**Supplementary information**

# Inhibition of Wnt/β-Catenin pathway and Histone acetyltransferase activity by Rimonabant: a therapeutic target for colon cancer.

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**Table S1** The panel of 306 targets used in this study, with specified information about the grid used for docking calculations.[a]

| Target | PDB code | Center coordinates | | | Size of grid along axis | | |
|---|---|---|---|---|---|---|---|
| | | x | y | z | x | y | z |
| 14_3_3_epsilon | 2BR9 | -17.799 | 2.054 | 20.299 | 16 | 16 | 22 |
| 14_3_3_gamma | 2B05 | -68.008 | -35.843 | -65.126 | 22 | 16 | 14 |
| 14_3_3_sigma | 1YWT | 26.322 | 42.314 | 62.000 | 22 | 16 | 14 |
| 14_3_3_theta | 2BTP | 28.243 | -20.467 | 33.117 | 22 | 18 | 16 |
| 14_3_3_zeta | 1QJA | 20.373 | -11.190 | 43.447 | 20 | 16 | 18 |
| 17hsd3 | 3KLM | -3.194 | 5.222 | -12.194 | 18 | 16 | 22 |
| CPA | 1CBX | -1.042 | 33.136 | -6.050 | 21 | 21 | 21 |
| CPU | 3D67 | 41.827 | 38.616 | 42.591 | 26 | 24 | 20 |
| EPHa3 | 3DZQ | -6.623 | 16.238 | 56.390 | 20 | 20 | 22 |
| EPHb4 | 2X9F | 12.385 | 6.033 | 11.642 | 20 | 20 | 20 |
| a2a_ago | 2YDV | 32.098 | 7.921 | -17.681 | 16 | 24 | 24 |
| a2a_ant | 3EML | -9.394 | -9.004 | 52.769 | 18 | 24 | 28 |
| abl2 | 3HMI | -30.312 | 8.541 | -15.143 | 18 | 14 | 18 |
| abl | 2HYY | 16.615 | 60.851 | 42.083 | 36 | 38 | 36 |
| aif | 1M6I | 2.760 | 51.263 | 23.172 | 20 | 14 | 28 |
| akap13 | 2LG1 | 6.045 | 1.351 | -0.883 | 54 | 42 | 44 |
| akt1 | 3MVH | 17.474 | -1.885 | 27.396 | 20 | 20 | 20 |
| akt2 | 3D0E | 21.279 | -18.979 | 8.086 | 20 | 22 | 24 |
| alk5 | 2WOU | 2.423 | 8.157 | 4.369 | 20 | 16 | 16 |
| alk | 2XP2 | 29.411 | 46.982 | 8.863 | 16 | 16 | 16 |
| alk_alternative | 3AOX | -18.736 | 13.648 | -3.639 | 26 | 28 | 28 |
| aman2 | 3DDF | 29.685 | 64.280 | 10.770 | 24 | 24 | 32 |
| ape1 | 2ISI | 30.330 | 10.876 | 32.821 | 16 | 16 | 16 |
| arf6 | 2W83 | 43.175 | 0.447 | 15.647 | 20 | 22 | 22 |
| arid3a | 2KK0 | 2.951 | -3.134 | -1.349 | 58 | 52 | 44 |
| ask1 | 3VW6 | -2.118 | 7.449 | 27.148 | 22 | 22 | 22 |
| atad2 | 3DAI | -12.463 | 41.138 | 3.561 | 56 | 52 | 52 |
| aurkinA | 2W1D | 2.999 | 34.523 | 3.684 | 22 | 22 | 22 |
| aurkinB | 2VG0 | 10.028 | -0.449 | 2.834 | 24 | 22 | 22 |
| bap1 | 2W15 | 10.534 | 12.859 | 21.170 | 14 | 14 | 14 |
| bcl2a1 | 2VM6 | -4.000 | 9.651 | 58.187 | 26 | 16 | 16 |
| bcl2 | 2O21 | 3.249 | 5.600 | 3.161 | 16 | 16 | 16 |
| bcl6 | 3LBZ | -4.609 | 2.416 | 20.623 | 22 | 20 | 20 |
| bclw | 1ZY3 | 1.000 | -10.592 | 2.873 | 26 | 22 | 16 |
| bclxl | 1BXL | 4.000 | -11.550 | 1.062 | 24 | 16 | 16 |
| brca | 4IGK | 13.608 | -14.986 | 10.561 | 26 | 26 | 26 |
| brd2_bd1 | 2YDW | 23.395 | 11.443 | -11.573 | 18 | 18 | 16 |
| brd2_bd2 | 3ONI | 44.077 | 42.044 | -9.953 | 16 | 16 | 16 |
| brd3_bd1 | 3S91 | 46.055 | 5.436 | 12.948 | 20 | 18 | 18 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| brd3_bd2 | 3S92 | 32.502 | 24.434 | 17.841 | 20 | 18 | 18 |
| brd4_bd1 | 3MXF | 30.178 | 15.747 | -1.351 | 20 | 20 | 20 |
| brd4_bd2 | 2YEM | -5.795 | -3.216 | -17.316 | 20 | 20 | 20 |
| brd9_4nqn | 4NQN | -15.756 | 14.283 | -14.566 | 18 | 22 | 22 |
| brd9_alt | 5IGN | 61.555 | -2.412 | 24.086 | 18 | 20 | 18 |
| brd9 | 4XY9 | 59.389 | -4.155 | 25.545 | 16 | 18 | 14 |
| brdt | 4KCX | 28.538 | -24.103 | 5.784 | 16 | 20 | 24 |
| btk | 3PIX | 19.034 | 7.855 | -3.847 | 22 | 16 | 20 |
| bubr1k | 3SI5 | 13.993 | 7.667 | 21.534 | 30 | 24 | 24 |
| cSRC | 3F3V | -4.939 | 33.779 | -7.177 | 24 | 20 | 22 |
| cabp7 | 2WOR | 0.197 | 5.214 | 5.850 | 22 | 16 | 30 |
| calmodulin | 3EWT | 26.150 | 16.896 | 41.536 | 20 | 20 | 20 |
| camKIIB | 3BHH | 19.194 | 68.631 | 32.637 | 22 | 24 | 22 |
| caspase1 | 2FQQ | 52.000 | 28.170 | 39.946 | 16 | 14 | 12 |
| caspase2 | 1PYO | -2.478 | 24.046 | 27.105 | 22 | 18 | 18 |
| caspase3 | 3EDQ | -7.472 | -8.883 | 9.361 | 16 | 16 | 18 |
| caspase7 | 1SHL | 52.800 | 13.900 | 5.432 | 30 | 30 | 30 |
| caspase8 | 1QTN | -9.591 | 32.000 | 43.500 | 16 | 16 | 18 |
| cathepsinB | 1GMY | 31.019 | 35.506 | 35.000 | 12 | 22 | 24 |
| cathepsinG | 1AU8 | 13.299 | 41.721 | 3.414 | 16 | 18 | 24 |
| cathepsinK | 2R6N | 32.090 | 7.855 | 3.945 | 20 | 16 | 16 |
| cathepsinL | 3HWN | 33.000 | -27.000 | -12.966 | 24 | 18 | 16 |
| ca_2 | 2X7S | 21.428 | 32.153 | 19.042 | 24 | 24 | 24 |
| cbfa2t1 | 2OD1 | -1.262 | 0.080 | -1.406 | 36 | 42 | 48 |
| cbp | 2RNY | -21.832 | -3.546 | -4.244 | 38 | 26 | 26 |
| cbp_brd | 4NR7 | 19.487 | 27.582 | -2.837 | 20 | 20 | 20 |
| cbp_brd_wat | 4NR7 | 19.487 | 27.582 | -2.837 | 20 | 20 | 20 |
| cdc42_no_alf3 | 2NGR | 27.969 | 0.399 | 9.383 | 24 | 18 | 20 |
| cdk2 | 2VV9 | 1.153 | 25.016 | 8.894 | 16 | 18 | 16 |
| cdk2_altern | 2WFY | 41.893 | 25.613 | 1.032 | 18 | 18 | 18 |
| cdk2_alt | 2WIH | 28.753 | 5.411 | 61.065 | 20 | 20 | 20 |
| cdk4 | 3G33 | -44.623 | -23.874 | -58.372 | 32 | 30 | 28 |
| cdk5 | 1H4L | 31.964 | -19.457 | 34.006 | 30 | 32 | 30 |
| cdk6 | 2F2C | 30.249 | 22.000 | 60.500 | 14 | 16 | 12 |
| cdk7 | 1UA2 | 42.707 | -3.136 | 23.335 | 30 | 30 | 30 |
| cdk8 | 3RGF | -6.073 | 2.926 | 28.602 | 38 | 38 | 40 |
| cdk9 | 3BLQ | 49.918 | -19.584 | -11.700 | 16 | 14 | 14 |
| chetk_alpha | 4GC8 | 22.040 | -10.419 | 8.546 | 20 | 26 | 22 |
| chk1 | 2QHN | 17.400 | -2.427 | 10.285 | 16 | 14 | 14 |
| chk2 | 2W7X | 46.710 | -14.819 | -10.824 | 16 | 16 | 22 |
| ciap1 | 3D9U | 6.049 | 16.721 | 11.491 | 14 | 20 | 16 |
| ck2 | 3FL5 | 23.097 | 6.627 | 17.825 | 20 | 22 | 22 |
| ck2_alt | 3PE1 | 21.455 | -32.592 | 18.621 | 20 | 28 | 26 |
| clk1 | 1Z57 | 5.753 | 12.504 | 22.896 | 30 | 30 | 30 |
| clk3 | 2WU6 | 36.404 | 59.008 | 16.400 | 12 | 16 | 16 |
| cmet | 2WGJ | 21.882 | 80.521 | 3.407 | 14 | 14 | 18 |
| cox_1 | 3N8X | -18.561 | -49.009 | -1.877 | 24 | 22 | 22 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| cox_1_3kk6 | 3KK6 | -31.141 | 42.768 | -7.323 | 22 | 22 | 22 |
| cox_2 | 3NT1 | -42.655 | -52.344 | -23.765 | 22 | 24 | 20 |
| cxcr4 | 2K05 | -5.086 | -3.516 | 3.094 | 20 | 24 | 22 |
| cyp19a1 | 4GL5 | 84.199 | 53.199 | 51.321 | 22 | 26 | 28 |
| dal1 | 3BIN | 47.246 | 74.157 | 0.758 | 24 | 18 | 30 |
| dapk | 3EH9 | -21.618 | 1.723 | -12.865 | 22 | 20 | 18 |
| dcr3 | 3K51 | -18.656 | 7.259 | 35.418 | 30 | 22 | 40 |
| ddb1 | 3I7P | 19.163 | 37.871 | 41.208 | 26 | 22 | 24 |
| ddx53 | 3IUY | -1.479 | 8.845 | 31.644 | 18 | 14 | 18 |
| dhfr | 1PD8 | 30.179 | 15.695 | -0.515 | 22 | 20 | 22 |
| diaminoox | 3HIG | -30.099 | -11.287 | 74.580 | 14 | 14 | 20 |
| dlc2 | 2H80 | 2.363 | -5.667 | 3.381 | 52 | 42 | 42 |
| dnmt3a | 3A1B | 34.666 | -6.035 | 13.225 | 24 | 24 | 20 |
| dnmt3l | 2QRV | 60.000 | 100.605 | 19.871 | 20 | 30 | 12 |
| dyrk_1a | 3ANQ | 4.690 | 28.024 | 12.200 | 26 | 22 | 26 |
| egfr | 2J6M | -50.000 | 0.373 | -18.696 | 14 | 12 | 22 |
| ejc | 3EX7 | -32.961 | 11.428 | 27.119 | 22 | 24 | 20 |
| enolase1_gr1 | 2PSN | 81.332 | -20.050 | -6.650 | 22 | 20 | 18 |
| enolase1_gr2 | 2PSN | 60.597 | -19.041 | 20.178 | 20 | 24 | 18 |
| enolase2_gr1 | 1TE6 | 46.142 | 36.062 | 24.468 | 22 | 22 | 24 |
| enolase2_gr2 | 1TE6 | 31.119 | 51.339 | 3.344 | 22 | 20 | 26 |
| enolase3_gr1 | 2XSX | -32.828 | 12.580 | 2.201 | 22 | 26 | 22 |
| enolase3_gr2 | 2XSX | 0.684 | 4.118 | -3.291 | 22 | 22 | 18 |
| erbB2 | 1S78 | 18.505 | 27.000 | 214.145 | 20 | 30 | 20 |
| erbB4 | 2R4B | -14.146 | 11.917 | -3.129 | 20 | 20 | 20 |
| erbB4_alt | 3BBT | -37.517 | 49.803 | 16.476 | 28 | 18 | 34 |
| erk1 | 2ZOQ | 28.863 | 6.828 | 17.411 | 30 | 30 | 30 |
| erk2 | 2OJG | -13.188 | 13.830 | 41.302 | 22 | 16 | 18 |
| errA | 3K6P | 36.477 | -1.714 | 35.201 | 20 | 24 | 20 |
| errB_ant | homology_modeling | 19.541 | 42.088 | 29.426 | 20 | 20 | 22 |
| errB_apo | homology_modeling | -16.371 | -5.373 | -29.356 | 20 | 20 | 20 |
| errB_gsk | homology_modeling | -53.704 | 121.991 | 2.500 | 22 | 22 | 22 |
| errB_gsk_h2o | homology_modeling | -53.704 | 121.991 | 2.500 | 22 | 22 | 22 |
| errG_ant | 1S9Q | 19.659 | 42.116 | 30.043 | 18 | 18 | 20 |
| errG_apo | 2E2R | -16.371 | -5.373 | -29.356 | 20 | 22 | 20 |
| errG_gsk | 2GPP | -53.703 | 122.879 | 1.944 | 20 | 24 | 22 |
| errG_gsk_h2o | 2GPP | -53.703 | 122.879 | 1.944 | 20 | 24 | 22 |
| e-cadherin | 2O72 | 40.500 | 12.000 | 55.000 | 30 | 30 | 30 |
| fadk1 | 3BZ3 | 10.246 | 1.881 | 2.017 | 24 | 20 | 26 |
| fak | 3BZ3 | 9.988 | 3.459 | 4.865 | 16 | 16 | 16 |
| fgf1 | 1HKN | -19.795 | -5.075 | 36.612 | 16 | 16 | 16 |
| fgfr1 | 1AGW | 8.727 | 4.577 | 19.000 | 14 | 10 | 20 |
| fgfr2 | 2PVF | 21.792 | -6.259 | -2.777 | 18 | 16 | 18 |
| flt3 | 3QS7 | -3.435 | 37.259 | -61.682 | 40 | 26 | 28 |
| fpps_allo | 3N1V | 4.461 | 78.308 | 28.791 | 22 | 20 | 20 |
| fpps_ipp | 1ZW5 | 13.086 | 33.007 | -6.741 | 18 | 18 | 18 |
| fpps_no_ipp | 1ZW5 | 11.806 | 33.007 | -6.741 | 22 | 18 | 20 |

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|---|---|---|---|---|---|---|---|
| fscn1 | 3LLP | 30.918 | 10.585 | 7.519 | 22 | 22 | 22 |
| ftase | 1LD8 | 17.110 | 135.160 | -1.069 | 16 | 14 | 16 |
| fxr | 1OSV | 21.179 | 42.946 | 12.608 | 26 | 24 | 20 |
| galectin1 | 1W6M | 0.871 | 60.097 | 25.245 | 16 | 16 | 12 |
| galectin3 | 1KJL | -1.495 | -7.002 | 0.865 | 20 | 16 | 12 |
| galectin7 | 3GAL | 5.147 | 8.086 | 28.917 | 16 | 12 | 16 |
| grb7 | 2QMS | 32.870 | 19.585 | 46.920 | 18 | 26 | 16 |
| gsk3 | 3F7Z | 0.590 | 13.013 | 17.987 | 30 | 30 | 30 |
| gstm2_2 | 3GUR | 10.202 | -7.431 | 16.808 | 26 | 24 | 26 |
| gstp1 | 2A2R | 10.846 | 7.407 | 26.035 | 14 | 14 | 14 |
| haspin | 3E7V | 12.731 | -10.431 | -10.993 | 24 | 20 | 22 |
| hdac1 | 4BKX | -44.755 | 16.619 | -5.512 | 16 | 16 | 24 |
| hdac2 | 3MAX | 69.400 | 33.500 | -0.297 | 18 | 20 | 20 |
| hdac3 | 4A69 | 34.423 | 60.188 | 26.892 | 23 | 29 | 25 |
| hdac4 | 2VQM | 16.376 | -10.087 | 2.960 | 18 | 24 | 34 |
| hdac6 | homology_modeling | 18.908 | -9.000 | -0.126 | 20 | 22 | 23 |
| hdac7 | 3C0Z | -35.000 | -32.700 | -23.000 | 27 | 27 | 27 |
| hdac8b | 1VKG | 21.859 | 69.000 | 72.500 | 23 | 23 | 23 |
| hdac8 | 1T64 | 107.700 | 59.300 | 26.383 | 24 | 24 | 27 |
| hgfr_cmet_alt | 2WD1 | 104.332 | 21.278 | 140.166 | 20 | 20 | 18 |
| hla1 | 3BO8 | -19.175 | 19.257 | -4.369 | 22 | 42 | 22 |
| hmt | 3HNA | -10.912 | -1.472 | 24.020 | 32 | 20 | 22 |
| hras | 2UZI | 6.723 | 25.453 | 26.054 | 18 | 20 | 22 |
| hsc70 | 3FZH | 17.063 | -4.127 | -0.134 | 20 | 20 | 22 |
| hsp70_allo_site | 3JXU | 5.808 | -30.125 | 18.937 | 14 | 14 | 12 |
| hsp90 | 2WI6 | 34.663 | 9.291 | 27.661 | 16 | 14 | 14 |
| hspa1a | 3JXU | -5.677 | -17.671 | 16.741 | 26 | 28 | 26 |
| hspa1lA | 3GDQ | 12.887 | 9.377 | 7.092 | 22 | 34 | 32 |
| hspa1lB | 3GDQ | 12.887 | 9.377 | 7.092 | 22 | 34 | 32 |
| hspa2 | 3I33 | -15.025 | -5.569 | 7.634 | 28 | 26 | 24 |
| hspa5 | 3IUC | -6.578 | -0.465 | 1.186 | 34 | 32 | 30 |
| hspa6A | 3FE1 | -2.351 | -4.413 | 21.062 | 28 | 26 | 24 |
| hspa6B | 3FE1 | -2.351 | -4.413 | 21.062 | 28 | 26 | 24 |
| ido | 2D0T | 60.151 | 53.354 | 19.000 | 36 | 36 | 36 |
| igf | 3F5P | 80.817 | 51.567 | 149.088 | 26 | 20 | 16 |
| irak4 | 2NRU | 30.739 | 6.930 | -2.308 | 20 | 20 | 24 |
| jak1 | 3EYG | 12.000 | 13.903 | -14.249 | 20 | 16 | 16 |
| jak2 | 3E64 | 33.332 | 34.394 | 37.000 | 14 | 22 | 14 |
| jak3 | 1YVJ | 8.374 | -13.359 | -7.996 | 16 | 16 | 16 |
| jmjd3 | 2XXZ | 45.578 | 45.880 | 4.878 | 15 | 15 | 15 |
| jmjd3_4ask | 4ASK | 44.186 | 44.880 | 7.000 | 20 | 20 | 20 |
| jmjd3_akg | 2XXZ | 40.000 | 45.910 | 5.455 | 18 | 18 | 18 |
| jnk1 | 4IZY | -13.979 | 5.567 | -22.334 | 24 | 28 | 22 |
| jnk2 | 3NPC | 53.345 | 47.600 | 9.200 | 32 | 34 | 36 |
| jnk3 | 2ZDT | 47.427 | 6.999 | 31.001 | 22 | 24 | 18 |
| jnk3_alt | 3KVX | -25.515 | 32.554 | 12.483 | 28 | 18 | 22 |
| kga | 3VOY | -5.021 | 18.201 | 16.327 | 24 | 24 | 28 |

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|---|---|---|---|---|---|---|---|
| kif11 | 3CJO | 18.757 | 15.434 | 107.995 | 22 | 18 | 24 |
| kif15 | 4BN2 | -21.874 | 16.722 | -51.467 | 20 | 24 | 20 |
| kit_kinase | 3G0E | 33.268 | -4.448 | -76.442 | 30 | 30 | 30 |
| kit_kinase_alternative | 4HVS | 21.659 | -2.264 | 7.637 | 24 | 28 | 20 |
| lck | 3AD4 | -25.151 | -1.321 | -7.567 | 24 | 20 | 20 |
| lox | 3O8Y | 3.055 | 17.715 | -0.739 | 22 | 26 | 22 |
| lsd1 | 2EJR | 23.606 | 44.189 | 50.526 | 26 | 32 | 30 |
| lyn | 2ZVA | 18.550 | -10.780 | 25.417 | 24 | 22 | 28 |
| mcl1 | 3D7V | 12.500 | -22.982 | 22.500 | 26 | 26 | 26 |
| mdm2 | 3EQS | -3.945 | -2.024 | 6.550 | 22 | 28 | 18 |
| mdmx | 3EQY | -15.391 | 19.122 | 15.766 | 28 | 20 | 16 |
| mdmx_alternative | 4N5T | 9.882 | 21.234 | -14.170 | 20 | 26 | 20 |
| mek1 | 3DV3 | 39.338 | -11.778 | -1.356 | 16 | 18 | 18 |
| mek1_adp | 1S9J | 32.376 | 29.688 | 39.434 | 24 | 24 | 18 |
| mek1_no_adp_no_lig | 1S9J | 32.376 | 29.688 | 39.434 | 24 | 24 | 18 |
| mek2_adp | 1S9I | 38.839 | 101.877 | 46.799 | 32 | 24 | 30 |
| mek2_no_adp_no_lig | 1S9I | 38.839 | 101.877 | 46.799 | 26 | 18 | 24 |
| mek4_anp | 3ALN | 16.902 | -1.048 | -26.289 | 22 | 20 | 20 |
| mek4_no_anp | 3ALN | 16.902 | -1.048 | -26.289 | 22 | 20 | 20 |
| mek5_pb1_domain | 1WI0 | -0.416 | -0.860 | -0.263 | 46 | 46 | 46 |
| metap2 | 1YW9 | 16.517 | 30.297 | 20.282 | 16 | 16 | 20 |
| mhp37 | 3E78 | 30.969 | 32.012 | 31.058 | 30 | 22 | 22 |
| mif | 3B9S | -28.479 | 12.851 | -15.782 | 24 | 22 | 20 |
| mk2 | 3M42 | 36.903 | 2.935 | 15.901 | 18 | 18 | 20 |
| mlk1 | 3DTC | 21.917 | 38.957 | 32.260 | 22 | 22 | 22 |
| ml_iap | 3F7H | 79.515 | 65.841 | 16.928 | 30 | 20 | 20 |
| mmp3 | 1HY7 | -1.500 | 49.563 | 56.892 | 18 | 12 | 26 |
| mmp8 | 2OY2 | -11.500 | -3.134 | 5.371 | 26 | 28 | 30 |
| mmp13 | 830C | -5.196 | 26.703 | 52.731 | 14 | 14 | 20 |
| mpges_1_4al1 | 4AL1 | 8.554 | -9.254 | -4.804 | 20 | 20 | 24 |
| mpges_1_no_gsh | 4AL0 | 10.304 | -11.033 | -8.384 | 24 | 20 | 30 |
| mpges_1_with_gsh | 4AL0 | 10.304 | -11.033 | -8.384 | 24 | 20 | 30 |
| mps1 | 4H7X | 49.683 | 54.589 | 56.182 | 32 | 30 | 36 |
| mrp1 | 2CBZ | -18.000 | 47.285 | 3.763 | 18 | 14 | 18 |
| msk1 | 3KN5 | 24.505 | 37.471 | 76.124 | 18 | 24 | 20 |
| mthfs | 3HY3 | 4.247 | 15.887 | -10.368 | 18 | 20 | 18 |
| mtor | 3FAP | -9.212 | 26.369 | 36.057 | 20 | 20 | 20 |
| mtsp1 | 3NCL | 21.607 | 28.392 | 27.485 | 20 | 20 | 20 |
| nek2 | 2XKF | -27.131 | 19.628 | -18.874 | 20 | 20 | 22 |
| nek7 | 2WQN | -9.772 | -31.792 | -46.457 | 20 | 18 | 20 |
| nm23_h2 | 3BBB | -24.262 | -21.020 | 45.862 | 18 | 26 | 24 |
| nnos | 3JT4 | 11.695 | 0.011 | 25.550 | 16 | 16 | 16 |
| nq02 | 3TZB | 17.082 | 1.632 | -6.666 | 24 | 24 | 28 |
| nqo1 | 2F1O | 10.513 | 11.320 | -4.000 | 16 | 16 | 20 |
| nr3c4 | 2Q7K | 25.465 | 2.178 | 4.975 | 26 | 26 | 24 |
| orf73 | 2YPY | 0.743 | 45.269 | 21.521 | 24 | 18 | 32 |
| p38 | 3HEG | 0.206 | 2.797 | 20.549 | 24 | 28 | 30 |

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|---|---|---|---|---|---|---|---|
| p53_mut | 2X0V | 125.393 | 103.818 | -42.832 | 18 | 18 | 16 |
| p300 | 3BIY | -17.116 | 17.800 | 2.628 | 18 | 32 | 16 |
| palb2 | 3EU7 | -11.743 | -8.240 | 6.425 | 26 | 24 | 26 |
| pan_bcr_abl | 3IK3 | 3.533 | -1.334 | 16.867 | 28 | 28 | 22 |
| parp | 2JVN | -1.605 | -0.821 | 4.533 | 40 | 48 | 50 |
| pcaf | 2RNW | 13.278 | -1.754 | 2.797 | 16 | 24 | 18 |
| pcna | 1VYJ | -43.984 | 66.000 | 36.537 | 20 | 20 | 20 |
| pd1_chain_b | 3BIK | 8.343 | -3.970 | -25.030 | 40 | 22 | 30 |
| pd1_chain_c | 3BIK | 4.343 | -30.970 | -4.030 | 36 | 30 | 28 |
| pdk1 | 3NAX | 5.483 | -3.504 | 9.156 | 34 | 34 | 34 |
| pdk2 | 4MP2 | 10.608 | 3.673 | -37.761 | 20 | 20 | 22 |
| pd | 3BIK | 2.876 | -14.538 | -25.455 | 22 | 24 | 24 |
| peroxiredoxin_1 | 2RII | -6.836 | 9.736 | -13.002 | 14 | 14 | 18 |
| peroxiredoxin_hORF6 | 1PRX | 18.838 | 2.806 | 1.665 | 20 | 22 | 22 |
| pgm | 1YFK | 3.188 | -2.533 | 53.526 | 14 | 14 | 14 |
| pi3k | 3ENE | 45.329 | 12.738 | 29.269 | 22 | 22 | 24 |
| pig3 | 2J8Z | 26.715 | 19.374 | -18.999 | 22 | 22 | 22 |
| pimkin | 3JYA | 5.477 | 82.059 | 1.200 | 36 | 36 | 36 |
| pka | 3L9L | 29.205 | 3.090 | 8.632 | 18 | 20 | 18 |
| pka_c_alpha | 4AXA | 6.566 | 10.987 | 0.767 | 22 | 26 | 22 |
| pkb_alpha | 2UVM | 16.822 | 7.994 | 18.563 | 18 | 22 | 18 |
| pkca | 3IW4 | 5.236 | 29.781 | 51.904 | 16 | 16 | 16 |
| pkcbII | 2I0E | 38.888 | 55.638 | 34.802 | 16 | 16 | 20 |
| pkct | 2JED | 58.284 | 15.628 | -3.697 | 16 | 16 | 20 |
| pkc_eta | 3TXO | 21.080 | 11.783 | 16.450 | 24 | 20 | 20 |
| pkc_iota | 3A8W | 5.500 | -21.705 | -12.402 | 22 | 24 | 24 |
| pkc_iota_2 | 1ZRZ | -8.918 | 20.387 | 20.039 | 24 | 24 | 22 |
| pkc_iota_apo | 3A8X | 20.567 | 3.010 | -43.634 | 28 | 24 | 20 |
| pkm2 | 4G1N | 0.453 | -12.672 | 47.009 | 30 | 30 | 28 |
| plk1 | 3FVH | 0.655 | 12.362 | 9.376 | 22 | 12 | 14 |
| pnk | 2W3O | 28.835 | -5.080 | -23.878 | 16 | 22 | 22 |
| pop | 3DDU | -4.757 | 13.470 | 34.000 | 20 | 16 | 20 |
| ppar_g | 3AN3 | 18.921 | 73.753 | 11.153 | 24 | 26 | 24 |
| prp31 | 2OZB | -5.633 | -29.445 | 10.077 | 30 | 28 | 28 |
| pten | 1D5R | 32.000 | 87.025 | 24.255 | 14 | 14 | 12 |
| pxr | 1M13 | 14.282 | 74.983 | 0.974 | 30 | 36 | 32 |
| pyk2 | 3FZS | -2.502 | -2.819 | 13.265 | 20 | 20 | 20 |
| rac1 | 4GZL | -10.630 | -6.059 | 12.325 | 28 | 20 | 18 |
| rack1 | 4AOW | -7.151 | -63.398 | -5.935 | 22 | 20 | 40 |
| raf | 3C4C | 6.651 | 24.264 | 34.675 | 36 | 36 | 36 |
| rar | 4DQM | -2.149 | -21.501 | 14.594 | 20 | 14 | 26 |
| ras | 3GFT | 11.333 | 33.635 | 19.939 | 22 | 18 | 20 |
| ret | 2X2K | -9.887 | 8.110 | 10.108 | 22 | 18 | 18 |
| rihb | 3B9X | -16.483 | 13.405 | 15.473 | 24 | 24 | 24 |
| ring3 | 4FLP | 11.621 | 6.748 | -53.930 | 20 | 22 | 20 |
| rnase_a | 4G8V | 34.391 | 0.156 | 11.313 | 22 | 34 | 28 |
| rock1 | 3TWJ | 16.506 | 33.311 | 15.984 | 18 | 20 | 26 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| rxr | 4M8H | 61.454 | 46.549 | 30.542 | 24 | 14 | 22 |
| s6k_alpha1 | 2Z7Q | 2.918 | -2.632 | 23.470 | 22 | 26 | 22 |
| sirt1 | 4I5I | 46.030 | -26.747 | 18.672 | 26 | 32 | 26 |
| soyb_lox | 1HU9 | 25.999 | 3.901 | 12.148 | 26 | 22 | 32 |
| srpk | 1WBP | 20.000 | 39.793 | 7.000 | 16 | 20 | 14 |
| stat1_s1 | 1YVL | -15.427 | -1.000 | 126.502 | 22 | 26 | 22 |
| stat1_s2 | 1YVL | -17.904 | -15.031 | 114.432 | 26 | 24 | 24 |
| stat3 | 1BG1 | 96.616 | 73.201 | 68.027 | 22 | 22 | 22 |
| strad_alpha | 3GNI | 2.435 | -20.980 | -28.236 | 26 | 20 | 28 |
| survivin | 1XOX | -25.152 | -39.750 | -77.198 | 24 | 24 | 36 |
| syk | 3FQH | -4.383 | -5.583 | 10.308 | 20 | 20 | 18 |
| tank1 | 2RF5 | -13.446 | -20.332 | -24.937 | 20 | 20 | 22 |
| tank2 | 3KR8 | 38.766 | -11.747 | -12.114 | 16 | 16 | 18 |
| tao2 | 2GCD | 45.644 | 56.288 | 0.502 | 22 | 20 | 20 |
| tdp1 | 1RFF | 7.194 | 54.070 | -1.204 | 36 | 36 | 36 |
| tie2 | 2OO8 | 54.000 | 2.432 | 73.772 | 14 | 16 | 20 |
| tip1 | 2L4T | -7.260 | -6.905 | 6.757 | 32 | 26 | 32 |
| top2B_3qx3 | 3QX3 | 33.969 | 94.096 | 50.851 | 28 | 30 | 26 |
| top2B_4g0v | 4G0V | 33.969 | 94.096 | 50.851 | 28 | 30 | 26 |
| topII | 1ZXM | 28.160 | 33.381 | 32.264 | 30 | 30 | 30 |
| topII_atp | 1QZR | 35.098 | -0.762 | 38.389 | 22 | 20 | 22 |
| topI | 1K4T | 21.005 | -3.741 | 28.466 | 16 | 22 | 10 |
| tp | 1UOU | -4.500 | 2.335 | 27.725 | 28 | 24 | 28 |
| ts | 3NCL | 0.231 | 13.226 | 17.549 | 16 | 20 | 16 |
| upa | 2VIP | 27.065 | 8.579 | 28.568 | 18 | 16 | 16 |
| vegfr1 | 1FLT | 19.812 | -3.886 | 8.346 | 24 | 28 | 30 |
| vegfr2 | 3EWH | 14.078 | -6.092 | 8.682 | 36 | 36 | 36 |
| wee1 | 1X8B | 4.307 | 53.947 | 25.912 | 16 | 16 | 16 |
| wif1 | 2YGN | 6.798 | -14.342 | 16.307 | 28 | 26 | 16 |
| xiap | 1TFT | -6.421 | -11.133 | 3.653 | 20 | 18 | 18 |
| zap70 | 1U59 | 11.166 | 5.172 | 54.018 | 22 | 18 | 20 |
| zf21 | 2RRF | 1.475 | -2.295 | -0.414 | 56 | 48 | 42 |

a. After visual inspection, we noticed that the reported grid dimensions were too small for some “blanks”, causing poor predicted binding affinity values. In these cases (cutoff = -4.0 kcal/mol), we enlarged the grid dimensions of the specific target of 6 points along the x,y,z axes.

**Table S2**. Final ranking of 166 interacting targets of SR141716, from the highest to the lowest normalized V values, and related original predicted binding affinities before normalization. The averaged predicted binding affinity calculated for the 30 “blanks” against each target is reported in the last column. The remaining 140 targets from the original panel of 306 items were not considered for the normalization due to the poor predicted binding affinities with SR141716 (cutoff=-7.5 kcal/mol).

| Position in the ranking | Target | PDB code | V | Predicted binding affinity of SR141716 (kcal/mol) | Averaged predicted binding affinity calculated for "blanks" (kcal/mol) |
|---|---|---|---|---|---|
| 1 | a2a_ant | 3EML | 1.256 | -11.4 | -9.1 |
| 2 | erbB4 | 2R4B | 1.221 | -10.2 | -8.4 |
| 3 | p300 | 3BIY | 1.214 | -11.2 | -9.2 |
| 4 | upa | 2VIP | 1.197 | -9.1 | -7.6 |
| 5 | brd9 | 4XY9 | 1.196 | -8.8 | -7.4 |
| 6 | topI | 1K4T | 1.183 | -11.0 | -9.3 |
| 7 | chk2 | 2W7X | 1.182 | -10.4 | -8.8 |
| 8 | mlk1 | 3DTC | 1.179 | -10.8 | -9.2 |
| 9 | mek1_adp | 1S9J | 1.166 | -9.6 | -8.2 |
| 10 | jak1 | 3EYG | 1.163 | -9.4 | -8.1 |
| 11 | alk5 | 2WOU | 1.143 | -9.7 | -8.5 |
| 12 | lsd1 | 2EJR | 1.128 | -9.9 | -8.8 |
| 13 | lsd1_FAD | 2EJR | 1.127 | -9.9 | -8.8 |
| 14 | cdk2_alt | 2WIH | 1.126 | -9.9 | -8.8 |
| 15 | dcr3 | 3K51 | 1.118 | -7.6 | -6.8 |
| 16 | enolase3_gr1 | 2XSX | 1.102 | -7.5 | -6.8 |
| 17 | lyn | 2ZVA | 1.100 | -9.3 | -8.5 |
| 18 | pkc_eta | 3TXO | 1.100 | -10.0 | -9.1 |
| 19 | camKIIB | 3BHH | 1.097 | -9.1 | -8.3 |
| 20 | mmp13 | 830C | 1.093 | -9.7 | -8.9 |
| 21 | cdk2 | 2VV9 | 1.092 | -9.5 | -8.7 |
| 22 | abl | 2HYY | 1.092 | -9.5 | -8.7 |
| 23 | ring3 | 4FLP | 1.091 | -8.9 | -8.2 |
| 24 | ppar_g | 3AN3 | 1.087 | -9.4 | -8.6 |
| 25 | CPU | 3D67 | 1.083 | -8.9 | -8.2 |
| 26 | pkct | 2JED | 1.083 | -10.4 | -9.6 |
| 27 | hsp90 | 2WI6 | 1.080 | -8.7 | -8.1 |
| 28 | aif | 1M6I | 1.080 | -10.7 | -9.9 |
| 29 | mek1_no_adp_no_lig | 1S9J | 1.074 | -9.2 | -8.6 |
| 30 | EPHb4 | 2X9F | 1.071 | -9.1 | -8.5 |
| 31 | jnk3 | 2ZDT | 1.071 | -9.0 | -8.4 |
| 32 | s6k_alpha1 | 2Z7Q | 1.071 | -8.8 | -8.2 |
| 33 | alk | 2XP2 | 1.068 | -8.3 | -7.8 |

| | | | | | |
|---|---|---|---|---|---|
| 34 | erbB4_alt | 3BBT | 1.066 | -9.3 | -8.7 |
| 35 | survivin | 1XOX | 1.065 | -9.0 | -8.5 |
| 36 | brd9_alt | 5IGN | 1.065 | -8.5 | -8.0 |
| 37 | atad2 | 3DAI | 1.065 | -8.0 | -7.5 |
| 38 | pkca | 3IW4 | 1.064 | -9.4 | -8.8 |
| 39 | akt1 | 3MVH | 1.063 | -9.7 | -9.1 |
| 40 | clk1 | 1Z57 | 1.062 | -9.7 | -9.1 |
| 41 | msk1 | 3KN5 | 1.062 | -9.2 | -8.7 |
| 42 | igf | 3F5P | 1.062 | -8.8 | -8.3 |
| 43 | bap1 | 2W15 | 1.059 | -8.4 | -7.9 |
| 44 | gsk3 | 3F7Z | 1.057 | -9.0 | -8.5 |
| 45 | mmp8 | 2OY2 | 1.055 | -9.3 | -8.8 |
| 46 | tank2 | 3KR8 | 1.054 | -8.3 | -7.9 |
| 47 | metap2 | 1YW9 | 1.053 | -8.7 | -8.3 |
| 48 | calmodulin | 3EWT | 1.053 | -8.2 | -7.8 |
| 49 | mdm2 | 3EQS | 1.052 | -8.0 | -7.6 |
| 50 | pcaf | 2RNW | 1.050 | -8.1 | -7.7 |
| 51 | fgfr2 | 2PVF | 1.049 | -9.2 | -8.8 |
| 52 | mk2 | 3M42 | 1.048 | -8.1 | -7.7 |
| 53 | zap70 | 1U59 | 1.047 | -9.0 | -8.6 |
| 54 | pyk2 | 3FZS | 1.046 | -8.7 | -8.3 |
| 55 | fak | 3BZ3 | 1.046 | -8.6 | -8.2 |
| 56 | clk3 | 2WU6 | 1.045 | -9.7 | -9.3 |
| 57 | mek1 | 3DV3 | 1.045 | -8.9 | -8.5 |
| 58 | top2B | 3QX3 | 1.043 | -9.8 | -9.4 |
| 59 | hsc70 | 3FZH | 1.043 | -8.9 | -8.5 |
| 60 | 17hsd3 | 3KLM | 1.040 | -7.7 | -7.4 |
| 61 | ftase | 1LD8 | 1.039 | -8.9 | -8.6 |
| 62 | hla1 | 3BO8 | 1.038 | -8.3 | -8.0 |
| 63 | jnk1 | 4IZY | 1.036 | -8.3 | -8.0 |
| 64 | hdac2 | 3MAX | 1.034 | -7.9 | -7.6 |
| 65 | tdp1 | 1RFF | 1.033 | -7.7 | -7.5 |
| 66 | hdac8b | 1VKG | 1.031 | -9.1 | -8.8 |
| 67 | cdk9 | 3BLQ | 1.029 | -8.4 | -8.2 |
| 68 | mps1 | 4H7X | 1.028 | -7.7 | -7.5 |
| 69 | dapk | 3EH9 | 1.027 | -8.9 | -8.7 |
| 70 | pkc_iota_apo | 3A8X | 1.026 | -9.1 | -8.9 |
| 71 | wif1 | 2YGN | 1.025 | -9.8 | -9.6 |
| 72 | pkc_iota_2 | 1ZRZ | 1.025 | -8.8 | -8.6 |
| 73 | ca_2 | 2X7S | 1.024 | -8.7 | -8.5 |
| 74 | hspa6B | 3FE1 | 1.023 | -7.6 | -7.4 |
| 75 | EPHa3 | 3DZQ | 1.022 | -8.2 | -8.0 |
| 76 | pop | 3DDU | 1.022 | -7.9 | -7.7 |
| 77 | nq02 | 3TZB | 1.021 | -9.6 | -9.4 |
| 78 | dyrk_1a | 3ANQ | 1.021 | -9.4 | -9.2 |
| 79 | pimkin | 3JYA | 1.021 | -8.9 | -8.7 |
| 80 | pkc_iota | 3A8W | 1.021 | -8.7 | -8.5 |

| | | | | | |
|---|---|---|---|---|---|
| 81 | mtor | 3FAP | 1.021 | -10.4 | -10.2 |
| 82 | CPA | 1CBX | 1.019 | -7.7 | -7.6 |
| 83 | lck | 3AD4 | 1.018 | -8.2 | -8.1 |
| 84 | ck2_alt | 3PE1 | 1.018 | -8.1 | -8.0 |
| 85 | topII | 1ZXM | 1.018 | -7.9 | -7.8 |
| 86 | haspin | 3E7V | 1.017 | -8.7 | -8.6 |
| 87 | fadk1 | 3BZ3 | 1.017 | -8.6 | -8.5 |
| 88 | irak4 | 2NRU | 1.016 | -9.3 | -9.2 |
| 89 | cmet | 2WGJ | 1.015 | -8.9 | -8.8 |
| 90 | mthfs | 3HY3 | 1.015 | -8.0 | -7.9 |
| 91 | brd3_bd1 | 3S91 | 1.013 | -7.8 | -7.7 |
| 92 | caspase3 | 3EDQ | 1.011 | -7.6 | -7.5 |
| 93 | pka_c_alpha | 4AXA | 1.010 | -9.6 | -9.5 |
| 94 | rack1 | 4AOW | 1.010 | -9.1 | -9.0 |
| 95 | cdk7 | 1UA2 | 1.009 | -9.1 | -9.0 |
| 96 | bclw | 1ZY3 | 1.008 | -9.1 | -9.0 |
| 97 | srpk | 1WBP | 1.008 | -7.9 | -7.8 |
| 98 | fpps_allo | 3N1V | 1.007 | -8.1 | -8.0 |
| 99 | caspase7 | 1SHL | 1.003 | -8.8 | -8.8 |
| 100 | jnk3_alt | 3KVX | 1.002 | -8.3 | -8.3 |
| 101 | brdt | 4KCX | 1.002 | -8.3 | -8.3 |
| 102 | ret | 2X2K | 1.001 | -8.1 | -8.1 |
| 103 | hspa1lB | 3GDQ | 0.998 | -8.3 | -8.3 |
| 104 | fgfr1 | 1AGW | 0.998 | -7.9 | -7.9 |
| 105 | btk | 3PIX | 0.995 | -8.0 | -8.0 |
| 106 | nek2 | 2XKF | 0.994 | -8.0 | -8.0 |
| 107 | mek2_no_adp_no_lig | 1S9I | 0.992 | -8.3 | -8.4 |
| 108 | rar | 4DQM | 0.990 | -8.6 | -8.7 |
| 109 | mtsp1 | 3NCL | 0.990 | -8.4 | -8.5 |
| 110 | pdk1 | 3NAX | 0.989 | -8.7 | -8.8 |
| 111 | jmjd3_akg | 2XXZ | 0.989 | -7.7 | -7.8 |
| 112 | pkcbII | 2I0E | 0.988 | -8.7 | -8.8 |
| 113 | brd9_4nqn | 4NQN | 0.988 | -8.0 | -8.1 |
| 114 | mpges_1_4al1 | 4AL1 | 0.987 | -8.9 | -9.0 |
| 115 | ts | 3NCL | 0.987 | -8.6 | -8.7 |
| 116 | topII_atp | 1QZR | 0.985 | -9.1 | -9.2 |
| 117 | rock1 | 3TWJ | 0.985 | -8.3 | -8.4 |
| 118 | jak3 | 1YVJ | 0.981 | -8.3 | -8.5 |
| 119 | p38 | 3HEG | 0.981 | -8.1 | -8.3 |
| 120 | top2B_4g0v | 4G0V | 0.975 | -8.7 | -8.9 |
| 121 | mek4_no_anp | 3ALN | 0.975 | -8.3 | -8.5 |
| 122 | cox_2 | 3NT1 | 0.974 | -8.0 | -8.2 |
| 123 | gstp1 | 2A2R | 0.972 | -7.6 | -7.8 |
| 124 | pka | 3L9L | 0.965 | -9.4 | -9.7 |
| 125 | a2a_ago | 2YDV | 0.965 | -9.0 | -9.3 |
| 126 | erk2 | 2OJG | 0.965 | -8.1 | -8.4 |
| 127 | brd4_bd2 | 2YEM | 0.965 | -7.9 | -8.2 |

| | | | | | |
|---|---|---|---|---|---|
| 128 | mmp3 | 1HY7 | 0.964 | -8.7 | -9.0 |
| 129 | cox_1_3kk6 | 3KK6 | 0.963 | -7.5 | -7.8 |
| 130 | jak2 | 3E64 | 0.962 | -8.6 | -8.9 |
| 131 | cSRC | 3F3V | 0.962 | -8.5 | -8.8 |
| 132 | kga | 3VOY | 0.956 | -8.0 | -8.4 |
| 133 | cdk4 | 3G33 | 0.956 | -7.6 | -8.0 |
| 134 | chetk_alpha | 4GC8 | 0.951 | -8.0 | -8.4 |
| 135 | aurkinA | 2W1D | 0.951 | -7.9 | -8.3 |
| 136 | erk1 | 2ZOQ | 0.950 | -8.2 | -8.6 |
| 137 | cdk5 | 1H4L | 0.948 | -7.9 | -8.3 |
| 138 | pi3k | 3ENE | 0.944 | -8.1 | -8.6 |
| 139 | mhp37 | 3E78 | 0.943 | -8.3 | -8.8 |
| 140 | brd3_bd2 | 3S92 | 0.943 | -7.5 | -8.0 |
| 141 | kif11 | 3CJO | 0.941 | -8.2 | -8.7 |
| 142 | pan_bcr_abl | 3IK3 | 0.941 | -8.1 | -8.6 |
| 143 | bcl2 | 2O21 | 0.939 | -7.7 | -8.2 |
| 144 | errG_ant | 1S9Q | 0.934 | -8.5 | -9.1 |
| 145 | diaminoox | 3HIG | 0.932 | -8.3 | -8.9 |
| 146 | bclxl | 1BXL | 0.929 | -7.6 | -8.2 |
| 147 | tao2 | 2GCD | 0.928 | -8.2 | -8.8 |
| 148 | arid3a | 2KK0 | 0.928 | -7.5 | -8.1 |
| 149 | jmjd3 | 2XXZ | 0.927 | -7.5 | -8.1 |
| 150 | ejc | 3EX7 | 0.926 | -8.4 | -9.1 |
| 151 | mpges_1_no_gsh | 4AL0 | 0.920 | -8.0 | -8.7 |
| 152 | vegfr2 | 3EWH | 0.915 | -8.2 | -9.0 |
| 153 | strad_alpha | 3GNI | 0.910 | -7.8 | -8.6 |
| 154 | hspa2 | 3I33 | 0.909 | -8.4 | -9.2 |
| 155 | wee1 | 1X8B | 0.909 | -8.1 | -8.9 |
| 156 | pxr | 1M13 | 0.906 | -8.7 | -9.6 |
| 157 | fpps_no_ipp | 1ZW5 | 0.902 | -7.5 | -8.3 |
| 158 | hmt | 3HNA | 0.898 | -7.9 | -8.8 |
| 159 | cdk8 | 3RGF | 0.898 | -7.5 | -8.4 |
| 160 | nnos | 3JT4 | 0.892 | -8.4 | -9.4 |
| 161 | dhfr | 1PD8 | 0.890 | -8.6 | -9.7 |
| 162 | ras | 3GFT | 0.890 | -7.9 | -8.9 |
| 163 | sirt1 | 4I5I | 0.885 | -8.3 | -9.4 |
| 164 | jnk2 | 3NPC | 0.885 | -7.7 | -8.7 |
| 165 | pkm2 | 4G1N | 0.812 | -7.9 | -9.7 |
| 166 | errB_ant | homology_modeling | 0.797 | -7.7 | -9.7 |

**Supplementary information**

**Figure legends**

**Supplementary Figure S1. Effect of SR141716 treatment on the apoptotic protein expression profiles in CRC cell lines.**

(**a**), Quantitative analysis of representative western blots, showed in Figure 1d, carried out for cleaved Caspase 3 and cleaved PARP in HCT116 and SW48 cells treated with SR141716 (SR, 10μM). Results (arbitrary units; cleaved form/total form/GAPDH) were expressed as mean ± SD of three independent experiments (unpaired two tailed Student's *t*-test *p<0,05, **p<0,01, ***p<0,005 *vs* control). (**b**), Cells were treated with SR141716 (SR, 10μM) for 48h and cell lysates were used to evaluate the protein expression through a Human Apoptosis Antibody Array (Abcam- Cambridge, UK). Left panel shows representative proteomic membrane pictures. Experiments were performed in duplicate. The squares highlighted the significantly modulated proteins not previously analyzed by western blot assay. In the right panel, densitometric analysis of the membrane spots was reported. The analysis was obtained through TotalLab$^{TM}$ software and array data normalization was performed according to manufacturer's instructions. Data were expressed as mean ± SD (unpaired two tailed Student's *t*-test *p<0,05 *vs* control)

**Supplementary Figure S2. Effect of SR141716 on canonical Wnt/β-Catenin pathway.**

Quantitative analysis of representative western blots in Figure 4a showing Wnt3, Dvl3, Fzd7 LRP6 (**a**) and p-GSK3β (**b**) protein levels in HCT116 and SW48 treated with SR141716 or vehicle alone. (**c**), Quantitative analysis of representative western blot for APC showed in Figure 4b and carried out on whole cell extracts from indicated cell lines treated with the compound (SR, 10μM). Results (arbitrary units) were expressed as mean ± SD of three independent experiments (unpaired two tailed Student's *t*-test *p<0,05, **p<0,01, ***p<0,005 *vs* control).

**Supplementary Figure S3. Effect of SR141716 on non canonical Wnt/β-Catenin pathway.**

Quantitative analysis of representative western blots reported in Figure 4c showing Wnt5A and ROR2 protein expression in HCT116 (**a**) and SW48 (**b**) treated with SR141716 (SR, 10μM) or vehicle. (**c**), Quantitative analysis of representative western blot for pCaMKII showed in Figure 4c Results (arbitrary units; phosphorylated form/total form/GAPDH) were expressed as mean ± SD of at least three independent experiments (unpaired two tailed Student's *t*-test *p<0,05, **p<0,01, ***p<0,005 *vs* control).

**Supplementary Figure S4. Transfection efficiency of luciferase assay and expression of ROR2 and LRP5 receptors in CRC cell lines.**

(**a**), Left panel: Fluorescence microphotographs of HCT116 cells transfected with a constitutively expressing GFP reporter construct, used as positive control in the luciferase assays (magnification 10x). Right panel: efficiency of the transfection procedure was calculated as percentage of green cells *versus* total cells (mean of cellular counts performed in at least 5 microphotographs from 4 independent experiments ± SD); unpaired two tailed Student's *t*-test **p<0,01. (**b**) Representative western blots and densitometric analysis of ROR2 and LRP5 receptors constitutively expressed in CRC cell lines used in the study. Results (arbitrary units; receptor/GAPDH) were expressed as mean ± SD. Cropped blots from full-length gels are displayed in b.

**Supplementary Figure S5. SR141716-induced downregulation of Wnt/β-Catenin target genes.**

Quantitative analysis of representative western blot depicted in Figure 5b and 5c for Cyclin D1, c-Myc, COX-2 in total extracts from HCT116 (**a**), SW48 (**b**), DLD1 (**c**) and SW620 (**d**) treated with the compound (SR, 10μM) for the indicated time. Results (arbitrary units) were expressed as mean ± SD (unpaired two tailed Student's *t*-test *p<0,05, **p<0,01, ***p<0,005 *vs* control).

**Supplementary Figure S6. β-Catenin localization and target genes expression in tumor sample from HCT116 xenograft.**

(**a**), Fixed tumor pieces were OCT-embedded, sectioned and labeled with fluorescent antibody against β-Catenin (green fluorescence). Nuclei were stained with Lamin A/C (red fluorescence). Localization of β-Catenin was analyzed in the orthogonal view of 0.5 µm thickness in the z plane. Data are representative of at least three experiments with similar results. (**b**), Quantification of western blot analysis for p-β-Catenin (left panel), Cyclin D1 and c-Myc (right panel) in tumors (n=6 per condition) from HCT116 xenografts s.c. treated with SR141716 or PBS/Glycerol for 42 weeks. Results (arbitrary units) were expressed as mean ± SEM.

**Supplementary Figure S7. SPR interaction analysis of SR141716 binding to immobilized control protein.**

Sensograms obtained from different injections (0.62, 1.25, 2.5, 4 and 5 µM) of SR141716 to immobilized myoglobin.

**Supplementary Figure S8.** Uncropped images for western blots displayed in main figure 1d.

**Supplementary Figure S9.** Uncropped images for western blots displayed in main figure 2.

**Supplementary Figure S10.** Uncropped images for western blots and gels displayed in main figure 3a and 3b, respectively.

**Supplementary Figure S11.** Uncropped images for western blots displayed in main figure 4a (left panel).

**Supplementary Figure S12.** Uncropped images for western blots displayed in main figure 4a (right panel).

**Supplementary Figure S13.** Uncropped images for western blots displayed in main figure 4b.

**Supplementary Figure S14.** Uncropped images for western blots displayed in main figure 4c.

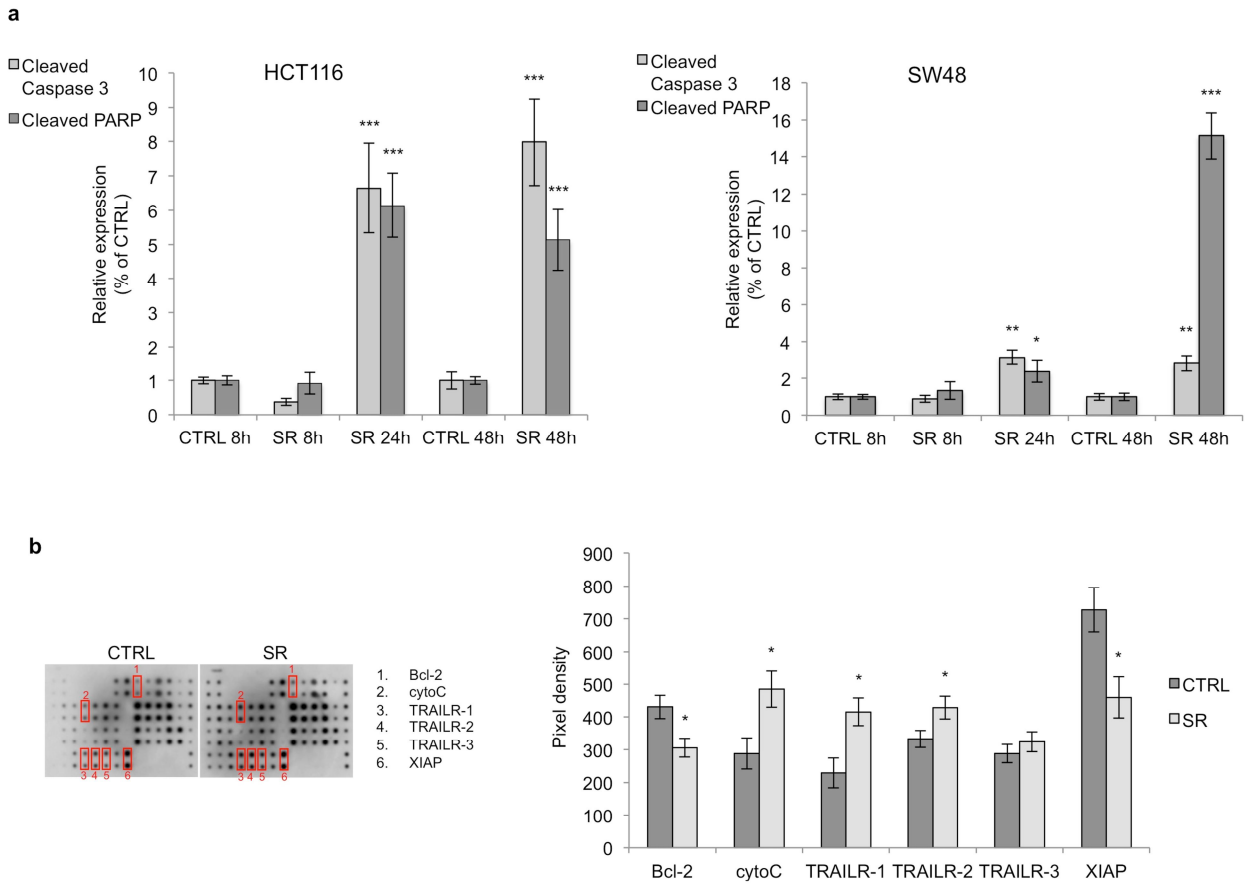
**Supplementary Figure S15.** Uncropped images for western blots displayed in main figure 5b and 5c (upper panel).

**Supplementary Figure S16.** Uncropped images for western blots displayed in main figure 5c (central and lower panel).

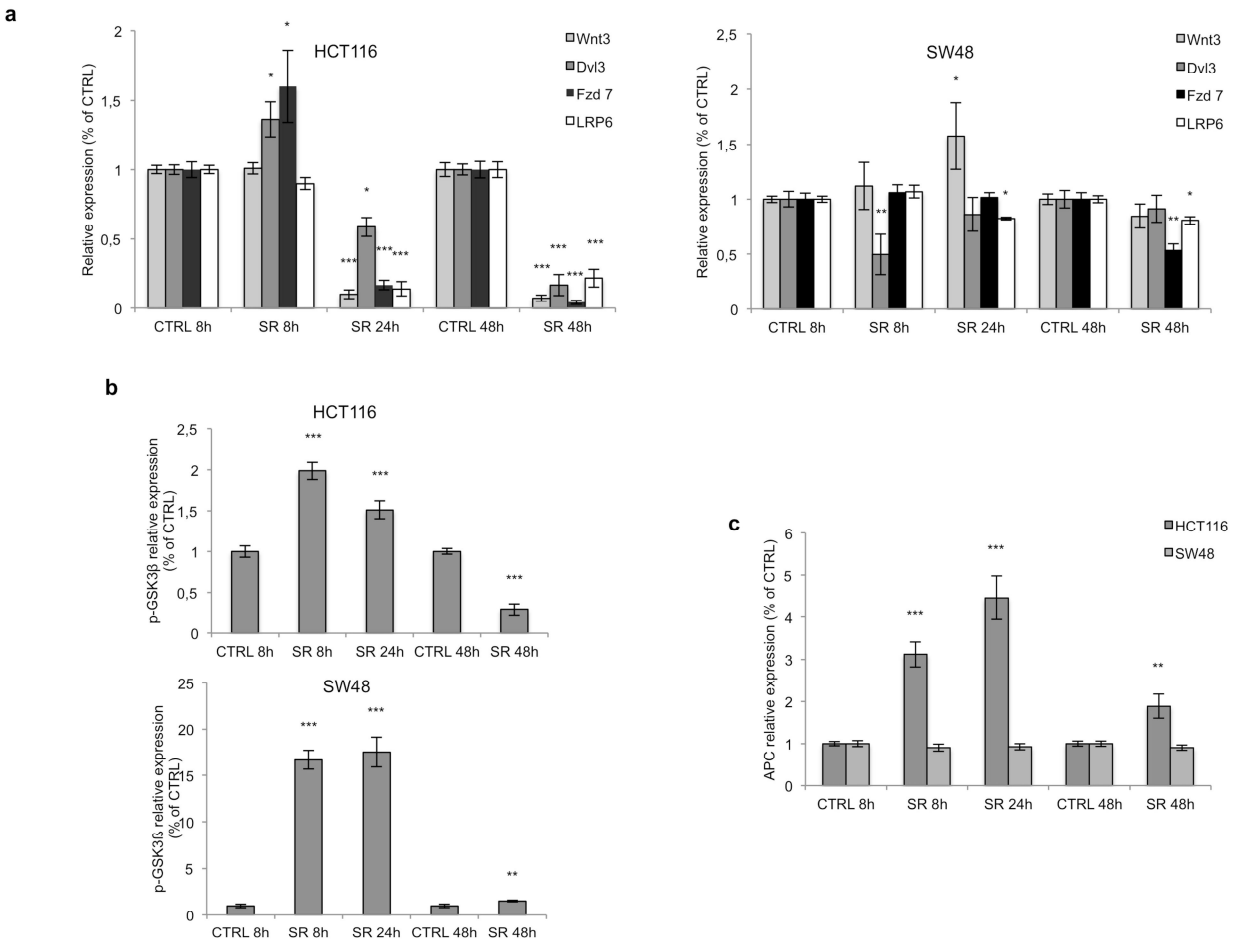
**Supplementary Figure S17.** Uncropped images for western blots displayed in main figure 6d.

**Supplementary Figure S18.** Uncropped images for western blots displayed in main figure 8.

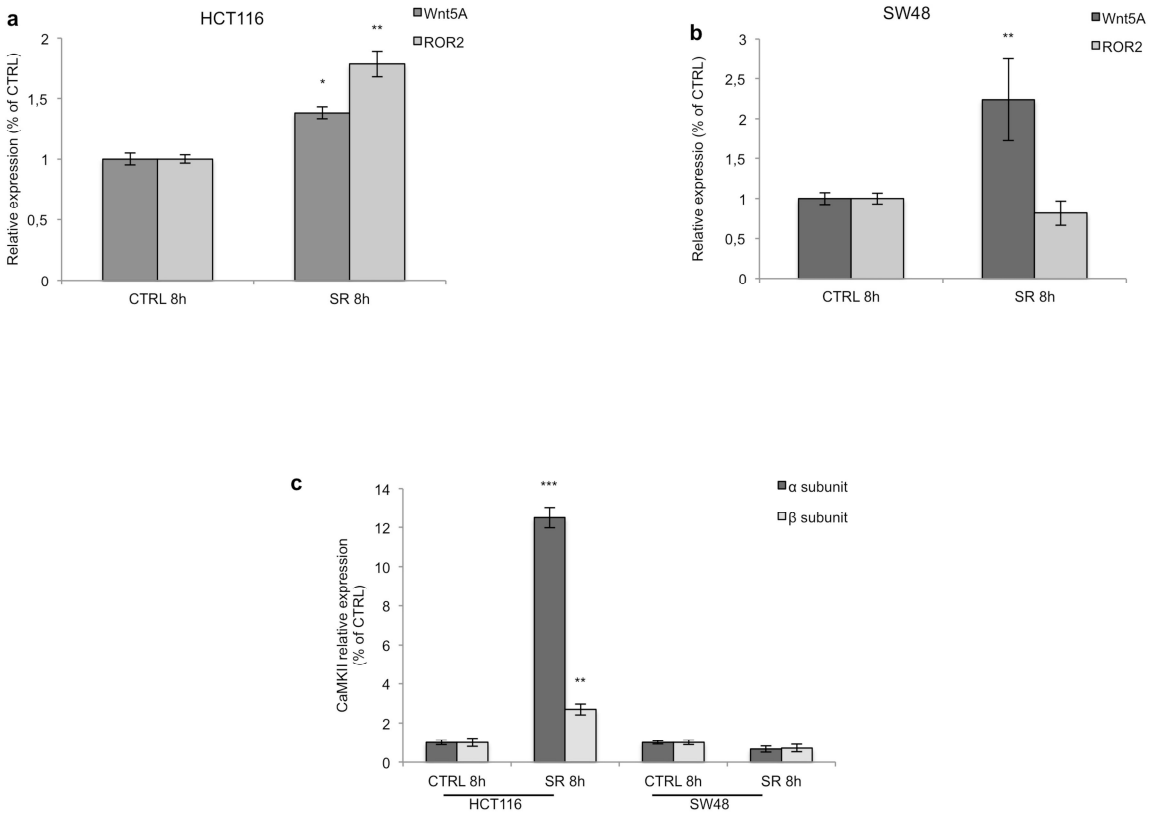
**Supplementary Figure S19.** Uncropped images for western blots displayed in supplementary figure 4b.



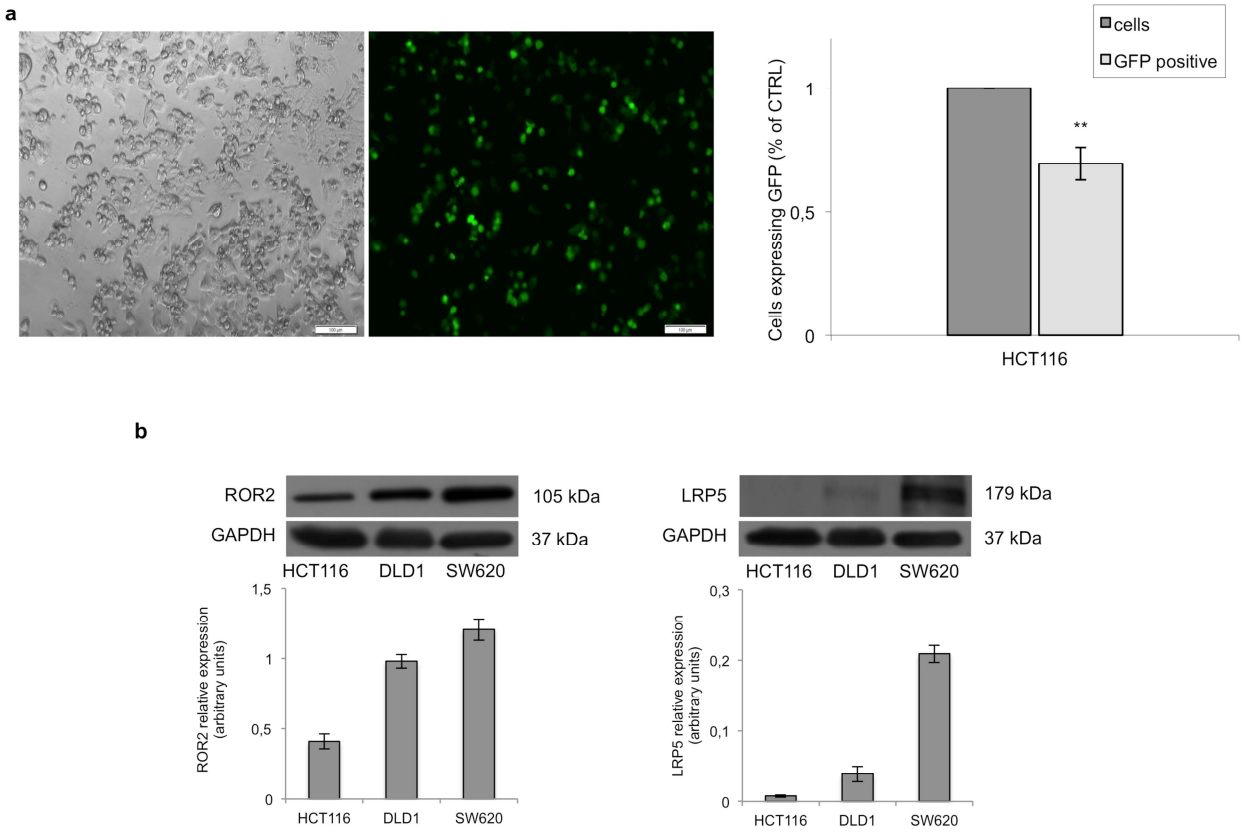

**Supplementary Figure S1**



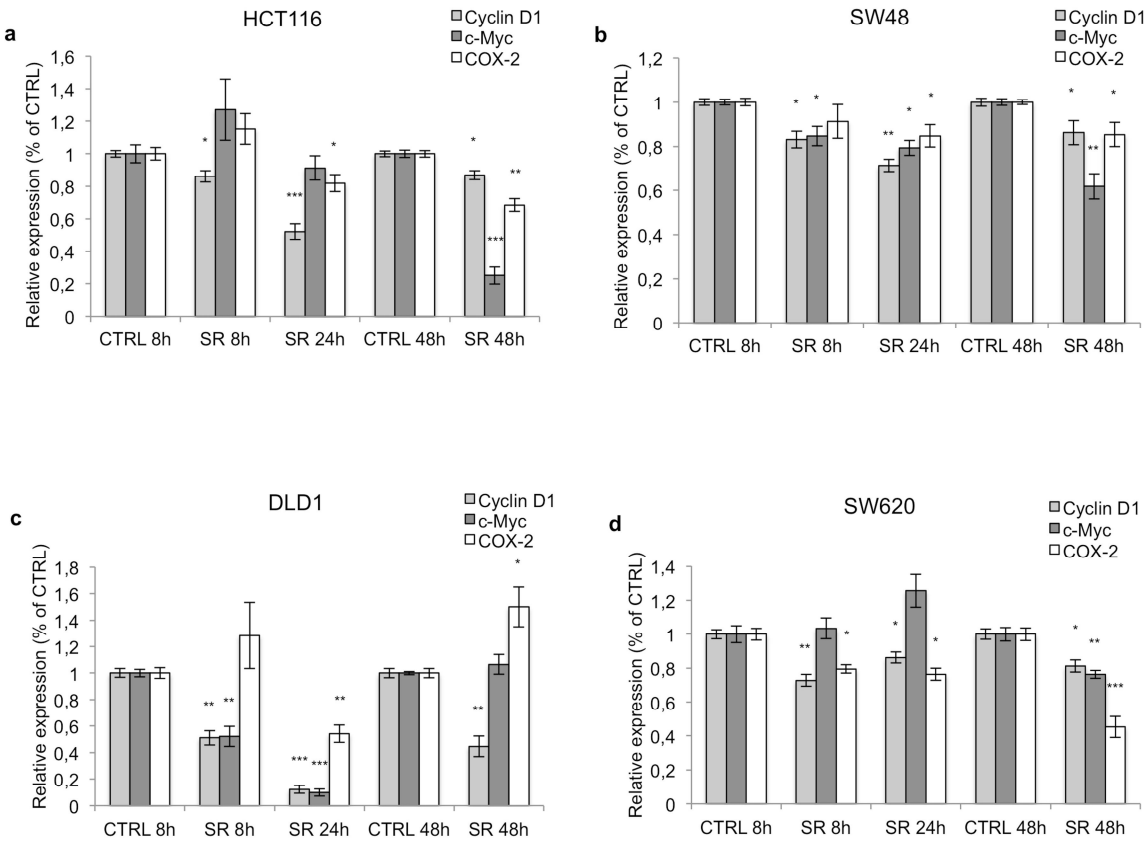

**Supplementary Figure S2**



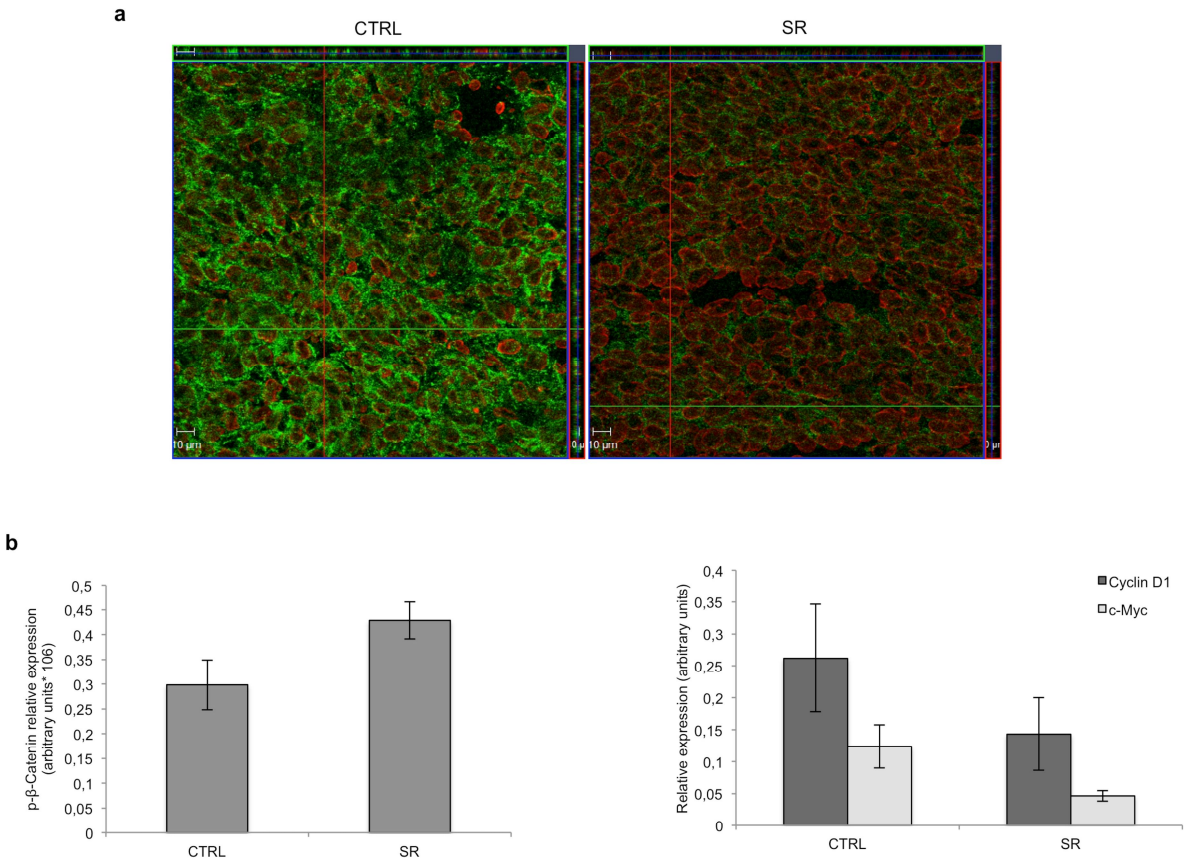

**Supplementary Figure S3**



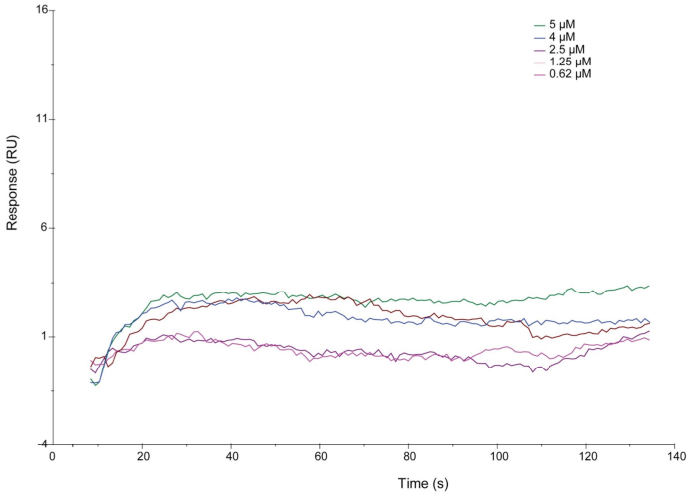

**Supplementary Figure S4**




**Supplementary Figure S5**

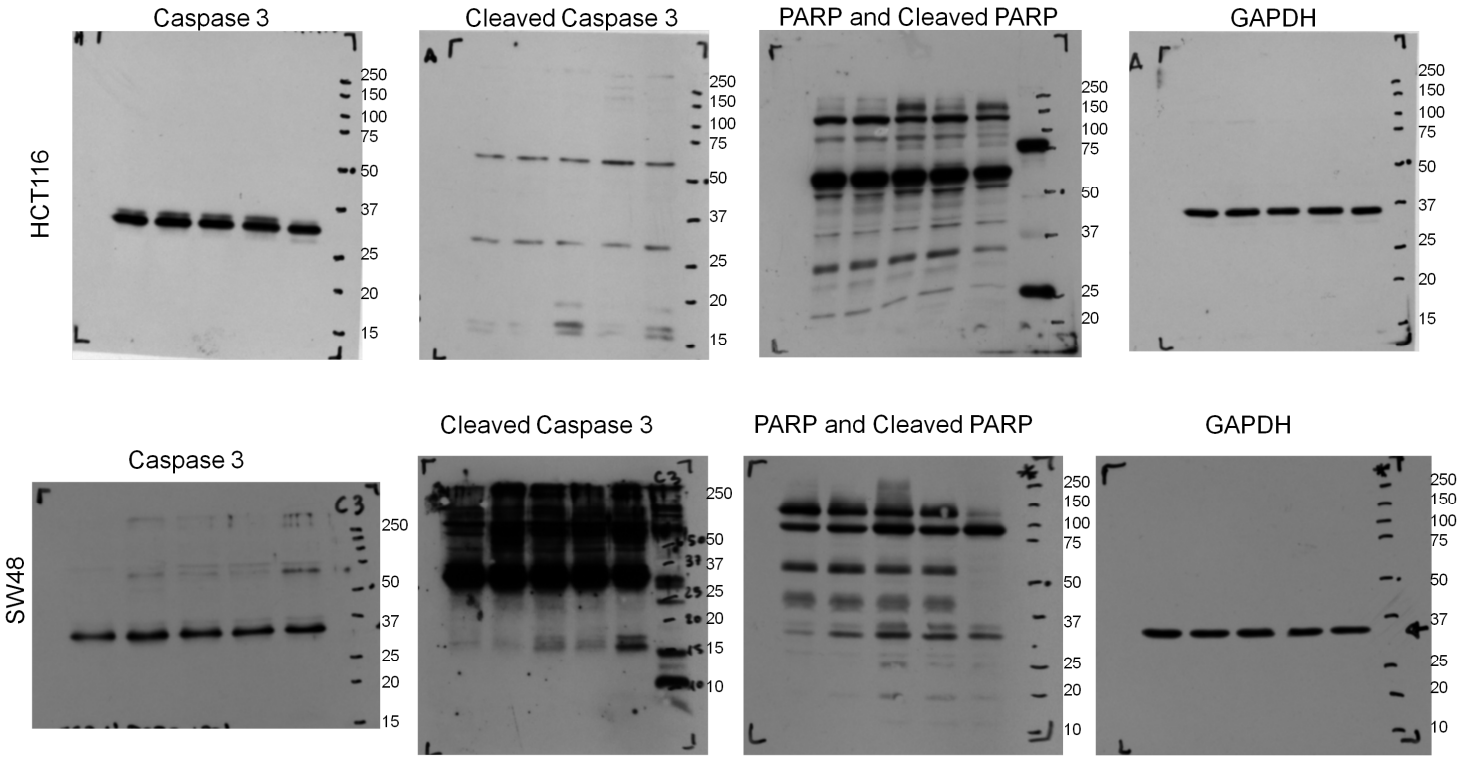



**Supplementary Figure S6**



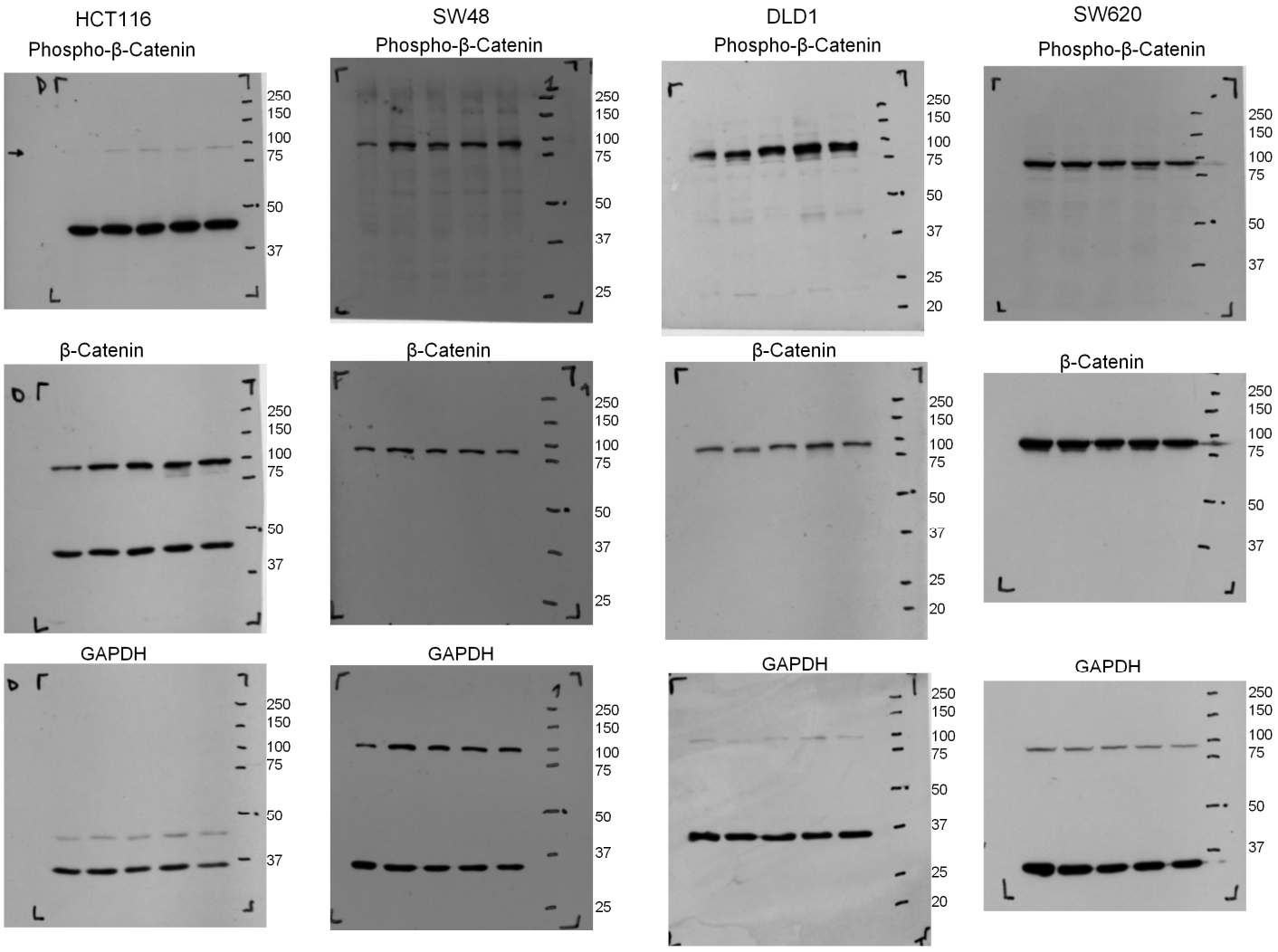

**Supplementary Figure S7**

**Figure 1 d**




**Supplementary Figure S8**

**Figure 2**




**Supplementary Figure S9**

**Figure 3 a**

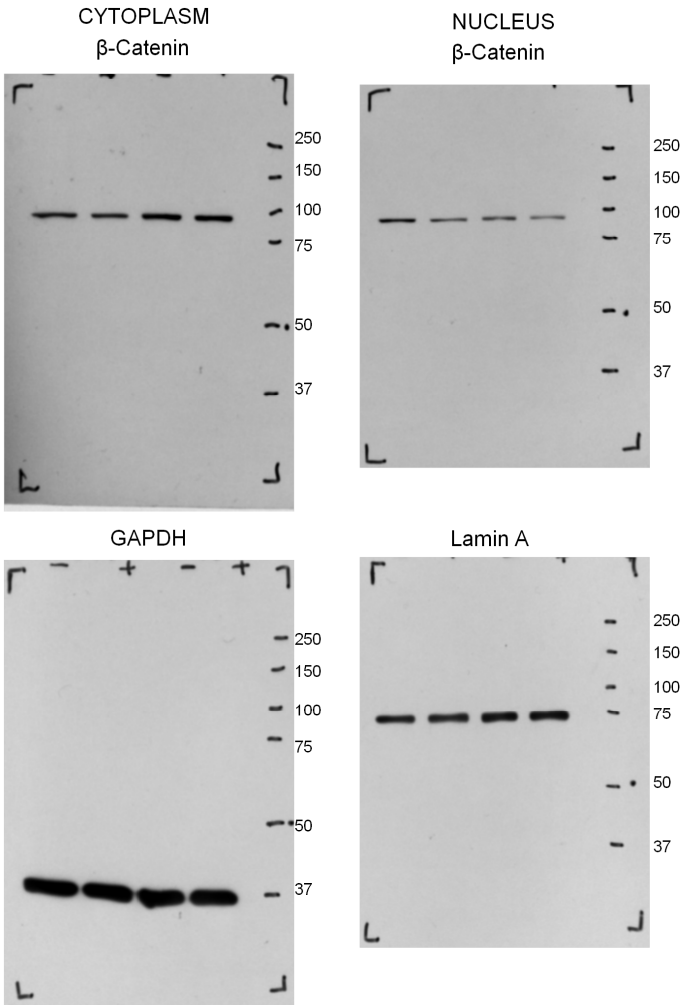
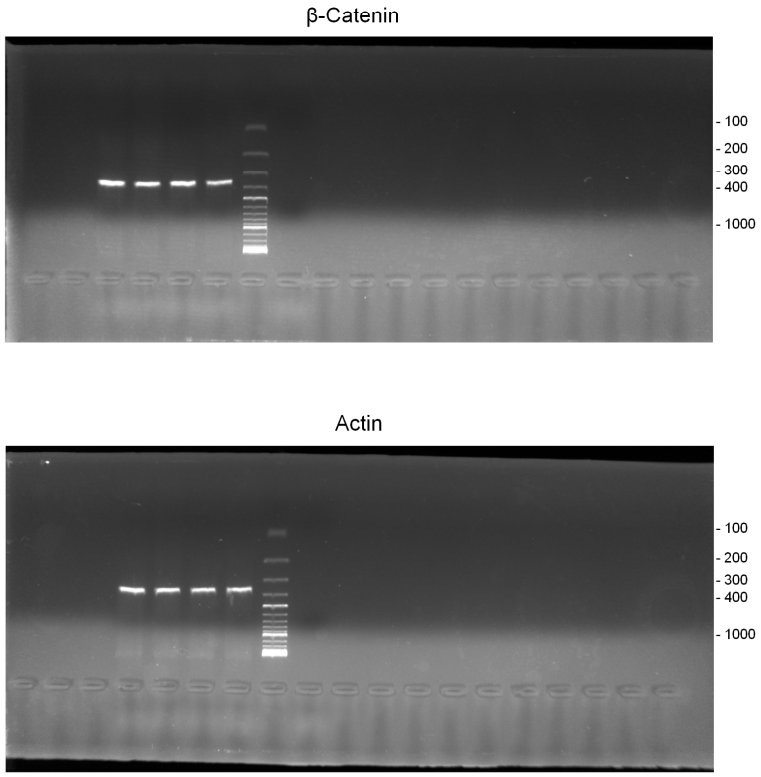
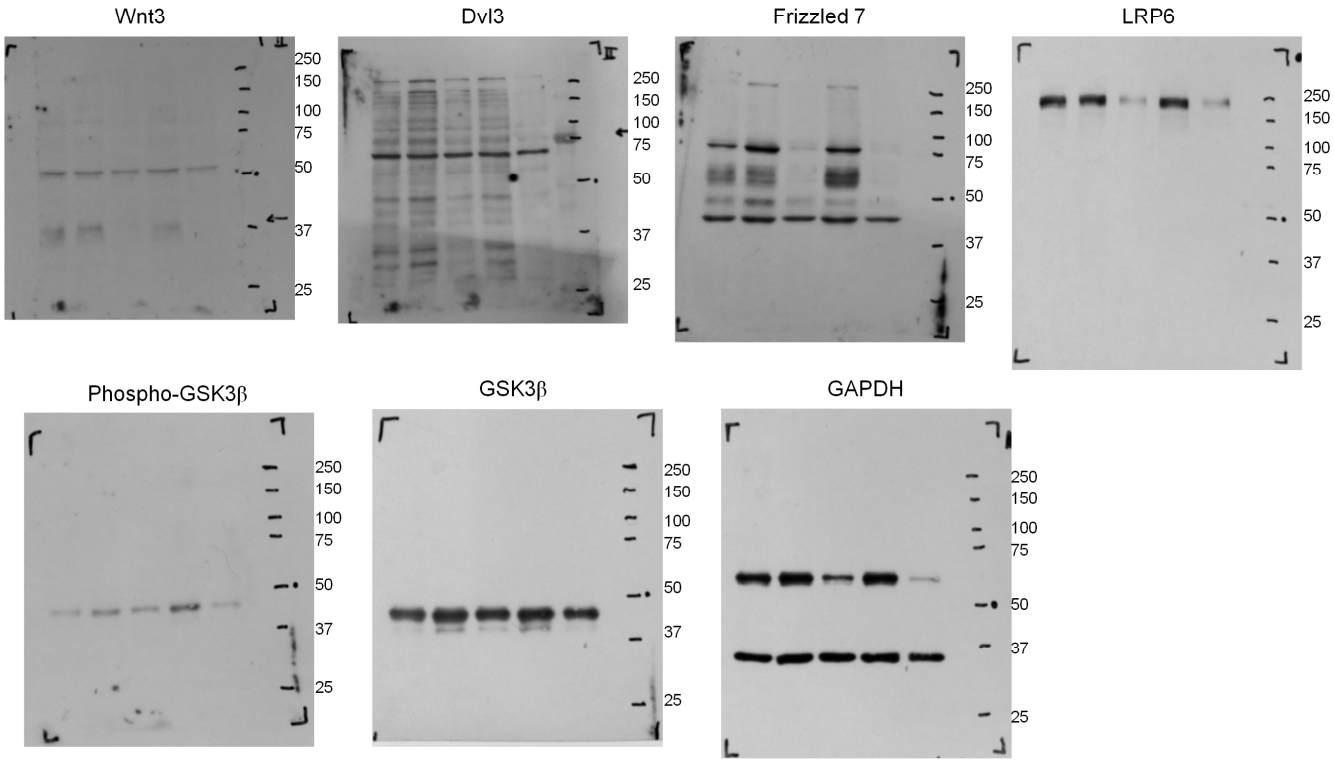



**Figure 3 b**



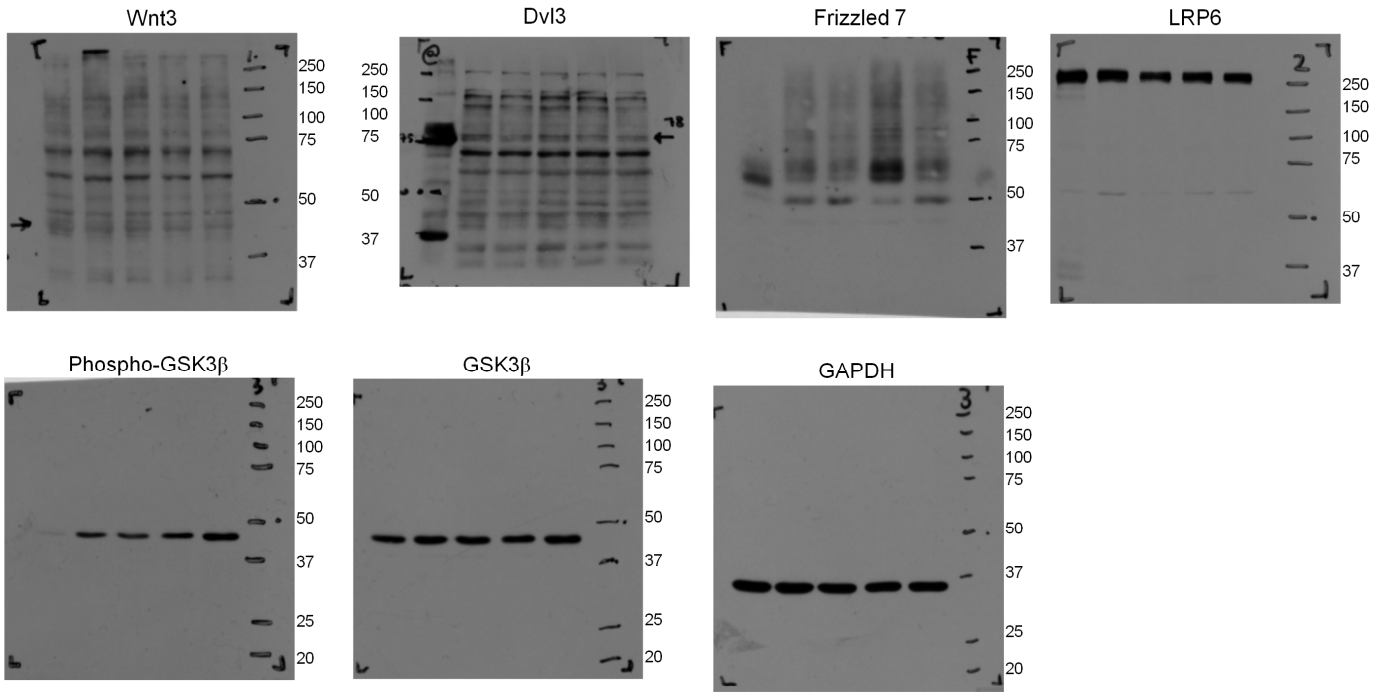

**Supplementary Figure S10**

**Figure 4 a (HCT116, left panel)**




**Supplementary Figure S11**

**Figure 4 a (SW48, right panel)**




**Supplementary Figure S12**

**Figure 4 b (HCT116, upper)**

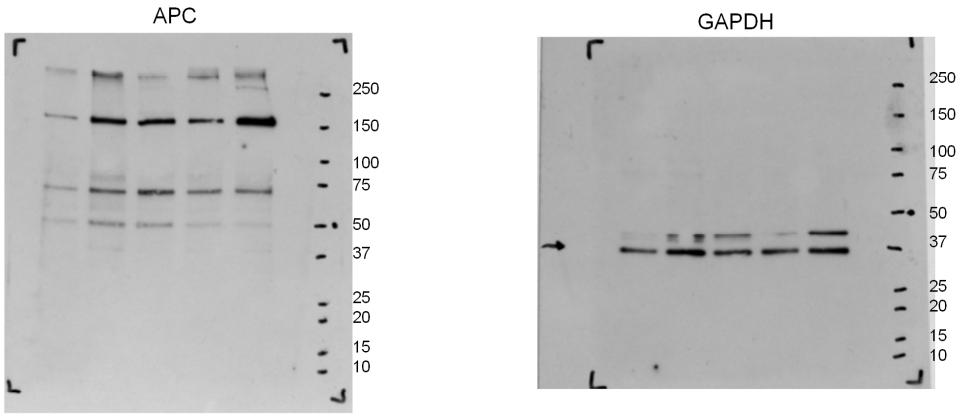
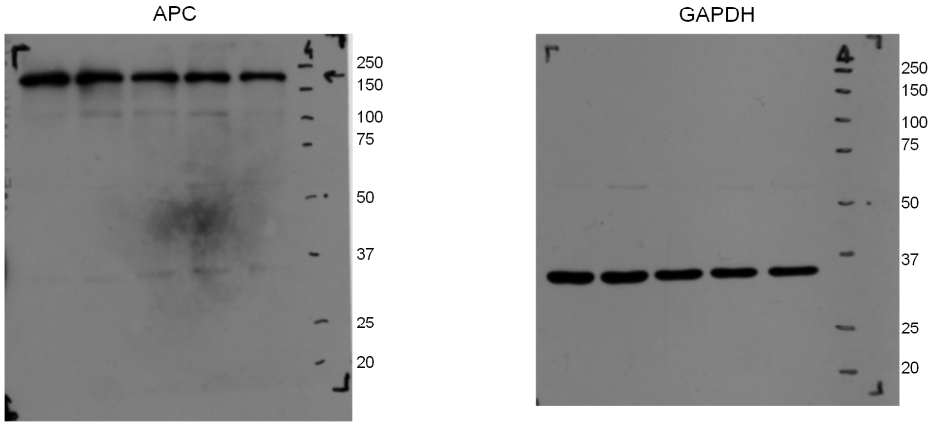



**Figure 4 b (SW48, lower)**




**Supplementary Figure S13**

**Figure 4 c (HCT116, left panel)**

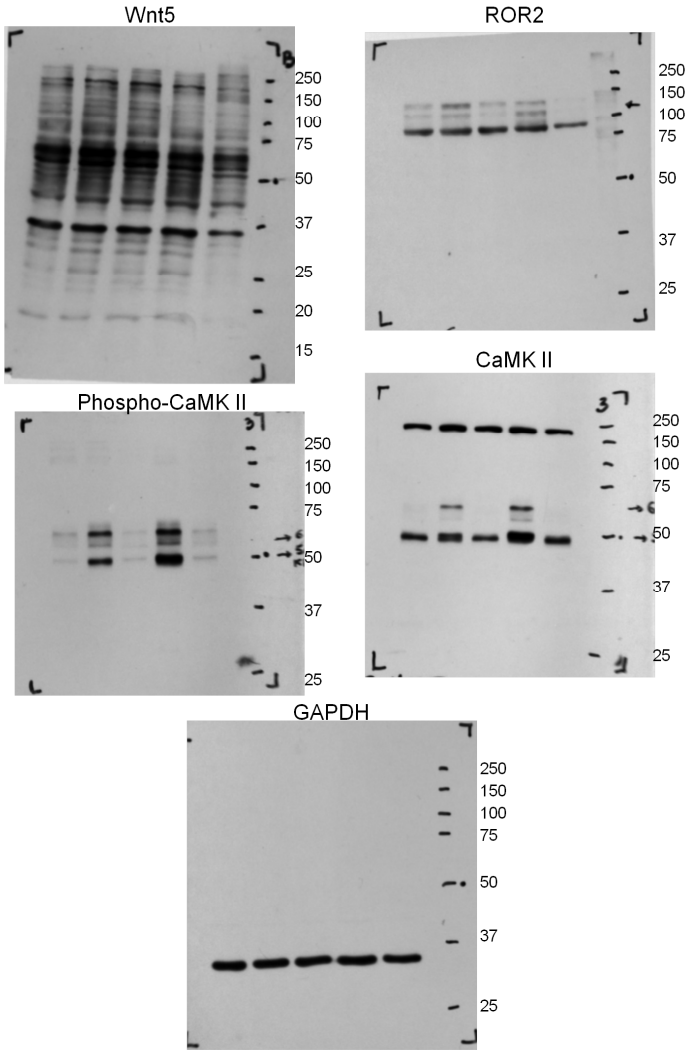
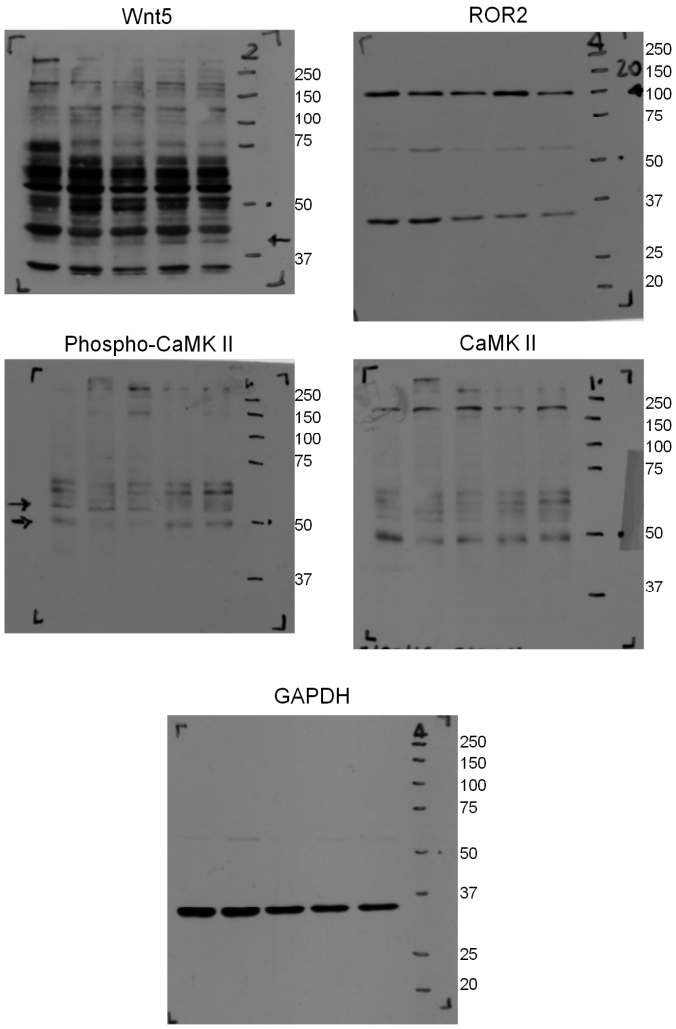



**Figure 4 c (SW48, right panel)**




**Supplementary Figure S14**

**Figure 5 b**

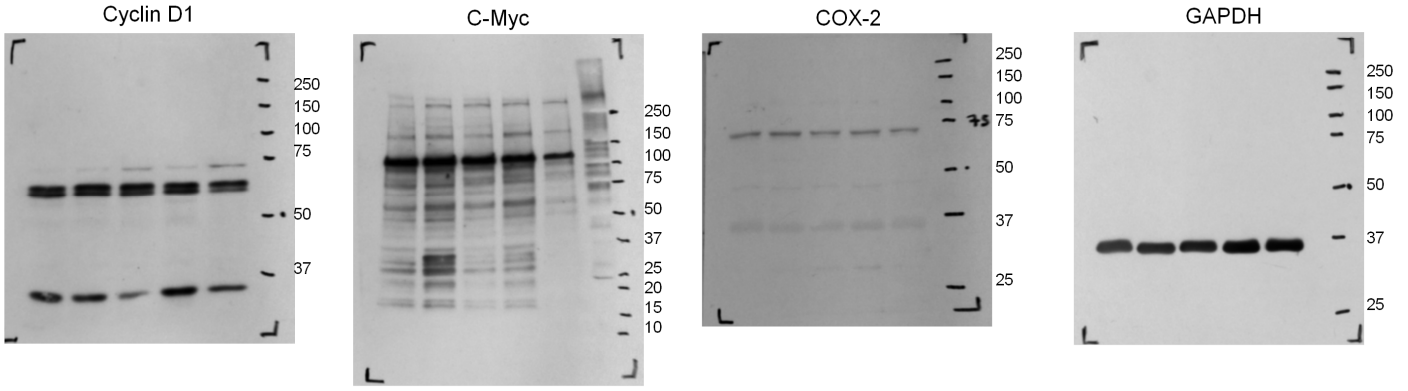
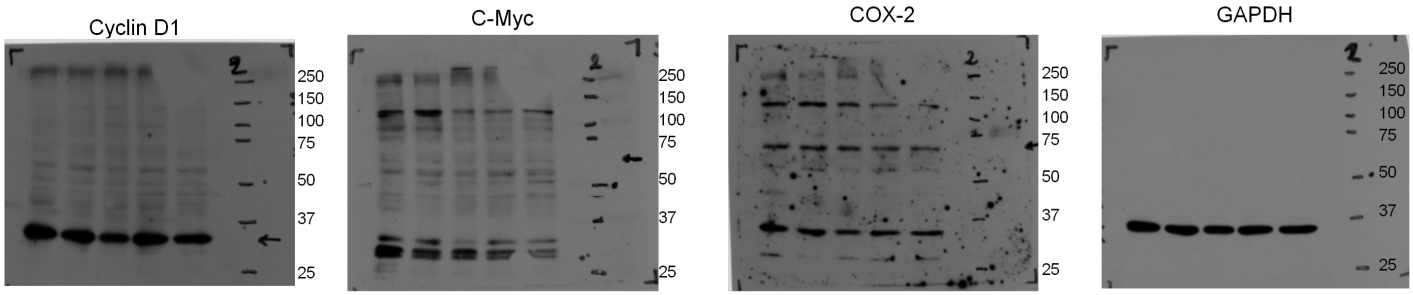



**Figure 5 c (SW48)**




**Supplementary Figure S15**

**Figure 5 c (DLD1)**

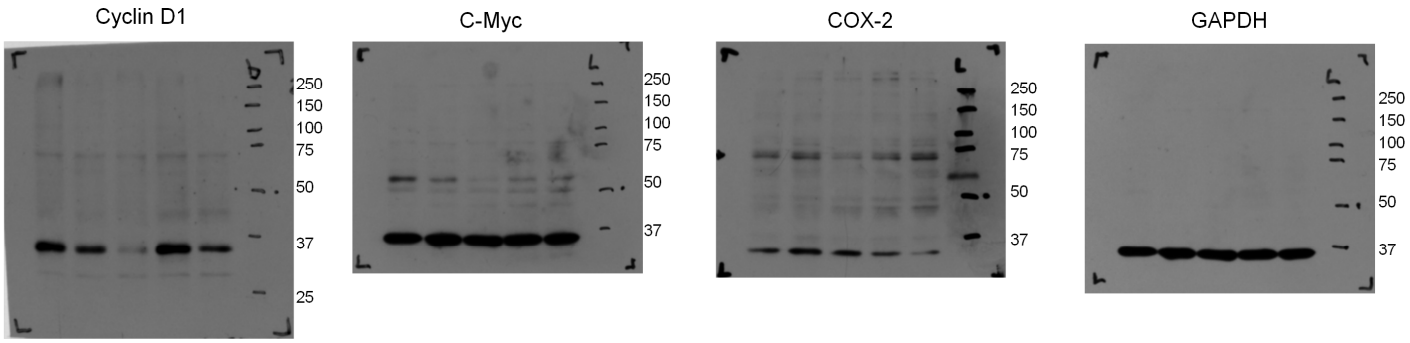
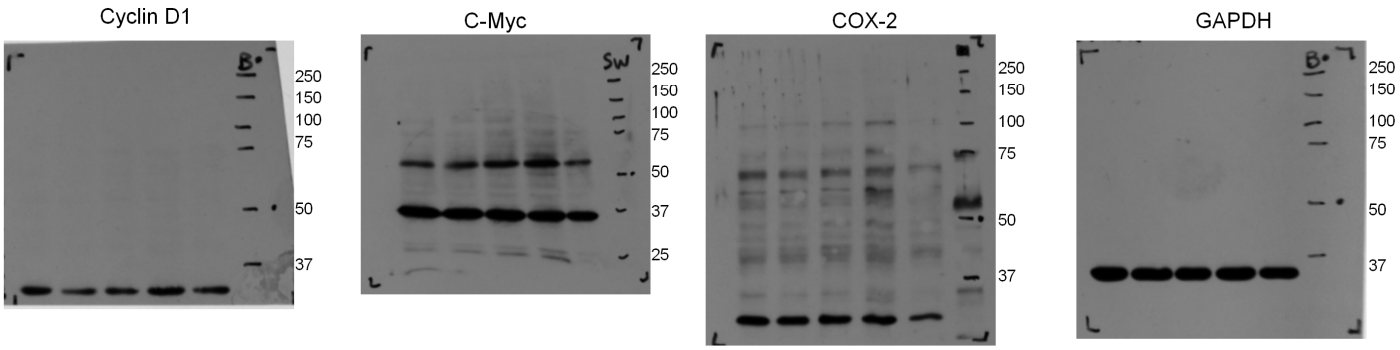
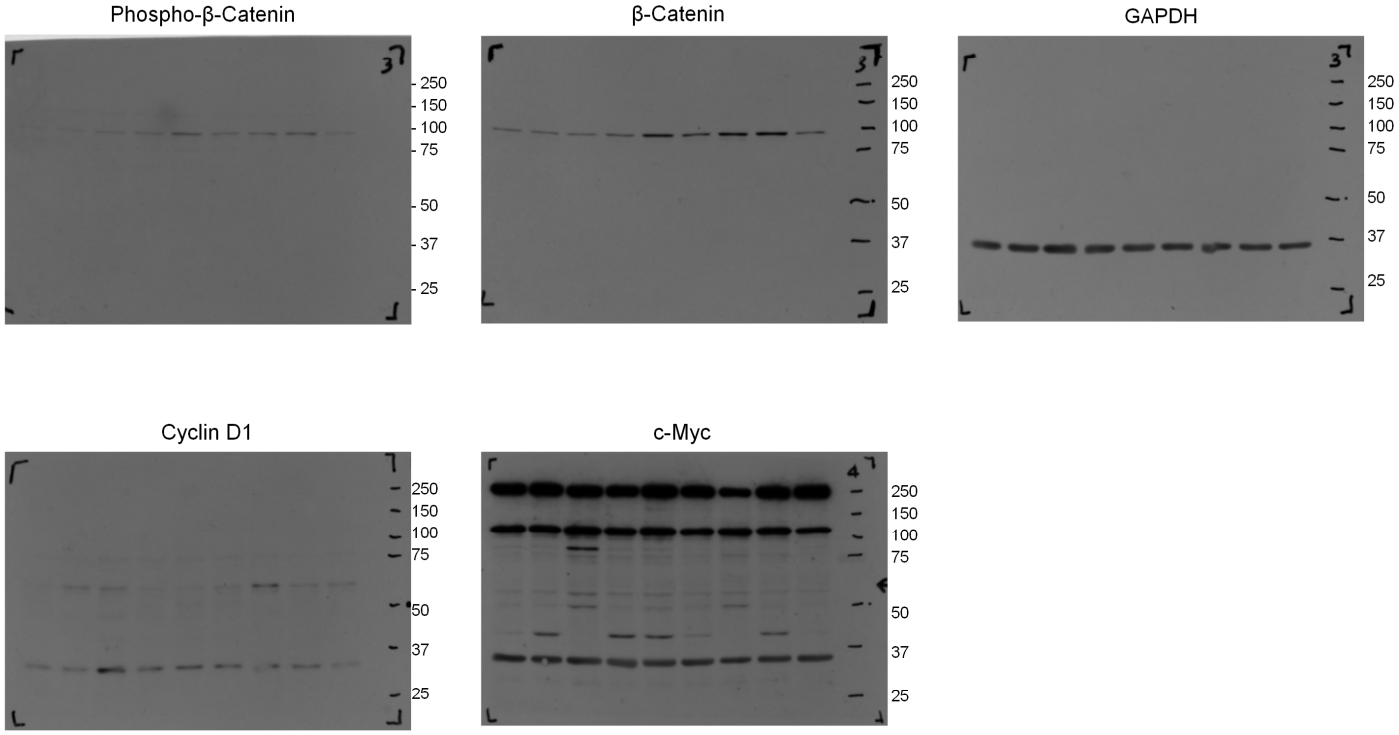



**Figure 5 c (SW620)**



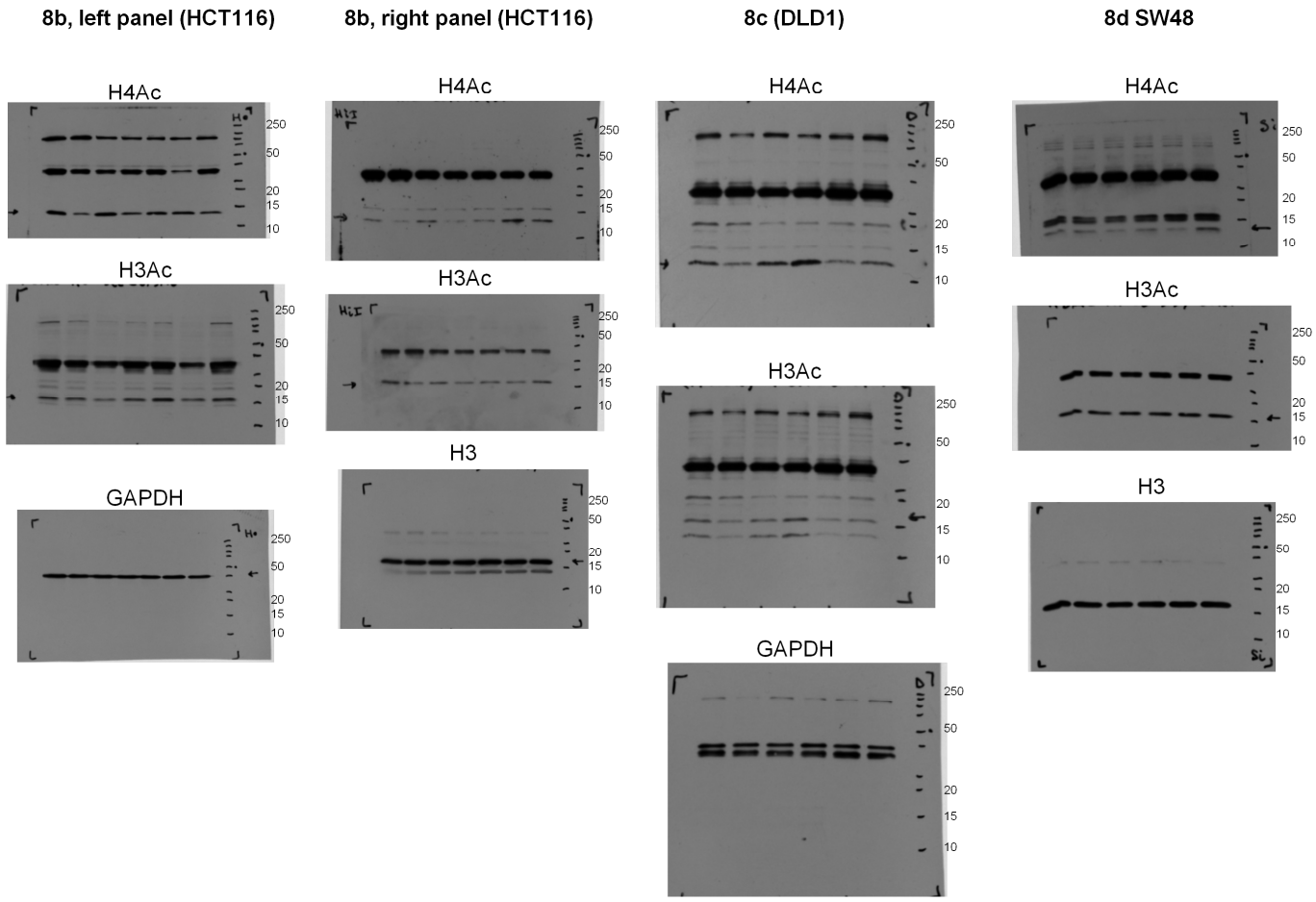

**Supplementary Figure S16**

**Figure 6 d**



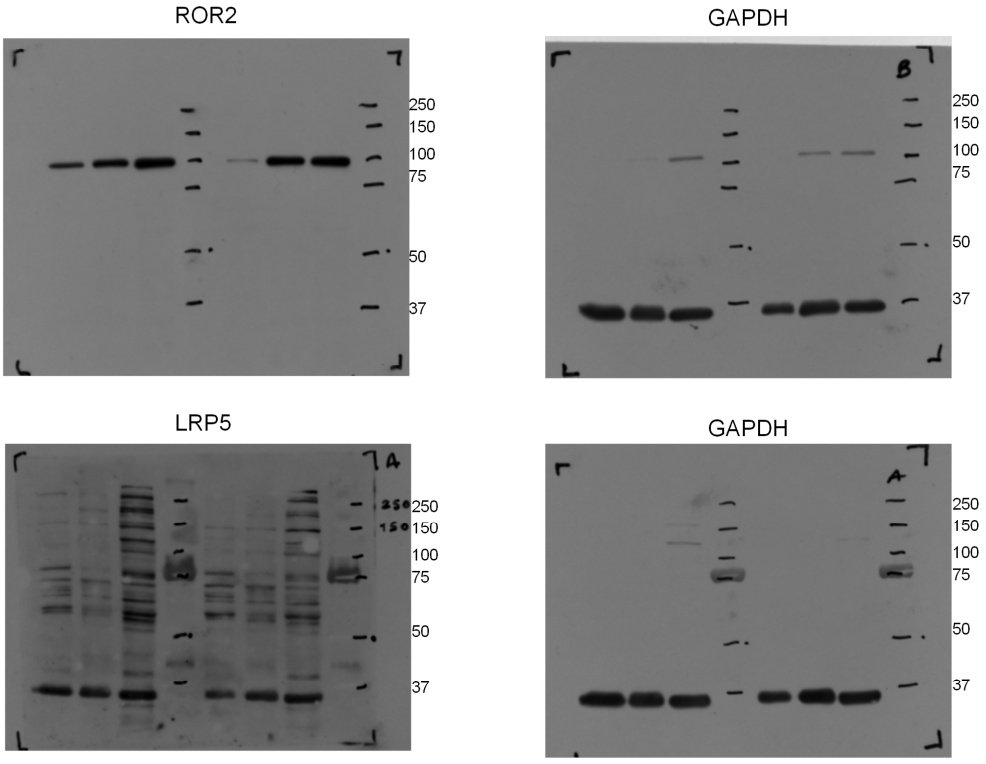

**Supplementary Figure S17**

**Figure 8**




**Supplementary Figure S18**

**Supplementary Figure 4 b**




**Supplementary Figure S19**