Cotargeting Plk1 and androgen receptor enhances the therapeutic sensitivity of paclitaxel-resistant prostate cancer

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Running Title
Cotargeting Plk1 and AR in taxol-resistant prostate cancer
Supplementary Figure 1.

Cells were treated with paclitaxel in a concentration-dependent manner in LNCaP, paclitaxel-resistant LNCaP (LNCaP\textsuperscript{TXR}), NCI-H460, and paclitaxel-resistant NCI-H460 (H460\textsuperscript{TXR}) cells for 48 h. The numbers of viable cells were then measured by a cell viability assay. The bar graph presents the mean values of half maximal growth inhibitory concentration (GI\textsubscript{50}, nM for paclitaxel).
Supplementary Table 1. A combination of BI 2536 and bicalutamide in paclitaxel-resistant LNCaP\textsuperscript{TXR} cells. LNCaP and LNCaP\textsuperscript{TXR} cells were treated with BI 2536 and bicalutamide in a concentration-dependent manner for 48 h. The percentages of viable cells were measured by a cell viability assay.

| Bicalutamide (μM) | 0          | 1          | 5          | 10         | 25         | 50         |
|-------------------|------------|------------|------------|------------|------------|------------|
|                   | LNCaP      | LNCaP\textsuperscript{TXR} | LNCaP      | LNCaP\textsuperscript{TXR} | LNCaP      | LNCaP\textsuperscript{TXR} |
| 0                 | 100.0 ± 0.1| 100.0 ± 1.1| 82.3 ± 0.9 | 73.2 ± 1.6 | 72.3 ± 1.3 | 67.6 ± 1.2 |
| 2.5               | 89.0 ± 0.1 | 96.0 ± 1.6 | 67.3 ± 0.9 | 67.4 ± 0.9 | 54.8 ± 1.3 | 60.1 ± 1.0 |
| 5.5               | 70.4 ± 1.3 | 79.7 ± 0.5 | 56.9 ± 0.8 | 58.8 ± 1.6 | 51.5 ± 1.3 | 53.2 ± 1.4 |
|                   | 48.9 ± 0.7 | 70.6 ± 1.1 | 43.7 ± 0.7 | 50.0 ± 1.4 | 36.9 ± 1.1 | 38.7 ± 1.0 |
|                   | 37.3 ± 0.4 | 48.6 ± 1.2 | 34.6 ± 1.1 | 38.1 ± 0.9 | 22.7 ± 1.8 | 28.6 ± 0.6 |
|                   | 29.5 ± 0.1 | 33.1 ± 0.8 | 25.0 ± 1.3 | 27.0 ± 1.1 | 17.3 ± 0.8 | 18.4 ± 0.4 |
Supplementary Table 2. A combination of volasertib and bicalutamide in paclitaxel-resistant LNCaP\textsuperscript{TXR} cells. LNCaP and LNCaP\textsuperscript{TXR} cells were treated with volasertib and bicalutamide in a concentration-dependent manner for 48 h. The percentages of viable cells were measured by a cell viability assay.

| Bicalutamide (μM) | 0 | 1 | 5 | 10 | 25 | 50 |
|-------------------|---|---|---|----|----|----|
| LNCaP             | 100.0 ± 0.1 | 89.0 ± 0.1 | 68.3 ± 1.1 | 50.9 ± 0.6 | 43.3 ± 0.3 | 29.5 ± 0.1 |
| LNCaP\textsuperscript{TXR} | 100.0 ± 1.1 | 92.3 ± 1.6 | 75.7 ± 0.5 | 69.8 ± 0.9 | 60.2 ± 1.0 | 49.1 ± 0.5 |
| LNCaP             | 81.1 ± 0.4 | 77.9 ± 0.7 | 57.1 ± 0.2 | 46.8 ± 0.9 | 39.8 ± 0.4 | 24.4 ± 0.4 |
| LNCaP\textsuperscript{TXR} | 72.1 ± 0.3 | 66.0 ± 1.4 | 60.4 ± 1.7 | 51.7 ± 1.1 | 44.4 ± 0.7 | 30.6 ± 1.1 |
| LNCaP             | 71.8 ± 1.4 | 58.2 ± 1.6 | 53.4 ± 0.9 | 39.9 ± 2.0 | 28.1 ± 0.4 | 17.5 ± 0.8 |
| LNCaP\textsuperscript{TXR} | 66.5 ± 1.4 | 63.1 ± 0.9 | 55.7 ± 1.5 | 40.4 ± 1.4 | 33.5 ± 1.1 | 19.7 ± 0.8 |
Supplementary Table 3. A combination of genistein and bicalutamide in paclitaxel-resistant LNCaP\textsuperscript{TXR} cells. LNCaP and LNCaP\textsuperscript{TXR} cells were treated with genistein and bicalutamide in a concentration-dependent manner for 48 h. The percentages of viable cells were measured by a cell viability assay.

| Bicalutamide (μM) | Genistein (μM) | 0  | 1  | 5  | 10 | 25 | 50 |
|-------------------|----------------|----|----|----|----|----|----|
|                   | LNCaP          | 100.0 ± 1.4 | 87.9 ± 1.3 | 79.9 ± 1.2 | 70.4 ± 1.1 | 60.8 ± 1.0 | 38.4 ± 1.4 |
|                   | LNCaP\textsuperscript{TXR} | 100.0 ± 0.8 | 77.7 ± 2.3 | 64.0 ± 1.3 | 50.5 ± 0.5 | 46.1 ± 1.8 | 37.3 ± 1.1 |
| 2.5               | LNCaP          | 82.0 ± 1.1 | 66.2 ± 1.2 | 61.0 ± 1.5 | 54.2 ± 1.3 | 47.8 ± 1.3 | 37.3 ± 2.2 |
|                   | LNCaP\textsuperscript{TXR} | 74.0 ± 1.2 | 69.8 ± 1.6 | 59.3 ± 1.6 | 48.2 ± 0.9 | 35.3 ± 1.5 | 25.7 ± 0.6 |
| 5.5               | LNCaP          | 71.0 ± 1.6 | 65.4 ± 1.5 | 55.6 ± 1.2 | 48.4 ± 1.2 | 40.5 ± 0.8 | 36.1 ± 0.6 |
|                   | LNCaP\textsuperscript{TXR} | 68.5 ± 1.2 | 55.2 ± 2.3 | 48.6 ± 0.9 | 37.9 ± 0.6 | 30.3 ± 1.2 | 19.8 ± 0.3 |
**Supplementary Table 4. Oligonucleotide sequence of PCR primers used in this study**

| Gene | Forward primer (5’-3’) | Reverse primer (5’-3’) |
|------|------------------------|-----------------------|
| MDR1 | 5’-ATATCAGCAGCCCACATCAT-3’ | 5’-GAAGCACTGGGATGTCCGTT-3’ |
| MRP1 | 5’-CAGTGACCTCTGGTCTTAAAC-3’ | 5’-ATCCACCTTGGAACTCTCTTTC-3’ |
| PLK1 | 5’-AAGAGATCCCCGGAGGTCTCTA-3’ | 5’-TCATTCAGGAAAAGGGTTGCC-3’ |
| AR   | 5’-CGCTGAAGGGAACAGAAGTA-3’ | 5’-CCTCTTCCTTCCTCTGTAGTT-3’ |
| PSA  | 5’-CTTGTAGCCTCTCGTGCGCAG-3’ | 5’-GACCTTCATAGCATCCGAGCAG-3’ |
Supplementary Figure 2

**Figure 1D**

**Figure 4F**

**Figure 5D**