



Figure 15. Distribution in the cell cycle of HeLa cells treated with naringenin and naringenin-EC₂₅ cisplatin (16 µM) for 24 and 48 h. A) Distribution in the different phases of the cell cycle at 24 h and 48h. $p < 0.05$ according to Tukey's mean test, $n=6$; B) Cell cycle distribution histograms at 24 h and 48h. Positive proliferation control (vehicle); Negative proliferation control (Starvation).

Relative area of invasion (um)
of spheroids 24h

| 0 | 100 | 300 | 500 |
|--------|--------|-------|-------|
| 8.556 | 2.985 | 2.071 | 1.424 |
| 23.811 | 3.623 | 2.825 | 3.181 |
| 9.684 | 11.907 | 1.654 | 1.579 |
| 12.653 | 5.235 | 0.439 | 0.937 |
| 5.719 | 7.664 | 1.264 | 0.685 |
| 19.656 | 5.198 | 1.142 | 1.587 |
| 10.074 | 6.785 | 0.951 | 0.565 |
| 7.772 | 3.156 | 1.023 | 0.916 |
| 8.151 | 5.015 | 2.878 | 0.483 |
| 10.637 | 2.974 | 1.633 | 1.125 |
| 2.314 | 18 | 1.49 | 2.245 |
| 15.916 | 6.595 | 3.738 | 1.777 |

Relative area of invasion (um) At 48h

| 0 | 100 | 300 | 500 |
|--------|--------|--------|-------|
| 10.504 | 30.406 | 6.874 | 3.489 |
| 36.233 | 12.097 | 4.904 | 3.624 |
| 35.195 | 28.374 | 7.442 | 2.022 |
| 30.246 | 17.254 | 11.797 | 9.41 |
| 24.265 | 19.636 | 5.015 | 0.867 |
| 49.956 | 9.318 | 5.421 | 3.151 |
| 15.402 | 6.164 | 7.21 | 2.8 |
| 17.053 | 13.36 | 5.595 | 3.503 |
| 37.462 | 12.894 | 6.198 | 0.728 |
| 35.933 | 18.11 | 12.102 | 2.747 |
| 12.821 | 21.753 | 7.256 | 2.21 |

Relative area of invasion (um)
Combination of naringenin +
cis-platinum

| Vehicle | EC25 | EC25+Nar | EC50 | EC50+Nar |
|---------|--------|----------|--------|----------|
| 8.556 | 4.637 | 12.937 | 13.056 | 2.64 |
| 23.811 | 9.846 | 8.88 | 5.946 | 6.568 |
| 9.684 | 9.932 | 5.002 | 4.117 | 2.38 |
| 12.653 | 20.645 | 3.425 | 3.482 | 4.152 |

| | | | | |
|--------|--------|-------|-------|--------|
| 5.719 | 13.165 | 9.438 | 9.709 | 1.393 |
| 19.656 | 11.304 | 5.114 | 1.618 | 3.465 |
| 10.074 | 19.502 | 2.218 | 9.348 | 9.742 |
| 7.772 | 14.863 | 8.973 | 3.323 | 11.284 |
| 8.151 | 20.025 | 2.543 | 4.395 | 5.71 |
| 10.637 | 23.761 | 9.488 | 4.935 | 5.003 |
| 2.314 | 14.768 | 6.802 | 5.698 | 6.372 |