

Supplementary Information 1:

List of top 100 ranking lethal pairs that shows a significant transition in drop in efficiency of Human Cancer Protein Interaction Network: Gene 1 and Gene 2 indicates the interacting partners of lethal pairs.

| Rank | Gene 1 | Gene 2 |
|------|---------|--------|
| 1. | CTNNB1 | TP53 |
| 2. | TP53 | YWHAG |
| 3. | CREBBP | TP53 |
| 4. | EP300 | TP53 |
| 5. | CSNK2A1 | TP53 |
| 6. | SMAD3 | TP53 |
| 7. | AR | TP53 |
| 8. | RB1 | TP53 |
| 9. | BRCA1 | TP53 |
| 10. | SUMO4 | TP53 |
| 11. | BCL2 | TP53 |
| 12. | EGFR | TP53 |
| 13. | PTK2 | TP53 |
| 14. | SMAD2 | TP53 |
| 15. | SRC | TP53 |
| 16. | HDAC1 | TP53 |
| 17. | CDK1 | TP53 |
| 18. | CASP3 | TP53 |
| 19. | ABL1 | TP53 |
| 20. | ESR1 | TP53 |
| 21. | FLNA | TP53 |
| 22. | CAV1 | TP53 |
| 23. | TP53 | UBE2I |
| 24. | PTCH1 | TP53 |
| 25. | EWSR1 | TP53 |
| 26. | AKT1 | TP53 |
| 27. | HIF1A | TP53 |
| 28. | STAT3 | TP53 |
| 29. | SMURF2 | TP53 |
| 30. | PRKCD | TP53 |
| 31. | SMAD4 | TP53 |
| 32. | BAT3 | TP53 |
| 33. | TP53 | VIM |
| 34. | RAD51 | TP53 |
| 35. | MAGI1 | TP53 |
| 36. | JUN | TP53 |
| 37. | TP53 | YWHAZ |
| 38. | HMGB1 | TP53 |
| 39. | RAC1 | TP53 |

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| 40. | CNOT7 | TP53 |
| 41. | TGFBR1 | TP53 |
| 42. | PPP2R1B | TP53 |
| 43. | IGF1 | TP53 |
| 44. | ERBB2 | TP53 |
| 45. | DYNLL1 | TP53 |
| 46. | PP2CA | TP53 |
| 47. | HSP90AA1 | TP53 |
| 48. | TP53 | ZBTB16 |
| 49. | PCNA | TP53 |
| 50. | MAPK3 | TP53 |
| 51. | FYN | TP53 |
| 52. | CDKN2A | TP53 |
| 53. | IGF1R | TP53 |
| 54. | HRAS | TP53 |
| 55. | APP | TP53 |
| 56. | SP1 | TP53 |
| 57. | SMAD5 | TP53 |
| 58. | PTEN | TP53 |
| 59. | PRNP | TP53 |
| 60. | MAPK1 | TP53 |
| 61. | EEF1A1 | TP53 |
| 62. | DAPK1 | TP53 |
| 63. | DACH1 | TP53 |
| 64. | CREBBP | EP300 |
| 65. | CREBBP | CTNNB1 |
| 66. | ACTB | TP53 |
| 67. | TP53 | XRCC6 |
| 68. | RUNX1 | TP53 |
| 69. | AURKA | TP53 |
| 70. | TP53 | YWHAB |
| 71. | MET | TP53 |
| 72. | GSK3B | TP53 |
| 73. | FN1 | TP53 |
| 74. | COL1A1 | TP53 |
| 75. | RELA | TP53 |
| 76. | NFKB1 | TP53 |
| 77. | MMP9 | TP53 |
| 78. | CEACAM1 | TP53 |
| 79. | CDKN1A | TP53 |
| 80. | CADM1 | TP53 |
| 81. | TP53 | TSC2 |
| 82. | RASA1 | TP53 |
| 83. | MAPK14 | TP53 |
| 84. | INS | TP53 |
| 85. | TP53 | UBB |
| 86. | TP53 | TRAF6 |
| 87. | PTPN6 | TP53 |
| 88. | PRKCZ | TP53 |
| 89. | PARP1 | TP53 |

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| 90. | CDK4 | TP53 |
| 91. | BTRC | TP53 |
| 92. | TP53 | VHL |
| 93. | TLR2 | TP53 |
| 94. | SOCS1 | TP53 |
| 95. | SMARCA4 | TP53 |
| 96. | NDRG1 | TP53 |
| 97. | KAT2B | TP53 |
| 98. | HSPA1A | TP53 |
| 99. | ETS1 | TP53 |
| 100 | CTNNB1 | EP300 |