 0.2424242 | 0.00651 | 0.090909 | 0.56131 | 0.1515152 | 0.31951 |
| Negative regulation of FGFR1 signaling | 0.2424242 | 0.00651 | 0.090909 | 0.56131 | 0.1212121 | 0.5263 |
| Nuclear signaling by ERBB4 | 0.2592593 | 0.00728 | 0.111111 | 0.42523 | 0.2592593 | 0.02778 |
| Caspase activation via extrinsic apoptotic signalling pathway | 0.2592593 | 0.00728 | 0.222222 | 0.02657 | 0.1851852 | 0.18623 |
| Signaling by NOTCH1 HD Domain Mutants in Cancer | 0.3333333 | 0.00732 | 0.066667 | 0.74723 | 0.2666667 | 0.08174 |
| Constitutive Signaling by NOTCH1 HD Domain Mutants | 0.3333333 | 0.00732 | 0.066667 | 0.74723 | 0.2666667 | 0.08174 |
| Regulation of innate immune responses to cytosolic DNA | 0.3333333 | 0.00732 | 0.066667 | 0.74723 | 0.2666667 | 0.08174 |
| Negative regulation of MET activity | 0.2857143 | 0.00772 | 0.142857 | 0.27741 | 0.1904762 | 0.21032 |
| Signaling by FGFR4 | 0.2195122 | 0.00797 | 0.073171 | 0.70886 | 0.1463415 | 0.32088 |
| MASTL Facilitates Mitotic Progression | 0.4 | 0.00804 | 0.2 | 0.2161 | 0.4 | 0.01988 |
| Interleukin-21 signaling | 0.4 | 0.00804 | 0.3 | 0.05033 | 0.3 | 0.09562 |
| Cellular responses to external stimuli | 0.1192843 | 0.00836 | 0.089463 | 0.46225 | 0.1689861 | 9.57E-05 |
| Rho GTPase cycle | 0.1521739 | 0.00882 | 0.108696 | 0.22592 | 0.1666667 | 0.03816 |
| RAB geranylgeranylation | 0.1875 | 0.00891 | 0.078125 | 0.67021 | 0.265625 | 0.0006 |
| Transcriptional regulation by RUNX3 | 0.1666667 | 0.00898 | 0.083333 | 0.61133 | 0.2083333 | 0.00507 |
| Pink/Parkin Mediated Mitophagy | 0.2727273 | 0.00984 | 0.090909 | 0.58579 | 0.2727273 | 0.03211 |
| TGF-beta receptor signaling in EMT (epithelial to mesenchymal transition) | 0.3125 | 0.00989 | 0.0625 | 0.76939 | 0.375 | 0.00623 |
| Glycogen storage diseases | 0.3125 | 0.00989 | 0.125 | 0.41481 | 0.125 | 0.55763 |
| Signaling by NOTCH1 | 0.1780822 | 0.01025 | 0.09589 | 0.45924 | 0.1780822 | 0.0664 |
| Signaling by FGFR1 | 0.2 | 0.0104 | 0.06 | 0.82574 | 0.12 | 0.5097 |
| Mitophagy | 0.2413793 | 0.01097 | 0.103448 | 0.47257 | 0.2068966 | 0.10385 |
| Negative regulation of FGFR3 signaling | 0.2413793 | 0.01097 | 0.068966 | 0.73504 | 0.137931 | 0.42297 |
| TRAF6 mediated IRF7 activation | 0.2413793 | 0.01097 | 0.172414 | 0.10443 | 0.2413793 | 0.04 |

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| Signaling by NOTCH1 PEST Domain Mutants in Cancer | 0.1896552 | 0.01103 | 0.068966 | 0.75939 | 0.1551724 | 0.20856 |
| Signaling by NOTCH1 in Cancer | 0.1896552 | 0.01103 | 0.068966 | 0.75939 | 0.1551724 | 0.20856 |
| Constitutive Signaling by NOTCH1 PEST Domain Mutants | 0.1896552 | 0.01103 | 0.068966 | 0.75939 | 0.1551724 | 0.20856 |
| Signaling by NOTCH1 HD+PEST Domain Mutants in Cancer | 0.1896552 | 0.01103 | 0.068966 | 0.75939 | 0.1551724 | 0.20856 |
| Constitutive Signaling by NOTCH1 HD+PEST Domain Mutants | 0.1896552 | 0.01103 | 0.068966 | 0.75939 | 0.1551724 | 0.20856 |
| RAB GEFs exchange GTP for GDP on RABs | 0.1666667 | 0.01119 | 0.088889 | 0.53633 | 0.1666667 | 0.08236 |
| Rab regulation of trafficking | 0.1532258 | 0.0115 | 0.08871 | 0.52817 | 0.1532258 | 0.10811 |
| Endosomal/Vacuolar pathway | 0.3636364 | 0.01176 | 0.181818 | 0.24972 | 0.2727273 | 0.12079 |
| Regulation by c-FLIP | 0.3636364 | 0.01176 | 0.363636 | 0.01167 | 0.2727273 | 0.12079 |
| Myoclonic epilepsy of Lafora | 0.3636364 | 0.01176 | 0.090909 | 0.63518 | 0.1818182 | 0.36087 |
| Type I hemidesmosome assembly | 0.3636364 | 0.01176 | 0.363636 | 0.01167 | 0.4545455 | 0.00483 |
| SUMOylation of immune response proteins | 0.3636364 | 0.01176 | 0.454545 | 0.0015 | 0.5454545 | 0.00059 |
| CASP8 activity is inhibited | 0.3636364 | 0.01176 | 0.363636 | 0.01167 | 0.2727273 | 0.12079 |
| Dimerization of procaspase-8 | 0.3636364 | 0.01176 | 0.363636 | 0.01167 | 0.2727273 | 0.12079 |
| VEGFA-VEGFR2 Pathway | 0.1616162 | 0.01198 | 0.111111 | 0.24745 | 0.2222222 | 0.00144 |
| Cyclin D associated events in G1 | 0.2045455 | 0.01274 | 0.136364 | 0.18366 | 0.1818182 | 0.12032 |
| G1 Phase | 0.2045455 | 0.01274 | 0.136364 | 0.18366 | 0.1818182 | 0.12032 |
| Transport of connexons to the plasma membrane | 0.2941176 | 0.01302 | 0.411765 | 0.00034 | 0.3529412 | 0.00872 |
| Regulation of MECP2 expression and activity | 0.2333333 | 0.01325 | 0.1 | 0.49556 | 0.1333333 | 0.44949 |
| Dectin-1 mediated noncanonical NF- κ B signaling | 0.1833333 | 0.01415 | 0.116667 | 0.26983 | 0.2333333 | 0.00636 |
| HSP90 chaperone cycle for steroid hormone receptors (SHR) | 0.1886792 | 0.01556 | 0.150943 | 0.08838 | 0.2641509 | 0.00188 |
| Regulation of PTEN gene transcription | 0.1803279 | 0.01594 | 0.147541 | 0.08238 | 0.1147541 | 0.5496 |
| Josephin domain DUBs | 0.3333333 | 0.01644 | NA | NA | 0.3333333 | 0.03896 |
| NF- κ B activation through FADD/RIP-1 pathway mediated by caspase-8 and -10 | 0.3333333 | 0.01644 | 0.333333 | 0.01632 | 0.4166667 | 0.00751 |
| Signaling by NTRK1 (TRKA) | 0.1666667 | 0.01748 | 0.089744 | 0.53074 | 0.2307692 | 0.00242 |
| RAF activation | 0.24 | 0.01863 | 0.12 | 0.3765 | 0.24 | 0.05691 |
| Constitutive Signaling by AKT1 E17K in Cancer | 0.24 | 0.01863 | 0.2 | 0.06209 | 0.28 | 0.01838 |
| Antigen activates B Cell Receptor (BCR) leading to generation of second messengers | 0.21875 | 0.0188 | 0.21875 | 0.0186 | 0.1875 | 0.14898 |
| Gap junction trafficking and regulation | 0.1914894 | 0.01935 | 0.191489 | 0.0191 | 0.2765957 | 0.00172 |
| Regulation of mRNA stability by proteins that bind AU-rich elements | 0.1590909 | 0.02048 | 0.090909 | 0.51012 | 0.1931818 | 0.01939 |
| Signaling by FGFR3 | 0.2 | 0.02092 | 0.05 | 0.87659 | 0.15 | 0.30005 |

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| Signaling by moderate kinase activity BRAF mutants | 0.2 | 0.02092 | 0.125 | 0.27015 | 0.175 | 0.16293 |
| Paradoxical activation of RAF signaling by kinase inactive BRAF | 0.2 | 0.02092 | 0.125 | 0.27015 | 0.175 | 0.16293 |
| Constitutive Signaling by Ligand-Responsive EGFR Cancer Variants | 0.2631579 | 0.02114 | NA | NA | 0.2631579 | 0.05639 |
| Signaling by EGFR in Cancer | 0.2631579 | 0.02114 | NA | NA | 0.2631579 | 0.05639 |
| Signaling by Ligand-Responsive EGFR Variants in Cancer | 0.2631579 | 0.02114 | NA | NA | 0.2631579 | 0.05639 |
| LDL clearance | 0.2631579 | 0.02114 | 0.210526 | 0.0785 | 0.3684211 | 0.00353 |
| PI3K/AKT Signaling in Cancer | 0.1546392 | 0.02138 | 0.175258 | 0.0042 | 0.1443299 | 0.20904 |
| Hemostasis | 0.1112903 | 0.0221 | 0.119355 | 0.00338 | 0.1564516 | 0.00056 |
| Initiation of Nuclear Envelope Reformation | 0.3076923 | 0.02213 | 0.230769 | 0.0987 | 0.2307692 | 0.17709 |
| Nuclear Envelope Reassembly | 0.3076923 | 0.02213 | 0.230769 | 0.0987 | 0.2307692 | 0.17709 |
| Triglyceride biosynthesis | 0.3076923 | 0.02213 | 0.307692 | 0.02197 | 0.0769231 | 0.79197 |
| Erythropoietin activates RAS | 0.3076923 | 0.02213 | 0.153846 | 0.31706 | 0.3076923 | 0.05135 |
| Cell-cell junction organization | 0.171875 | 0.02233 | 0.0625 | 0.82329 | 0.15625 | 0.1863 |
| Transcriptional activation of mitochondrial biogenesis | 0.1785714 | 0.02242 | 0.089286 | 0.55012 | 0.1785714 | 0.09788 |
| Other interleukin signaling | 0.2307692 | 0.02248 | 0.192308 | 0.07157 | 0.3076923 | 0.00652 |
| Signaling by VEGF | 0.1495327 | 0.02389 | 0.102804 | 0.33422 | 0.2056075 | 0.00401 |
| Degradation of beta-catenin by the destruction complex | 0.1585366 | 0.02563 | 0.085366 | 0.58514 | 0.2073171 | 0.00981 |
| Signaling by NOTCH4 | 0.1585366 | 0.02563 | 0.073171 | 0.73469 | 0.195122 | 0.02094 |
| Negative regulation of FGFR2 signaling | 0.2058824 | 0.02581 | 0.117647 | 0.3471 | 0.1470588 | 0.34302 |
| Signaling by Hippo | 0.25 | 0.0262 | 0.15 | 0.25289 | 0.2 | 0.18583 |
| TP53 Regulates Transcription of Genes Involved in Cytochrome C Release | 0.25 | 0.0262 | 0.3 | 0.00588 | 0.25 | 0.06842 |
| Listeria monocytogenes entry into host cells | 0.25 | 0.0262 | 0.1 | 0.53309 | 0.25 | 0.06842 |
| Deactivation of the beta-catenin transactivating complex | 0.1904762 | 0.02751 | 0.095238 | 0.50782 | 0.2142857 | 0.04332 |
| Beta-catenin independent WNT signaling | 0.137931 | 0.02812 | 0.075862 | 0.73427 | 0.1793103 | 0.01214 |
| Deubiquitination | 0.1212121 | 0.02878 | 0.087542 | 0.53094 | 0.1346801 | 0.14442 |
| SEMA3A-Plexin repulsion signaling by inhibiting Integrin adhesion | 0.2857143 | 0.02888 | 0.357143 | 0.00521 | 0.2142857 | 0.20749 |
| TP53 regulates transcription of several additional cell death genes whose specific roles in p53-dependent apoptosis remain uncertain | 0.2857143 | 0.02888 | 0.214286 | 0.1178 | 0.3571429 | 0.01565 |
| Interleukin-15 signaling | 0.2857143 | 0.02888 | 0.214286 | 0.1178 | 0.3571429 | 0.01565 |

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| EPH-Ephrin signaling | 0.1521739 | 0.02903 | 0.163043 | 0.01335 | 0.2717391 | 2.25E-05 |
| The role of GTSE1 in G2/M progression after G2 checkpoint | 0.16 | 0.02931 | 0.093333 | 0.48821 | 0.2133333 | 0.00913 |
| NIK-->noncanonical NF-kB signaling | 0.1694915 | 0.03123 | 0.101695 | 0.41432 | 0.220339 | 0.01365 |
| Signaling by SCF-KIT | 0.1860465 | 0.0313 | 0.232558 | 0.00334 | 0.2790698 | 0.00235 |
| Sphingolipid de novo biosynthesis | 0.1860465 | 0.0313 | 0.162791 | 0.07776 | 0.2325581 | 0.02004 |
| EPH-ephrin mediated repulsion of cells | 0.1764706 | 0.03161 | 0.176471 | 0.03123 | 0.2352941 | 0.01038 |
| CD209 (DC-SIGN) signaling | 0.2380952 | 0.03198 | 0.190476 | 0.10573 | 0.2857143 | 0.02576 |
| TP53 regulates transcription of additional cell cycle genes whose exact role in the p53 pathway remain uncertain | 0.2380952 | 0.03198 | 0.238095 | 0.03172 | 0.2857143 | 0.02576 |
| Interleukin-37 signaling | 0.2380952 | 0.03198 | 0.238095 | 0.03172 | 0.2857143 | 0.02576 |
| G2/M Transition | 0.128866 | 0.03277 | 0.07732 | 0.73118 | 0.1443299 | 0.1094 |
| RHO GTPases Activate WASPs and WAVEs | 0.1944444 | 0.03441 | 0.111111 | 0.3882 | 0.2777778 | 0.00552 |
| Cellular Senescence | 0.1282051 | 0.03458 | 0.082051 | 0.64541 | 0.1282051 | 0.29105 |
| Interleukin-2 family signaling | 0.1818182 | 0.03542 | 0.136364 | 0.18366 | 0.2045455 | 0.05619 |
| TP53 Regulates Metabolic Genes | 0.1511628 | 0.03627 | 0.081395 | 0.63625 | 0.1976744 | 0.01562 |
| Mitotic G2-G2/M phases | 0.127551 | 0.03648 | 0.076531 | 0.74535 | 0.1428571 | 0.11992 |
| Activation of BAD and translocation to mitochondria | 0.2666667 | 0.03671 | 0.133333 | 0.3829 | 0.4 | 0.00431 |
| YAP1- and WWTR1 (TAZ)-stimulated gene expression | 0.2666667 | 0.03671 | 0.133333 | 0.3829 | 0.2 | 0.23893 |
| phosphorylation site mutants of CTNNB1 are not targeted to the proteasome by the destruction complex | 0.2666667 | 0.03671 | 0.133333 | 0.3829 | 0.2 | 0.23893 |
| Misspliced GSK3beta mutants stabilize beta-catenin | 0.2666667 | 0.03671 | 0.133333 | 0.3829 | 0.2 | 0.23893 |
| S33 mutants of beta-catenin aren't phosphorylated | 0.2666667 | 0.03671 | 0.133333 | 0.3829 | 0.2 | 0.23893 |
| S37 mutants of beta-catenin aren't phosphorylated | 0.2666667 | 0.03671 | 0.133333 | 0.3829 | 0.2 | 0.23893 |
| S45 mutants of beta-catenin aren't phosphorylated | 0.2666667 | 0.03671 | 0.133333 | 0.3829 | 0.2 | 0.23893 |
| T41 mutants of beta-catenin aren't phosphorylated | 0.2666667 | 0.03671 | 0.133333 | 0.3829 | 0.2 | 0.23893 |
| The NLRP3 inflammasome | 0.2666667 | 0.03671 | 0.266667 | 0.03646 | 0.3333333 | 0.02132 |
| InIB-mediated entry of Listeria monocytogenes into host cell | 0.2666667 | 0.03671 | 0.066667 | 0.74723 | 0.2 | 0.23893 |
| N-Glycan antennae elongation | 0.2666667 | 0.03671 | 0.066667 | 0.74723 | 0.3333333 | 0.02132 |
| Signaling by NOTCH | 0.1234043 | 0.03777 | 0.07234 | 0.8287 | 0.1489362 | 0.05687 |
| Signaling by RAS mutants | 0.1698113 | 0.03942 | 0.113208 | 0.31792 | 0.1509434 | 0.25069 |
| Gap junction trafficking | 0.1777778 | 0.0399 | 0.177778 | 0.03946 | 0.2666667 | 0.00356 |
| Synthesis of active ubiquitin: roles of E1 and E2 enzymes | 0.2 | 0.04304 | 0.066667 | 0.75215 | 0.3 | 0.00479 |
| Molecules associated with elastic fibres | 0.1842105 | 0.04472 | 0.210526 | 0.01534 | 0.1578947 | 0.25925 |

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| Microtubule-dependent trafficking of connexons from Golgi to the plasma membrane | 0.25 | 0.04566 | 0.375 | 0.00165 | 0.3125 | 0.02818 |
| Glycogen synthesis | 0.25 | 0.04566 | 0.0625 | 0.76939 | 0.1875 | 0.27109 |
| Rap1 signalling | 0.25 | 0.04566 | 0.125 | 0.41481 | 0.3125 | 0.02818 |
| Ub-specific processing proteases | 0.1227273 | 0.04643 | 0.077273 | 0.74136 | 0.1272727 | 0.29036 |
| Transcriptional Regulation by MECP2 | 0.1636364 | 0.04844 | 0.109091 | 0.34988 | 0.1090909 | 0.60631 |
| Signaling by NTRKs | 0.1414141 | 0.04986 | 0.10101 | 0.36646 | 0.2020202 | 0.00724 |
| COPI-mediated anterograde transport | 0.1414141 | 0.04986 | 0.10101 | 0.36646 | 0.1616162 | 0.09271 |
| PI5P, PP2A and IER3 Regulate PI3K/AKT Signaling | 0.1414141 | 0.04986 | 0.161616 | 0.01175 | 0.1313131 | 0.33388 |
| NOTCH1 Intracellular Domain Regulates Transcription | 0.1702128 | 0.04994 | 0.106383 | 0.39452 | 0.1702128 | 0.15902 |
| Extracellular matrix organization | 0.1162791 | 0.05142 | 0.156146 | 6.26E-05 | 0.1461794 | 0.04732 |
| Non-integrin membrane-ECM interactions | 0.1525424 | 0.07033 | 0.237288 | 0.00044 | 0.2542373 | 0.00198 |
| Peptide ligand-binding receptors | 0.1210526 | 0.07042 | 0.163158 | 0.0005 | 0.1210526 | 0.40743 |
| cGMP effects | 0.0555556 | 0.80878 | 0.388889 | 0.00052 | NA | NA |
| Formation of tubulin folding intermediates by CCT/TriC | 0.1304348 | 0.32822 | 0.304348 | 0.0027 | 0.2608696 | 0.0394 |
| Nitric oxide stimulates guanylate cyclase | 0.0416667 | 0.88991 | 0.291667 | 0.00353 | NA | NA |
| Class A/1 (Rhodopsin-like receptors) | 0.0987654 | 0.26473 | 0.12963 | 0.00626 | 0.0833333 | 0.97115 |
| Prolactin receptor signaling | 0.2 | 0.1388 | 0.333333 | 0.00726 | 0.2 | 0.23893 |
| Gap junction assembly | 0.1764706 | 0.0726 | 0.235294 | 0.00777 | 0.2647059 | 0.01159 |
| Degradation of the extracellular matrix | 0.1142857 | 0.16554 | 0.15 | 0.01011 | 0.15 | 0.11223 |
| Negative regulation of the PI3K/AKT network | 0.1320755 | 0.07928 | 0.160377 | 0.01033 | 0.1226415 | 0.43021 |
| Erythropoietin activates Phosphoinositide-3-kinase (PI3K) | 0.2727273 | 0.06517 | 0.363636 | 0.01167 | 0.1818182 | 0.36087 |
| Vitamin B5 (pantothenate) metabolism | 0.1176471 | 0.44701 | 0.294118 | 0.01291 | 0.2352941 | 0.11907 |
| Cooperation of Prefoldin and TriC/CCT in actin and tubulin folding | 0.1 | 0.49705 | 0.233333 | 0.01311 | 0.2 | 0.11801 |
| GPCR ligand binding | 0.0919037 | 0.39853 | 0.118162 | 0.01371 | 0.0853392 | 0.98177 |
| Metabolism of vitamins and cofactors | 0.0899471 | 0.49473 | 0.137566 | 0.01376 | 0.1322751 | 0.23855 |
| Cytosolic tRNA aminoacylation | 0.0833333 | 0.63517 | 0.25 | 0.01511 | 0.375 | 0.00082 |
| Synthesis of very long-chain fatty acyl-CoAs | 0.0833333 | 0.63517 | 0.25 | 0.01511 | 0.2083333 | 0.12914 |
| Apoptotic cleavage of cellular proteins | 0.1315789 | 0.2375 | 0.210526 | 0.01534 | 0.1578947 | 0.25925 |
| Uptake and actions of bacterial toxins | 0.1612903 | 0.13067 | 0.225806 | 0.01568 | 0.1935484 | 0.13306 |
| Assembly of collagen fibrils and other multimeric structures | 0.1311475 | 0.16286 | 0.180328 | 0.01571 | 0.1967213 | 0.0397 |
| Caspase-mediated cleavage of cytoskeletal proteins | 0.1666667 | 0.28434 | 0.333333 | 0.01632 | 0.25 | 0.14807 |
| Constitutive Signaling by Aberrant PI3K in Cancer | 0.1267606 | 0.16741 | 0.169014 | 0.01948 | 0.0985915 | 0.71132 |

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| Metabolism of water-soluble vitamins and cofactors | 0.097561 | 0.39444 | 0.146341 | 0.02075 | 0.1463415 | 0.15725 |
| Ephrin signaling | 0.2105263 | 0.079 | 0.263158 | 0.02096 | 0.3157895 | 0.01569 |
| Prefoldin mediated transfer of substrate to CCT/TriC | 0.1153846 | 0.40239 | 0.230769 | 0.02226 | 0.1923077 | 0.16626 |
| Post-chaperonin tubulin folding pathway | 0.15 | 0.25393 | 0.25 | 0.02598 | 0.2 | 0.18583 |
| Inflammasomes | 0.2 | 0.09221 | 0.25 | 0.02598 | 0.25 | 0.06842 |
| Syndecan interactions | 0.1481481 | 0.2083 | 0.222222 | 0.02657 | 0.2222222 | 0.0784 |
| Tryptophan catabolism | 0.0714286 | 0.72375 | 0.285714 | 0.02867 | 0.1428571 | 0.48409 |
| Chaperonin-mediated protein folding | 0.0860215 | 0.57711 | 0.150538 | 0.03103 | 0.1290323 | 0.36646 |
| Nuclear Envelope Breakdown | 0.1372549 | 0.15609 | 0.176471 | 0.03123 | 0.1568627 | 0.21833 |
| Signaling by BMP | 0.1785714 | 0.09343 | 0.214286 | 0.03139 | 0.1785714 | 0.20701 |
| Integrin cell surface interactions | 0.1294118 | 0.12327 | 0.152941 | 0.03286 | 0.2 | 0.01397 |
| Apoptotic execution phase | 0.0961538 | 0.48479 | 0.173077 | 0.03495 | 0.1346154 | 0.37848 |
| p130Cas linkage to MAPK signaling for integrins | 0.2 | 0.1388 | 0.266667 | 0.03646 | 0.1333333 | 0.52181 |
| Smooth Muscle Contraction | 0.0810811 | 0.64187 | 0.189189 | 0.03895 | 0.1081081 | 0.61978 |
| Fatty acyl-CoA biosynthesis | 0.0540541 | 0.84799 | 0.189189 | 0.03895 | 0.1351351 | 0.41383 |
| Triglyceride metabolism | 0.1081081 | 0.41027 | 0.189189 | 0.03895 | 0.1621622 | 0.23944 |
| Elastic fibre formation | 0.1555556 | 0.09522 | 0.177778 | 0.03946 | 0.1333333 | 0.40554 |
| Laminin interactions | 0.1333333 | 0.26692 | 0.2 | 0.04266 | 0.2666667 | 0.0162 |
| EPHA-mediated growth cone collapse | 0.1 | 0.49705 | 0.2 | 0.04266 | 0.2666667 | 0.0162 |
| Regulation of TP53 Activity through Acetylation | 0.1666667 | 0.11759 | 0.2 | 0.04266 | 0.1666667 | 0.2506 |
| Collagen formation | 0.0888889 | 0.53886 | 0.144444 | 0.04904 | 0.1444444 | 0.21928 |
| Platelet homeostasis | 0.0777778 | 0.68579 | 0.144444 | 0.04904 | 0.0555556 | 0.98086 |
| Protein folding | 0.0808081 | 0.64882 | 0.141414 | 0.04912 | 0.1212121 | 0.45315 |
| Response to elevated platelet cytosolic Ca2+ | 0.0970149 | 0.39463 | 0.119403 | 0.1252 | 0.2164179 | 0.00044 |
| Platelet activation, signaling and aggregation | 0.1145038 | 0.07868 | 0.091603 | 0.43925 | 0.1832061 | 0.00053 |
| EPHB-mediated forward signaling | 0.1666667 | 0.07079 | 0.142857 | 0.1574 | 0.3095238 | 0.00053 |
| HIV Infection | 0.1163793 | 0.07866 | 0.107759 | 0.16204 | 0.1853448 | 0.00079 |
| Axon guidance | 0.0998185 | 0.16996 | 0.094374 | 0.30193 | 0.1578947 | 0.0008 |
| RHO GTPases activate CIT | 0.1 | 0.5343 | 0.15 | 0.25289 | 0.4 | 0.00098 |
| RHO GTPases Activate ROCKs | 0.05 | 0.84092 | 0.1 | 0.53309 | 0.4 | 0.00098 |
| Platelet degranulation | 0.0930233 | 0.46055 | 0.116279 | 0.15695 | 0.2093023 | 0.00116 |
| HIV Life Cycle | 0.1192053 | 0.11188 | 0.119205 | 0.11023 | 0.1986755 | 0.00154 |
| Regulation of actin dynamics for phagocytic cup formation | 0.147541 | 0.08326 | 0.081967 | 0.62774 | 0.2459016 | 0.00282 |
| PCP/CE pathway | 0.1413043 | 0.05763 | 0.076087 | 0.70569 | 0.2173913 | 0.00304 |

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| Late Phase of HIV Life Cycle | 0.1304348 | 0.05713 | 0.115942 | 0.15009 | 0.1956522 | 0.00323 |
| Class I MHC mediated antigen processing & presentation | 0.1105121 | 0.07213 | 0.097035 | 0.2807 | 0.1590296 | 0.00454 |
| Sema4D in semaphorin signaling | 0.16 | 0.17156 | 0.16 | 0.17062 | 0.32 | 0.005 |
| Infectious disease | 0.0994764 | 0.2282 | 0.094241 | 0.34491 | 0.1570681 | 0.00558 |
| Oxygen-dependent proline hydroxylation of Hypoxia-inducible Factor Alpha | 0.1515152 | 0.06067 | 0.045455 | 0.93653 | 0.2272727 | 0.00625 |
| Sema4D induced cell migration and growth-cone collapse | 0.1428571 | 0.27853 | 0.142857 | 0.27741 | 0.3333333 | 0.00666 |
| Regulation of RUNX2 expression and activity | 0.1506849 | 0.05244 | 0.082192 | 0.62519 | 0.2191781 | 0.00699 |
| Fcgamma receptor (FCGR) dependent phagocytosis | 0.1395349 | 0.07168 | 0.081395 | 0.63625 | 0.2093023 | 0.00725 |
| BMAL1:CLOCK,NPAS2 activates circadian gene expression | 0.1851852 | 0.0824 | 0.148148 | 0.20721 | 0.2962963 | 0.00835 |
| Transcriptional regulation by RUNX2 | 0.1157025 | 0.1737 | 0.082645 | 0.6234 | 0.1900826 | 0.00893 |
| Regulation of Hypoxia-inducible Factor (HIF) by oxygen | 0.1466667 | 0.06168 | 0.04 | 0.96546 | 0.2133333 | 0.00913 |
| Cellular response to hypoxia | 0.1466667 | 0.06168 | 0.04 | 0.96546 | 0.2133333 | 0.00913 |
| Gastrin-CREB signalling pathway via PKC and MAPK | 0.2222222 | 0.06682 | 0.166667 | 0.20498 | 0.3333333 | 0.01185 |
| Clathrin-mediated endocytosis | 0.1214286 | 0.10576 | 0.1 | 0.34141 | 0.1785714 | 0.01443 |
| RHO GTPases activate PAKs | 0.0833333 | 0.63517 | 0.166667 | 0.15326 | 0.2916667 | 0.01463 |
| PTK6 Regulates RHO GTPases, RAS GTPase and MAP kinases | 0.2142857 | 0.11838 | 0.142857 | 0.35027 | 0.3571429 | 0.01565 |
| Negative regulation of NOTCH4 signaling | 0.1481481 | 0.09715 | 0.037037 | 0.95648 | 0.2222222 | 0.01632 |
| Signaling by Rho GTPases | 0.1013514 | 0.17035 | 0.083333 | 0.65123 | 0.1463964 | 0.01857 |
| p75NTR regulates axonogenesis | 0.1 | 0.60096 | 0.2 | 0.2161 | 0.4 | 0.01988 |
| Formation of Incision Complex in GG-NER | 0.0930233 | 0.52855 | 0.093023 | 0.52679 | 0.2325581 | 0.02004 |
| Detoxification of Reactive Oxygen Species | 0.1621622 | 0.10081 | 0.108108 | 0.40863 | 0.2432432 | 0.02017 |
| Signalning by ERBB2 | 0.14 | 0.1449 | 0.02 | 0.98987 | 0.22 | 0.02255 |
| Iron uptake and transport | 0.0862069 | 0.58411 | 0.137931 | 0.13138 | 0.2068966 | 0.02784 |
| CD28 co-stimulation | 0.1212121 | 0.32801 | 0.151515 | 0.15765 | 0.2424242 | 0.02833 |
| Plasma lipoprotein clearance | 0.1818182 | 0.06434 | 0.121212 | 0.32655 | 0.2424242 | 0.02833 |
| Formation of annular gap junctions | 0.2727273 | 0.06517 | 0.090909 | 0.63518 | 0.3636364 | 0.02847 |
| Calcineurin activates NFAT | 0.2727273 | 0.06517 | 0.181818 | 0.24972 | 0.3636364 | 0.02847 |
| Semaphorin interactions | 0.1076923 | 0.34358 | 0.153846 | 0.05498 | 0.2 | 0.0293 |
| Autodegradation of the E3 ubiquitin ligase COP1 | 0.1538462 | 0.08172 | 0.038462 | 0.94931 | 0.2115385 | 0.02959 |
| Host Interactions of HIV factors | 0.125 | 0.09409 | 0.085938 | 0.57185 | 0.171875 | 0.03095 |
| RHO GTPase Effectors | 0.0917722 | 0.42789 | 0.075949 | 0.79799 | 0.1487342 | 0.03198 |
| Gap junction degradation | 0.25 | 0.08142 | 0.083333 | 0.66715 | 0.3333333 | 0.03896 |

| | | | | | | |
|---|-----------|---------|----------|---------|-----------|---------|
| FCGR activation | 0.0833333 | 0.66798 | 0.083333 | 0.66715 | 0.3333333 | 0.03896 |
| PECAM1 interactions | 0.1666667 | 0.28434 | 0.25 | 0.081 | 0.3333333 | 0.03896 |
| Repression of WNT target genes | 0.1666667 | 0.28434 | 0.25 | 0.081 | 0.3333333 | 0.03896 |
| VEGFR2 mediated vascular permeability | 0.137931 | 0.24701 | 0.137931 | 0.24578 | 0.2413793 | 0.04 |
| Regulation of RAS by GAPs | 0.1323529 | 0.13889 | 0.029412 | 0.9854 | 0.1911765 | 0.04079 |
| Regulation of RUNX3 expression and activity | 0.1454545 | 0.10544 | 0.054545 | 0.87142 | 0.2 | 0.04289 |
| tRNA Aminoacylation | 0.0714286 | 0.72573 | 0.142857 | 0.1574 | 0.2142857 | 0.04332 |
| Regulation of PTEN stability and activity | 0.1304348 | 0.1481 | 0.057971 | 0.8652 | 0.1884058 | 0.04524 |
| COPI-independent Golgi-to-ER retrograde traffic | 0.1632653 | 0.0615 | 0.163265 | 0.06086 | 0.2040816 | 0.04618 |
| DAP12 signaling | 0.1666667 | 0.11759 | 0.133333 | 0.26563 | 0.2333333 | 0.04725 |
| SUMOylation of intracellular receptors | 0.1333333 | 0.26692 | 0.033333 | 0.93624 | 0.2333333 | 0.04725 |
| Interconversion of nucleotide di- and triphosphates | 0.1 | 0.49705 | 0.066667 | 0.75215 | 0.2333333 | 0.04725 |
| Antigen processing: Ubiquitination & Proteasome degradation | 0.0906149 | 0.45796 | 0.090615 | 0.45319 | 0.1456311 | 0.04775 |
| AUF1 (hnRNP D0) binds and destabilizes mRNA | 0.1428571 | 0.11411 | 0.035714 | 0.96267 | 0.1964286 | 0.04812 |
| Hh mutants that don't undergo autocatalytic processing are degraded by ERAD | 0.125 | 0.21738 | 0.017857 | 0.99417 | 0.1964286 | 0.04812 |

Table S3A. Enriched Reactome pathways from up-regulated genes at 2.5h pi. Significant Reactome pathways using up-regulated DEGs from STM, T3SS-1^{mut} or T3SS-2^{mut}-infected HIOs at 2.5h.

Table S3B: Reactome Pathways Downregulated 2.5h pi

| Description | STM | | T3SS-1 ^{mut} | | T3SS-2 ^{mut} | |
|---|------------|----------|-----------------------|---------|-----------------------|---------|
| | gene ratio | p-value | gene ratio | p-value | gene ratio | p-value |
| Mitochondrial translation initiation | 0.264368 | 2.40E-08 | 0.126437 | 0.03474 | 0.091954 | 0.4138 |
| Mitochondrial translation | 0.247312 | 9.26E-08 | 0.11828 | 0.05248 | 0.086022 | 0.4893 |
| Metabolism of RNA | 0.126113 | 1.04E-07 | 0.0727 | 0.35054 | 0.074184 | 0.7803 |
| Mitochondrial translation elongation | 0.252874 | 1.15E-07 | 0.126437 | 0.03474 | 0.08046 | 0.5697 |
| Mitochondrial translation termination | 0.252874 | 1.15E-07 | 0.126437 | 0.03474 | 0.08046 | 0.5697 |
| Mitotic Prometaphase | 0.181818 | 1.45E-07 | 0.045455 | 0.93222 | 0.106061 | 0.1267 |
| Cell Cycle | 0.123245 | 7.87E-07 | 0.049922 | 0.98097 | 0.087363 | 0.3051 |
| Cell Cycle, Mitotic | 0.125 | 3.52E-06 | 0.052239 | 0.9516 | 0.080224 | 0.5646 |
| Cell Cycle Checkpoints | 0.143345 | 9.73E-06 | 0.054608 | 0.85977 | 0.071672 | 0.7617 |
| AURKA Activation by TPX2 | 0.232877 | 1.05E-05 | 0.054795 | 0.74599 | 0.164384 | 0.0142 |
| Cilium Assembly | 0.160804 | 1.09E-05 | 0.055276 | 0.81059 | 0.140704 | 0.003 |
| mRNA Splicing | 0.162304 | 1.23E-05 | 0.078534 | 0.32912 | 0.099476 | 0.211 |
| Processing of Capped Intronless Pre-mRNA | 0.357143 | 1.28E-05 | 0.25 | 0.00228 | 0.178571 | 0.0725 |
| tRNA processing | 0.198113 | 1.50E-05 | 0.075472 | 0.44168 | 0.075472 | 0.6405 |
| Processing of Capped Intron-Containing Pre-mRNA | 0.148148 | 2.03E-05 | 0.065844 | 0.60323 | 0.090535 | 0.3318 |
| Regulation of PLK1 Activity at G2/M Transition | 0.204545 | 3.86E-05 | 0.045455 | 0.86172 | 0.147727 | 0.0252 |
| Resolution of Sister Chromatid Cohesion | 0.177419 | 5.67E-05 | 0.024194 | 0.9925 | 0.072581 | 0.6887 |
| M Phase | 0.124682 | 7.94E-05 | 0.035623 | 0.99848 | 0.07888 | 0.6013 |
| Translation | 0.134021 | 9.21E-05 | 0.09622 | 0.04248 | 0.054983 | 0.9682 |
| mRNA Splicing - Major Pathway | 0.153005 | 9.41E-05 | 0.081967 | 0.27197 | 0.092896 | 0.3201 |
| G2/M Transition | 0.149485 | 0.000108 | 0.056701 | 0.78415 | 0.103093 | 0.162 |
| Mitotic Spindle Checkpoint | 0.178571 | 0.000111 | 0.053571 | 0.78809 | 0.089286 | 0.4285 |
| Organelle biogenesis and maintenance | 0.132653 | 0.000115 | 0.061224 | 0.72516 | 0.132653 | 0.0016 |
| Amplification of signal from the kinetochores | 0.1875 | 0.000127 | 0.03125 | 0.96459 | 0.083333 | 0.5262 |
| Amplification of signal from unattached kinetochores via a MAD2 inhibitory signal | 0.1875 | 0.000127 | 0.03125 | 0.96459 | 0.083333 | 0.5262 |
| Mitotic G2-G2/M phases | 0.147959 | 0.00013 | 0.056122 | 0.79503 | 0.102041 | 0.1733 |
| Recruitment of mitotic centrosome proteins and complexes | 0.195122 | 0.000184 | 0.073171 | 0.49517 | 0.158537 | 0.0146 |
| Centrosome maturation | 0.195122 | 0.000184 | 0.073171 | 0.49517 | 0.158537 | 0.0146 |
| Processing of Intronless Pre-mRNAs | 0.368421 | 0.000214 | 0.315789 | 0.00127 | 0.210526 | 0.0632 |
| SUMOylation | 0.144385 | 0.00033 | 0.053476 | 0.83304 | 0.085561 | 0.4555 |
| Loss of Nlp from mitotic centrosomes | 0.2 | 0.000351 | 0.042857 | 0.86715 | 0.142857 | 0.0559 |

| | | | | | | | |
|--|----------|----------|----------|----------|----------|----------|--------|
| Loss of proteins required for interphase microtubule organization from the centrosome | | 0.2 | 0.000351 | 0.042857 | 0.86715 | 0.142857 | 0.0559 |
| Anchoring of the basal body to the plasma membrane | 0.173469 | 0.000506 | 0.05102 | 0.81034 | 0.132653 | 0.0538 | |
| tRNA modification in the nucleus and cytosol | 0.232558 | 0.000704 | 0.069767 | 0.57263 | 0.046512 | 0.8756 | |
| Recruitment of NuMA to mitotic centrosomes | 0.173913 | 0.000712 | 0.065217 | 0.60949 | 0.130435 | 0.069 | |
| RHO GTPases Activate Formins | 0.152174 | 0.000735 | 0.036232 | 0.96425 | 0.057971 | 0.8832 | |
| Separation of Sister Chromatids | 0.138298 | 0.000821 | 0.037234 | 0.97687 | 0.06383 | 0.8478 | |
| Intraflagellar transport | 0.211538 | 0.000907 | 0.038462 | 0.88016 | 0.115385 | 0.2462 | |
| Mitotic Metaphase and Anaphase | 0.135 | 0.000956 | 0.035 | 0.98625 | 0.07 | 0.7607 | |
| Mitotic Anaphase | 0.130653 | 0.001897 | 0.035176 | 0.98563 | 0.065327 | 0.8332 | |
| G0 and Early G1 | 0.259259 | 0.002282 | 0.111111 | 0.28104 | 0.074074 | 0.6576 | |
| SUMO E3 ligases SUMOylate target proteins | 0.132597 | 0.002286 | 0.055249 | 0.80251 | 0.082873 | 0.5105 | |
| Cleavage of Growing Transcript in the Termination Region | 0.179104 | 0.002475 | 0.134328 | 0.03817 | 0.104478 | 0.3025 | |
| RNA Polymerase II Transcription Termination | 0.179104 | 0.002475 | 0.134328 | 0.03817 | 0.104478 | 0.3025 | |
| Activation of E2F1 target genes at G1/S | 0.25 | 0.002858 | 0.107143 | 0.3002 | 0.142857 | 0.1897 | |
| G1/S-Specific Transcription | 0.25 | 0.002858 | 0.107143 | 0.3002 | 0.142857 | 0.1897 | |
| APC/C-mediated degradation of cell cycle proteins | 0.162791 | 0.002861 | 0.046512 | 0.84947 | 0.093023 | 0.4011 | |
| Regulation of mitotic cell cycle | 0.162791 | 0.002861 | 0.046512 | 0.84947 | 0.093023 | 0.4011 | |
| Peroxisomal lipid metabolism | 0.241379 | 0.00354 | 0.206897 | 0.01236 | 0.137931 | 0.2069 | |
| Transcription of E2F targets under negative control by p107 (RBL1) and p130 (RBL2) in complex with HDAC1 | 0.3125 | 0.004083 | 0.125 | 0.30067 | 0.0625 | 0.7432 | |
| Peroxisomal protein import | 0.174603 | 0.004526 | 0.174603 | 0.00335 | 0.126984 | 0.1375 | |
| Glyoxylate metabolism and glycine degradation | 0.225806 | 0.005267 | 0.129032 | 0.15945 | 0.064516 | 0.7309 | |
| Beta-catenin phosphorylation cascade | 0.294118 | 0.00545 | 0.235294 | 0.02537 | 0.235294 | 0.0441 | |
| Condensation of Prometaphase Chromosomes | 0.363636 | 0.005628 | NA | NA | 0.181818 | 0.2239 | |
| SLBP Dependent Processing of Replication-Dependent Histone Pre-mRNAs | 0.363636 | 0.005628 | 0.090909 | 0.54205 | 0.090909 | 0.6071 | |
| tRNA processing in the nucleus | 0.178571 | 0.005652 | 0.071429 | 0.54037 | 0.089286 | 0.4835 | |
| TP53 Regulates Transcription of Genes Involved in G2 Cell Cycle Arrest | 0.277778 | 0.007111 | 0.111111 | 0.35225 | 0.166667 | 0.1763 | |
| Activation of APC/C and APC/C:Cdc20 mediated degradation of mitotic proteins | 0.157895 | 0.007126 | 0.052632 | 0.77382 | 0.078947 | 0.5922 | |
| Activation of the TFAP2 (AP-2) family of transcription factors | 0.333333 | 0.007971 | 0.083333 | 0.57345 | 0.083333 | 0.6391 | |
| G2/M Checkpoints | 0.125 | 0.00821 | 0.059524 | 0.72279 | 0.059524 | 0.8865 | |

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|--|----------|----------|----------|---------|----------|--------|
| Transcription of E2F targets under negative control by DREAM complex | 0.263158 | 0.009095 | 0.157895 | 0.13715 | 0.052632 | 0.801 |
| Phosphorylation of the APC/C | 0.263158 | 0.009095 | 0.157895 | 0.13715 | 0.157895 | 0.1976 |
| DNA Repair | 0.107595 | 0.010218 | 0.075949 | 0.32856 | 0.094937 | 0.2118 |
| Regulation of APC/C activators between G1/S and early anaphase | 0.15 | 0.010678 | 0.05 | 0.80711 | 0.075 | 0.6428 |
| Chk1/Chk2(Cds1) mediated inactivation of Cyclin B:Cdk1 complex | 0.307692 | 0.010874 | 0.153846 | 0.22241 | 0.076923 | 0.6686 |
| SUMOylation of transcription cofactors | 0.177778 | 0.013094 | 0.088889 | 0.37188 | 0.133333 | 0.1559 |
| Mitochondrial tRNA aminoacylation | 0.238095 | 0.014141 | 0.238095 | 0.01206 | 0.238095 | 0.024 |
| Mitochondrial Fatty Acid Beta-Oxidation | 0.189189 | 0.01423 | 0.108108 | 0.24593 | 0.027027 | 0.957 |
| APC/C:Cdc20 mediated degradation of mitotic proteins | 0.146667 | 0.016621 | 0.053333 | 0.76482 | 0.08 | 0.579 |
| G2/M DNA damage checkpoint | 0.136842 | 0.016864 | 0.063158 | 0.64089 | 0.063158 | 0.7959 |
| RHO GTPase Effectors | 0.10443 | 0.016989 | 0.041139 | 0.98596 | 0.03481 | 0.9998 |
| Protein localization | 0.125984 | 0.01817 | 0.125984 | 0.01293 | 0.086614 | 0.4609 |
| mRNA decay by 5' to 3' exoribonuclease | 0.266667 | 0.018526 | 0.066667 | 0.65534 | 0.066667 | 0.7204 |
| mRNA 3'-end processing | 0.155172 | 0.020609 | 0.137931 | 0.04292 | 0.103448 | 0.3328 |
| TP53 Regulates Transcription of Cell Cycle Genes | 0.163265 | 0.021351 | 0.081633 | 0.43506 | 0.163265 | 0.0426 |
| Diseases associated with N-glycosylation of proteins | 0.235294 | 0.028845 | 0.235294 | 0.02537 | 0.058824 | 0.7641 |
| SUMOylation of DNA methylation proteins | 0.235294 | 0.028845 | 0.117647 | 0.32659 | 0.235294 | 0.0441 |
| Cyclin A/B1/B2 associated events during G2/M transition | 0.2 | 0.029191 | 0.04 | 0.83072 | 0.08 | 0.6153 |
| mRNA Splicing - Minor Pathway | 0.153846 | 0.029578 | 0.019231 | 0.97526 | 0.076923 | 0.6207 |
| SLBP independent Processing of Histone Pre-mRNAs | 0.3 | 0.029619 | 0.1 | 0.50833 | 0.1 | 0.5723 |
| Processing and activation of SUMO | 0.3 | 0.029619 | NA | NA | 0.1 | 0.5723 |
| APC:Cdc20 mediated degradation of cell cycle proteins prior to satisfaction of the cell cycle checkpoint | 0.136986 | 0.033427 | 0.054795 | 0.74599 | 0.068493 | 0.7192 |
| SUMOylation of DNA replication proteins | 0.159091 | 0.034503 | 0.022727 | 0.95624 | 0.045455 | 0.8836 |
| Regulation of TP53 Activity | 0.1125 | 0.035742 | 0.09375 | 0.13359 | 0.11875 | 0.0609 |
| DNA Replication | 0.11811 | 0.036225 | 0.070866 | 0.50814 | 0.062992 | 0.8216 |
| Beta-oxidation of very long chain fatty acids | 0.272727 | 0.038616 | 0.181818 | 0.1712 | 0.181818 | 0.2239 |
| CDC6 association with the ORC:origin complex | 0.272727 | 0.038616 | 0.090909 | 0.54205 | 0.090909 | 0.6071 |
| Regulation of TP53 Degradation | 0.166667 | 0.039893 | 0.083333 | 0.45191 | 0.083333 | 0.5704 |
| Synthesis of DNA | 0.117647 | 0.043252 | 0.067227 | 0.57455 | 0.058824 | 0.8612 |
| Dual incision in TC-NER | 0.136364 | 0.043416 | 0.106061 | 0.16414 | 0.060606 | 0.7962 |
| Transcriptional Regulation by TP53 | 0.09589 | 0.043664 | 0.093151 | 0.04104 | 0.109589 | 0.0321 |
| Activation of ATR in response to replication stress | 0.162162 | 0.044486 | 0.162162 | 0.03812 | 0.081081 | 0.5894 |

| | | | | | | |
|---|----------|----------|----------|---------|----------|--------|
| Regulation of TP53 Expression and Degradation | 0.162162 | 0.04486 | 0.081081 | 0.47009 | 0.081081 | 0.5894 |
| RNA Polymerase III Transcription Initiation From Type 3 Promoter | 0.178571 | 0.04534 | 0.107143 | 0.3002 | 0.107143 | 0.4015 |
| G1/S Transition | 0.114504 | 0.045722 | 0.061069 | 0.68279 | 0.068702 | 0.7492 |
| Fatty acid metabolism | 0.107345 | 0.047473 | 0.067797 | 0.55825 | 0.079096 | 0.5853 |
| Kinesins | 0.140351 | 0.047708 | 0.105263 | 0.19359 | 0.087719 | 0.4995 |
| HDR through Homologous Recombination (HRR) or Single Strand Annealing (SSA) | 0.113636 | 0.048348 | 0.060606 | 0.69099 | 0.106061 | 0.1856 |
| Post-chaperonin tubulin folding pathway | 0.2 | 0.049614 | 0.1 | 0.40244 | 0.05 | 0.8172 |
| Metabolism of cofactors | 0.2 | 0.049614 | 0.1 | 0.40244 | 0.05 | 0.8172 |
| Asparagine N-linked glycosylation | 0.072848 | 0.489383 | 0.115894 | 0.0015 | 0.109272 | 0.0498 |
| N-glycan trimming in the ER and Calnexin/Calreticulin cycle | 0.085714 | 0.459461 | 0.228571 | 0.00209 | 0.171429 | 0.0608 |
| VEGFR2 mediated cell proliferation | 0.142857 | 0.185177 | 0.285714 | 0.00225 | 0.095238 | 0.5191 |
| Membrane Trafficking | 0.055732 | 0.953318 | 0.095541 | 0.00501 | 0.074841 | 0.7532 |
| Neddylation | 0.098291 | 0.071906 | 0.115385 | 0.00526 | 0.128205 | 0.0085 |
| Retrograde transport at the Trans-Golgi-Network | 0.081633 | 0.46563 | 0.183673 | 0.00545 | 0.102041 | 0.3686 |
| Translesion Synthesis by POLH | 0.157895 | 0.149395 | 0.263158 | 0.00772 | 0.105263 | 0.4654 |
| Rab regulation of trafficking | 0.064516 | 0.666042 | 0.129032 | 0.0104 | 0.072581 | 0.6887 |
| TBC/RABGAPs | 0.130435 | 0.106304 | 0.173913 | 0.01194 | 0.086957 | 0.5218 |
| Biosynthesis of the N-glycan precursor (dolichol lipid-linked oligosaccharide, LLO) and transfer to a nascent protein | 0.089744 | 0.320034 | 0.141026 | 0.01675 | 0.115385 | 0.1818 |
| Vesicle-mediated transport | 0.052474 | 0.981945 | 0.089955 | 0.01696 | 0.073463 | 0.8001 |
| Acyl chain remodelling of PS | 0.086957 | 0.495233 | 0.217391 | 0.0178 | NA | NA |
| Regulation of KIT signaling | 0.0625 | 0.693816 | 0.25 | 0.02048 | 0.1875 | 0.1361 |
| Activation of PPARGC1A (PGC-1alpha) by phosphorylation | 0.2 | 0.156101 | 0.3 | 0.02671 | 0.3 | 0.0418 |
| Base-Excision Repair, AP Site Formation | 0.1 | 0.522653 | 0.3 | 0.02671 | 0.1 | 0.5723 |
| Ketone body metabolism | 0.1 | 0.522653 | 0.3 | 0.02671 | NA | NA |
| Calnexin/calreticulin cycle | 0.038462 | 0.854014 | 0.192308 | 0.0294 | 0.153846 | 0.1568 |
| Glycerophospholipid biosynthesis | 0.062016 | 0.708663 | 0.116279 | 0.03033 | 0.062016 | 0.8344 |
| TP53 Regulates Metabolic Genes | 0.116279 | 0.084355 | 0.127907 | 0.03226 | 0.104651 | 0.2645 |
| Antigen processing: Ubiquitination & Proteasome degradation | 0.097087 | 0.0512 | 0.097087 | 0.03312 | 0.116505 | 0.0179 |
| Phospholipid metabolism | 0.075472 | 0.443116 | 0.103774 | 0.03327 | 0.070755 | 0.7522 |
| GAB1 signalosome | 0.090909 | 0.556698 | 0.272727 | 0.0349 | 0.090909 | 0.6071 |
| Acyl chain remodelling of PG | 0.157895 | 0.149395 | 0.210526 | 0.03708 | NA | NA |
| Receptor-type tyrosine-protein phosphatases | 0.05 | 0.772306 | 0.2 | 0.04392 | 0.05 | 0.8172 |

| | | | | | | |
|---|----------|----------|----------|---------|----------|--------|
| Base Excision Repair | 0.128205 | 0.141533 | 0.153846 | 0.04771 | 0.076923 | 0.6257 |
| Resolution of Abasic Sites (AP sites) | 0.128205 | 0.141533 | 0.153846 | 0.04771 | 0.076923 | 0.6257 |
| DNA Damage Bypass | 0.102041 | 0.268957 | 0.142857 | 0.04796 | 0.102041 | 0.3686 |
| Translocation of SLC2A4 (GLUT4) to the plasma membrane | 0.114286 | 0.123536 | 0.128571 | 0.04852 | 0.071429 | 0.6839 |
| Reversible hydration of carbon dioxide | 0.083333 | 0.588317 | 0.083333 | 0.57345 | 0.416667 | 0.0017 |
| Deactivation of the beta-catenin transactivating complex | 0.119048 | 0.176699 | 0.095238 | 0.3241 | 0.214286 | 0.0058 |
| Fanconi Anemia Pathway | 0.125 | 0.152896 | 0.125 | 0.13581 | 0.2 | 0.0138 |
| Resolution of D-loop Structures through Holliday Junction Intermediates | 0.121212 | 0.20578 | 0.090909 | 0.39599 | 0.212121 | 0.0152 |
| Resolution of D-Loop Structures | 0.117647 | 0.221103 | 0.088235 | 0.41484 | 0.205882 | 0.0178 |
| Creation of C4 and C2 activators | NA | NA | NA | NA | 0.285714 | 0.0225 |
| CD28 dependent PI3K/Akt signaling | 0.090909 | 0.471552 | 0.136364 | 0.18817 | 0.227273 | 0.029 |
| Urea cycle | NA | NA | 0.1 | 0.50833 | 0.3 | 0.0418 |
| HDR through Homologous Recombination (HRR) | 0.089552 | 0.342698 | 0.104478 | 0.17325 | 0.149254 | 0.0434 |

Table S3B. Enriched Reactome pathways from down-regulated genes at 2.5h pi. Significant Reactome pathways using down-regulated DEGs from STM, T3SS-1^{mut} or T3SS-2^{mut}-infected HIOs at 2.5h.