

Supplementary Information for

Article

PI3K p110 α Blockade Enhances Anti-Tumor Efficacy of Abemaciclib in Human Colorectal Cancer Cells

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Table S1. Key genetic alterations in 9 colorectal cancer cell lines.

| | Primary resistance cell lines to CDK4/6 inhibitors | | | | | Sensitive cell lines to CDK4/6 inhibitors | | | |
|---------------|--|----------------|----------------|-------|----------------|---|----------------|--------|-----------------|
| | HCT-15 | DLD-1 | HCT-8 | SW480 | SNU-175 | SNU-C5 | HT-29 | Caco-2 | SNU-C4 |
| <i>CCND1</i> | WT | - | - | WT | WT | WT | WT | WT | WT |
| <i>CDKN2A</i> | WT | - | - | WT | DEL | Silent | WT | WT | WT |
| <i>RB1</i> | WT | - | - | WT | R798Q D921D | WT | WT | WT | WT |
| <i>KRAS</i> | G13D | G13D | G13D | G12V | A59T | WT | WT | WT | WT |
| <i>BRAF</i> | WT | WT | WT | WT | WT | V600E | V600E T119S | WT | D22N |
| <i>PIK3CA</i> | E545K D549N | E545K D549N | E545K D549N | WT | WT | H1047R | P449T | WT | E545G V71I |
| <i>PETN</i> | WT | WT | WT | WT | WT | WT | WT | WT | F288fs F288S |

Table S2. The synergistic activity of abemaciclib with BYL719 in HT-29, Caco-2, and, SNU-C4 cell lines.

| HT-29 | | | Caco-2 | | | SNU-C4 | | | | | | | | |
|-------|-------|-----------|--------------------|--------------------|------|--------|-----------|--------------------|--------------------|------|-------|-----------|--------------------|--------------------|
| Fa | CI | Est. S.D. | Abemaciclib | BYL719 | Fa | CI | Est. S.D. | Abemaciclib | BYL719 | Fa | CI | Est. S.D. | Abemaciclib | BYL719 |
| 0.02 | 0.011 | 0.025 | 2×10^{-6} | 10^{-5} | 0.02 | 0.513 | 0.579 | 2×10^{-4} | 9×10^{-4} | 0.02 | 0.336 | 1.306 | 2×10^{-4} | 2×10^{-4} |
| 0.05 | 0.025 | 0.04 | 3×10^{-5} | 2×10^{-4} | 0.05 | 0.472 | 0.387 | 0.001 | 0.006 | 0.05 | 0.313 | 0.805 | 0.001 | 0.001 |
| 0.1 | 0.048 | 0.057 | 3×10^{-4} | 0.001 | 0.1 | 0.447 | 0.271 | 0.005 | 0.026 | 0.1 | 0.299 | 0.549 | 0.005 | 0.005 |
| 0.15 | 0.072 | 0.068 | 9×10^{-4} | 0.004 | 0.15 | 0.437 | 0.212 | 0.012 | 0.065 | 0.15 | 0.293 | 0.432 | 0.013 | 0.011 |
| 0.2 | 0.098 | 0.077 | 0.002 | 0.012 | 0.2 | 0.432 | 0.173 | 0.024 | 0.131 | 0.2 | 0.29 | 0.359 | 0.026 | 0.022 |
| 0.25 | 0.127 | 0.084 | 0.005 | 0.026 | 0.25 | 0.429 | 0.145 | 0.043 | 0.233 | 0.25 | 0.288 | 0.307 | 0.045 | 0.038 |
| 0.3 | 0.158 | 0.089 | 0.01 | 0.051 | 0.3 | 0.43 | 0.124 | 0.072 | 0.385 | 0.3 | 0.287 | 0.267 | 0.073 | 0.062 |
| 0.35 | 0.193 | 0.092 | 0.019 | 0.096 | 0.35 | 0.432 | 0.108 | 0.113 | 0.608 | 0.35 | 0.286 | 0.235 | 0.113 | 0.096 |
| 0.4 | 0.234 | 0.094 | 0.035 | 0.174 | 0.4 | 0.435 | 0.096 | 0.174 | 0.933 | 0.4 | 0.286 | 0.209 | 0.17 | 0.145 |

| | | | | | | | | | | | | | | |
|------------|--------------|--------------|--------------|--------------|------------|--------------|--------------|-------------|--------------|------------|--------------|--------------|--------------|--------------|
| 0.45 | 0.28 | 0.095 | 0.061 | 0.306 | 0.45 | 0.44 | 0.088 | 0.261 | 1.405 | 0.45 | 0.286 | 0.187 | 0.252 | 0.215 |
| <u>0.5</u> | <u>0.335</u> | <u>0.096</u> | <u>0.107</u> | <u>0.533</u> | <u>0.5</u> | <u>0.447</u> | <u>0.083</u> | <u>0.39</u> | <u>2.099</u> | <u>0.5</u> | <u>0.286</u> | <u>0.171</u> | <u>0.371</u> | <u>0.316</u> |
| 0.55 | 0.401 | 0.098 | 0.186 | 0.928 | 0.55 | 0.457 | 0.083 | 0.583 | 3.135 | 0.55 | 0.287 | 0.159 | 0.545 | 0.464 |
| 0.6 | 0.482 | 0.108 | 0.327 | 1.634 | 0.6 | 0.469 | 0.087 | 0.879 | 4.722 | 0.6 | 0.288 | 0.153 | 0.807 | 0.687 |
| 0.65 | 0.583 | 0.134 | 0.59 | 2.948 | 0.65 | 0.484 | 0.095 | 1.347 | 7.239 | 0.65 | 0.289 | 0.155 | 1.215 | 1.035 |
| 0.7 | 0.716 | 0.19 | 1.108 | 5.539 | 0.7 | 0.505 | 0.107 | 2.126 | 11.43 | 0.7 | 0.291 | 0.165 | 1.882 | 1.603 |
| 0.75 | 0.899 | 0.296 | 2.218 | 11.09 | 0.75 | 0.534 | 0.124 | 3.515 | 18.89 | 0.75 | 0.294 | 0.185 | 3.047 | 2.596 |
| 0.8 | 1.166 | 0.489 | 4.912 | 24.56 | 0.8 | 0.575 | 0.147 | 6.248 | 33.59 | 0.8 | 0.298 | 0.22 | 5.29 | 4.506 |
| 0.85 | 1.602 | 0.873 | 12.86 | 64.29 | 0.85 | 0.639 | 0.183 | 12.54 | 67.41 | 0.85 | 0.304 | 0.276 | 10.31 | 8.787 |
| 0.9 | 2.447 | 1.792 | 46.16 | 230.8 | 0.9 | 0.756 | 0.246 | 31.64 | 170 | 0.9 | 0.313 | 0.372 | 25.04 | 21.33 |
| 0.95 | 4.888 | 5.312 | 363.8 | 1819 | 0.95 | 1.051 | 0.415 | 141 | 758 | 0.95 | 0.332 | 0.593 | 104.9 | 89.39 |
| 0.99 | 23.37 | 51.85 | 34787 | 2E+05 | 0.99 | 2.614 | 1.54 | 3830 | 20584 | 0.99 | 0.395 | 1.572 | 2486 | 2117 |

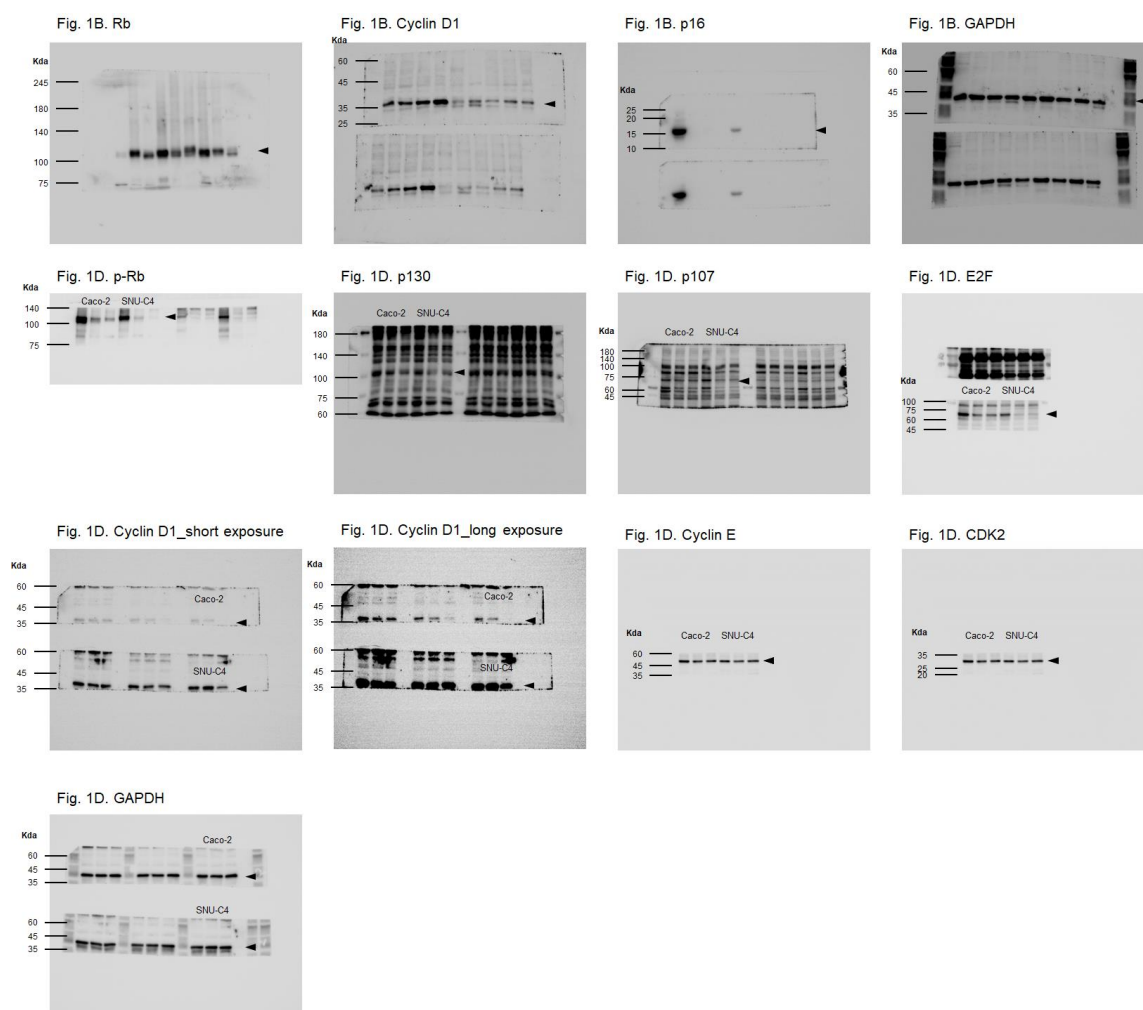


Figure S1. Uncropped Western blot images of indicated proteins in whole cell lysates from Caco-2 and SNU-C4 cells treated with and without abemaciclib, related to Figure 1B and 1D.

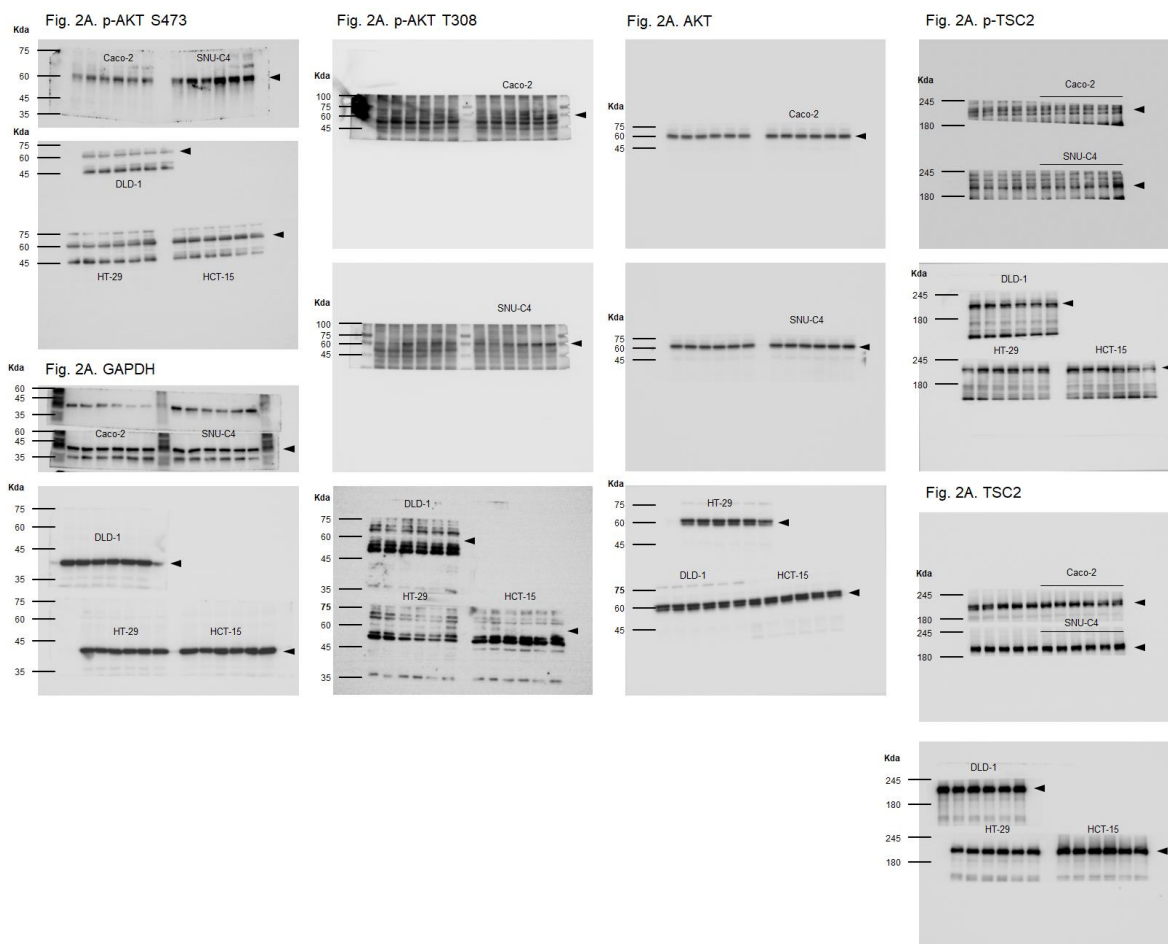


Figure S2. Uncropped Western blot images of indicated proteins in whole cell lysates from HCT-15, DLD-1, HT-29, Caco-2, and SNU-C4 cells treated with and without abemaciclib, related to Figure 2A.

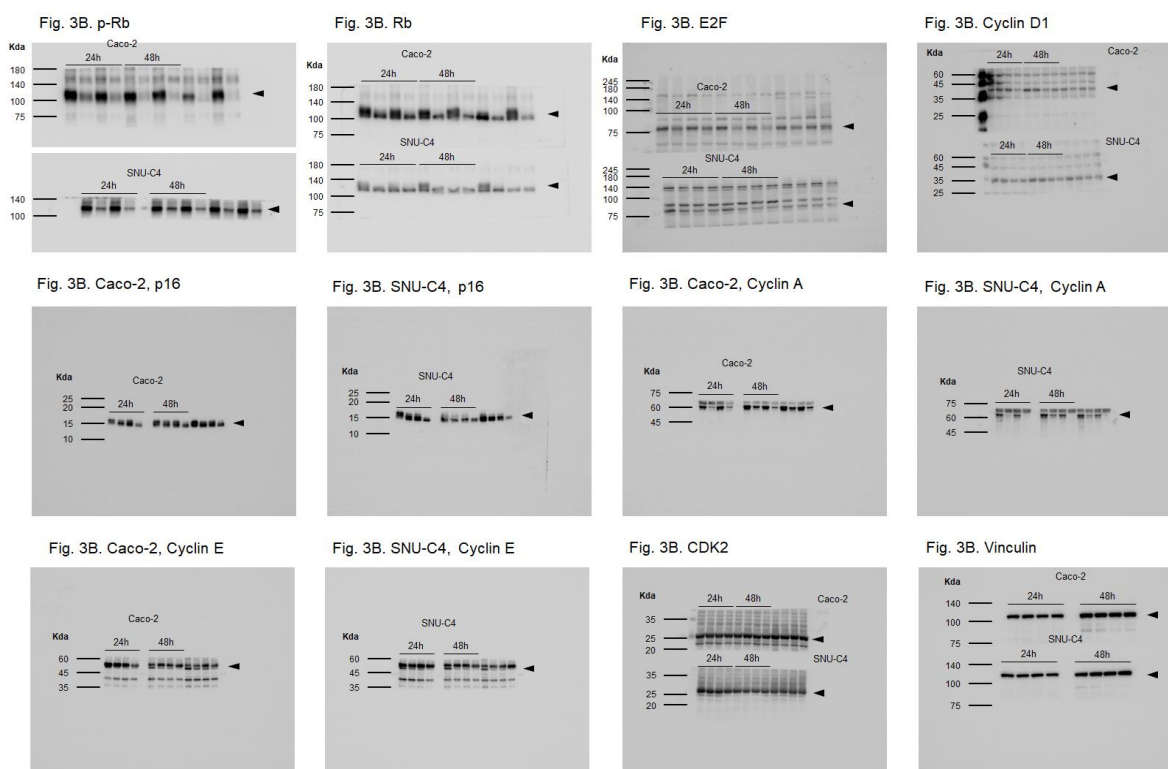


Figure 3S. Uncropped Western blot images of indicated proteins in whole cell lysates from Caco-2 and SNU-C4 cells treated with abemaciclib and/or BYL719, related to Figure 3B.