**Table S1. Comparison of the top 20 depleted hits between transduction replicates in Genome-wide CRISPR screen**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **HCT116 KRAS WT in-vitro screen** | | | | | |
| **1st infection** | | | **2nd infection** | | |
| **Gene Symbol** | **RIGER rank** | **RIGER *p*-value** | **Gene Symbol** | **RIGER rank** | **RIGER *p*-value** |
| PSMG4 | 1 | 0.000001 | RPL19 | 1 | 0.000001 |
| SOD2 | 2 | 0.000001 | RPL3 | 2 | 0.000001 |
| C18orf21 | 3 | 0.000008 | C15orf41 | 3 | 0.000011 |
| RPL19 | 4 | 0.000008 | MKI67IP | 4 | 0.000008 |
| POLR2D | 5 | 0.000014 | RPA3 | 5 | 0.000022 |
| CENPI | 6 | 0.000015 | ACTL6A | 6 | 0.000024 |
| LONP1 | 7 | 0.000017 | PPIL2 | 7 | 0.000028 |
| C15orf41 | 8 | 0.000018 | RPL13 | 8 | 0.000031 |
| PPIL2 | 9 | 0.000019 | LONP1 | 9 | 0.000032 |
| TCP1 | 10 | 0.00001 | PSMG4 | 10 | 0.000034 |
| MKI67IP | 11 | 0.000012 | TBCA | 11 | 0.000039 |
| RPL11 | 12 | 0.000014 | CENPI | 12 | 0.000044 |
| ATP6V0C | 13 | 0.000034 | PTPMT1 | 13 | 0.000047 |
| RAD9A | 14 | 0.000016 | LOC440243 | 14 | 0.000056 |
| RPL3 | 15 | 0.000041 | SBNO1 | 15 | 0.000056 |
| RPA3 | 16 | 0.000044 | CBWD2 | 16 | 0.00006 |
| FARSA | 17 | 0.000025 | NUP155 | 17 | 0.00006 |
| C9orf114 | 18 | 0.000051 | ATP6V0C | 18 | 0.00006 |
| RPP38 | 19 | 0.000056 | CBWD1 | 19 | 0.000064 |
| POLR1E | 20 | 0.000061 | POLR1E | 20 | 0.000078 |
| … | … | … | … | … | … |
| KRAS | 545 | 0.01438 | KRAS | 256 | 0.005787 |

Appears in the 20 top of other replicate infection

Appears in the 100 top of other replicate infection

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **HCT116 KRAS MUT in-vitro screen** | | | | | |
| **1st infection** | | | **2nd infection** | | |
| **Gene Symbol** | **RIGER rank** | **RIGER *p*-value** | **Gene Symbol** | **RIGER rank** | **RIGER *p*-value** |
| CENPI | 1 | 0.000001 | VARS | 1 | 0.000006 |
| LONP1 | 2 | 0.000001 | RARS2 | 2 | 0.000006 |
| C15orf41 | 3 | 0.000006 | PSMG4 | 3 | 0.000008 |
| PSMG4 | 4 | 0.000008 | RPL13 | 4 | 0.000014 |
| RPL19 | 5 | 0.000014 | POLR3H | 5 | 0.00001 |
| ATP6V0C | 6 | 0.000015 | RPL19 | 6 | 0.000021 |
| POLR3H | 7 | 0.000008 | RPL11 | 7 | 0.00001 |
| C18orf21 | 8 | 0.000019 | CENPI | 8 | 0.000026 |
| MYC | 9 | 0.000019 | SPC24 | 9 | 0.000028 |
| SPC24 | 10 | 0.000021 | C15orf41 | 10 | 0.000031 |
| VARS | 11 | 0.000022 | ALDOA | 11 | 0.000039 |
| RAD9A | 12 | 0.00001 | NUP155 | 12 | 0.000051 |
| TOP2A | 13 | 0.000031 | MYC | 13 | 0.000055 |
| PSMB7 | 14 | 0.000034 | RPS19 | 14 | 0.000065 |
| GINS4 | 15 | 0.000034 | PPIL2 | 15 | 0.000071 |
| RPL13A | 16 | 0.000039 | MKI67IP | 16 | 0.000037 |
| RPL34 | 17 | 0.000041 | MRPL33 | 17 | 0.000095 |
| RPA3 | 18 | 0.00005 | RAD9A | 18 | 0.000049 |
| RPL3 | 19 | 0.000056 | C9orf114 | 19 | 0.000125 |
| RPL13 | 20 | 0.000059 | C18orf21 | 20 | 0.000136 |
| … | … | … | … | … | … |
| KRAS | 189 | 0.002357 | KRAS | 117 | 0.001699 |

Appears in the 20 top of other replicate infection

Appears in the 100 top of other replicate infection

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **HCT116 KRAS WT in-vivo Xenograft Screen** | | | | | |
| **1st infection** | | | **2nd infection** | | |
| **Gene Symbol** | **RIGER rank** | **RIGER *p*-value** | **Gene Symbol** | **RIGER rank** | **RIGER *p*-value** |
| RPL19 | 1 | 0.000003 | C9orf114 | 1 | 0.000012 |
| MYC | 2 | 0.000005 | SPC24 | 2 | 0.000014 |
| RPL3 | 3 | 0.000008 | PPIL2 | 3 | 0.000017 |
| LAS1L | 4 | 0.000018 | RPL3 | 4 | 0.000019 |
| EXOSC1 | 5 | 0.000023 | CYBA | 5 | 0.00002 |
| ATP6V0C | 6 | 0.000056 | EXOSC10 | 6 | 0.000044 |
| SPC24 | 7 | 0.00006 | SBNO1 | 7 | 0.000056 |
| MOCS3 | 8 | 0.000064 | RPL10 | 8 | 0.000056 |
| EIF3F | 9 | 0.000064 | IL7R | 9 | 0.000067 |
| RPP21 | 10 | 0.000065 | SPRTN | 10 | 0.00007 |
| RPL13A | 11 | 0.000067 | N6AMT1 | 11 | 0.000076 |
| RPL23 | 12 | 0.000033 | TBCA | 12 | 0.000086 |
| PSMG4 | 13 | 0.000077 | ALDOA | 13 | 0.000101 |
| PTPMT1 | 14 | 0.000084 | POLR3H | 14 | 0.000058 |
| RPL13 | 15 | 0.000091 | WDR59 | 15 | 0.000174 |
| RPP38 | 16 | 0.000091 | RBM42 | 16 | 0.000212 |
| POLR1E | 17 | 0.000125 | NLE1 | 17 | 0.00024 |
| POP5 | 18 | 0.000055 | DCPS | 18 | 0.00024 |
| CENPI | 19 | 0.000163 | C15orf41 | 19 | 0.000241 |
| RPS18 | 20 | 0.000168 | INSR | 20 | 0.000243 |
| … | … | … | … | … | … |
| KRAS | 151 | 0.004931 | KRAS | 2391 | 0.1361 |

Appears in the 20 top of other replicate infection

Appears in the 100 top of other replicate infection

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **HCT116 KRAS MUT in-vivo Xenograft Screen** | | | | | |
| **1st infection** | | | **2nd infection** | | |
| **Gene Symbol** | **RIGER rank** | **RIGER *p*-value** | **Gene Symbol** | **RIGER rank** | **RIGER *p*-value** |
| LONP1 | 1 | 0.000006 | PSMG4 | 1 | 0.000008 |
| RPL3 | 2 | 0.000006 | RPL11 | 2 | 0.000005 |
| RPL34 | 3 | 0.000007 | NUP155 | 3 | 0.000015 |
| CENPI | 4 | 0.000008 | SPC24 | 4 | 0.000019 |
| PSMG4 | 5 | 0.000008 | CENPI | 5 | 0.000023 |
| WBP4 | 6 | 0.000012 | VARS | 6 | 0.000024 |
| JUNB | 7 | 0.000014 | POLR2D | 7 | 0.000039 |
| RPS19 | 8 | 0.000015 | RPL3 | 8 | 0.000052 |
| VARS | 9 | 0.000019 | SAFB | 9 | 0.00006 |
| RPS18 | 10 | 0.000022 | ZNHIT6 | 10 | 0.000065 |
| NOP58 | 11 | 0.000022 | C18orf21 | 11 | 0.000163 |
| C18orf21 | 12 | 0.000022 | GDF5 | 12 | 0.000183 |
| ATP6V0C | 13 | 0.000023 | GINS4 | 13 | 0.000226 |
| COPB2 | 14 | 0.000043 | SNRPD3 | 14 | 0.000107 |
| POLR3H | 15 | 0.000022 | REV3L | 15 | 0.000251 |
| RPL13A | 16 | 0.000052 | RPL13A | 16 | 0.000271 |
| C15orf41 | 17 | 0.000061 | TSR2 | 17 | 0.000119 |
| SMC6 | 18 | 0.000061 | RPL13 | 18 | 0.000301 |
| PPIL2 | 19 | 0.000064 | TOP2A | 19 | 0.000318 |
| GINS4 | 20 | 0.000079 | RBM17 | 20 | 0.00016 |
| … | … | … | … | … | … |
| KRAS | 82 | 0.000885 | KRAS | 97 | 0.003186 |

Appears in the 20 top of other replicate infection

Appears in the 100 top of other replicate infection