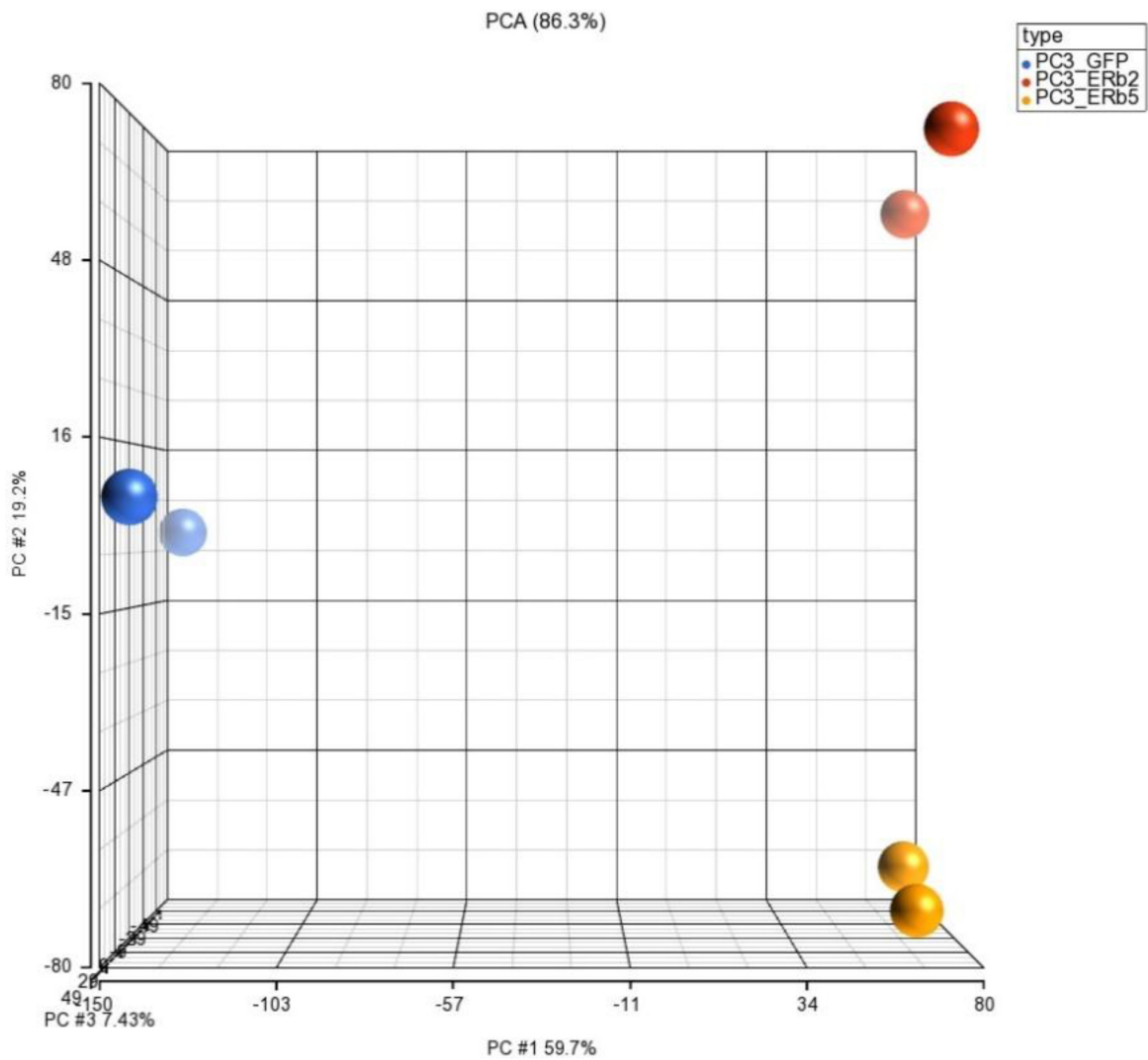
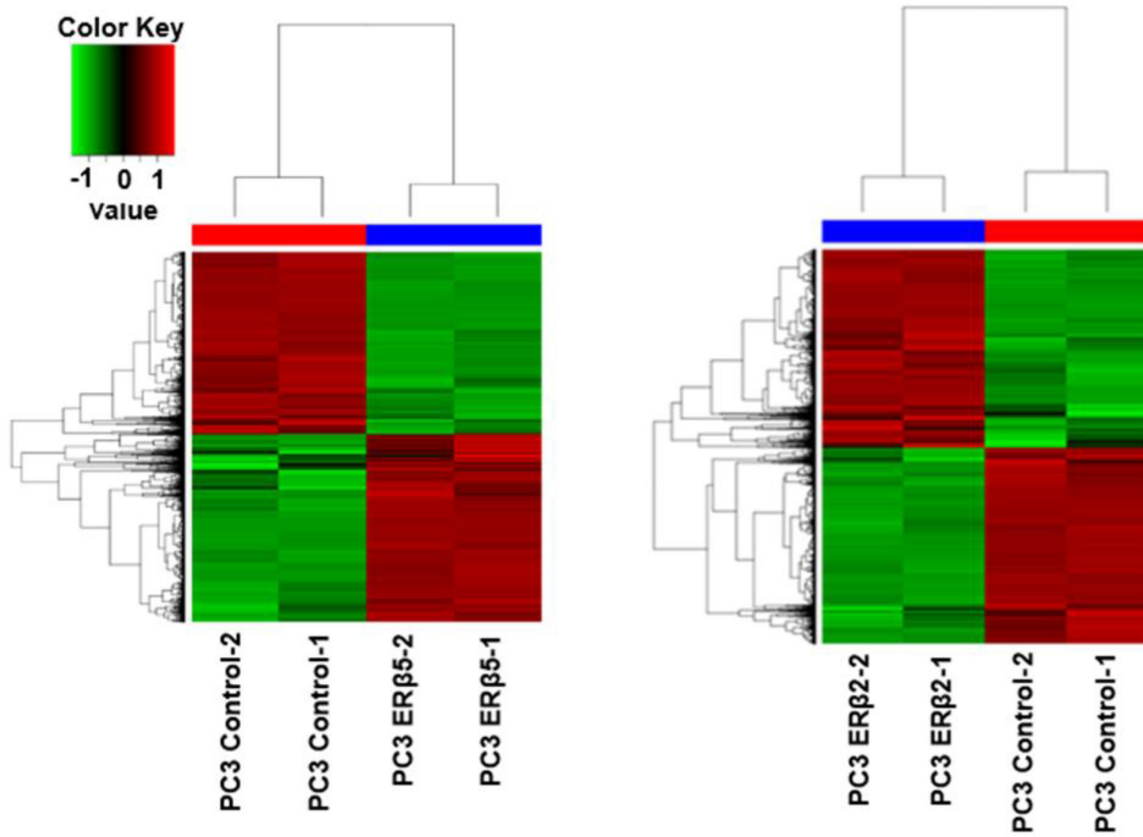


The estrogen receptor variants $\beta 2$ and $\beta 5$ induce stem cell characteristics and chemotherapy resistance in prostate cancer through activation of hypoxic signaling

SUPPLEMENTARY MATERIALS

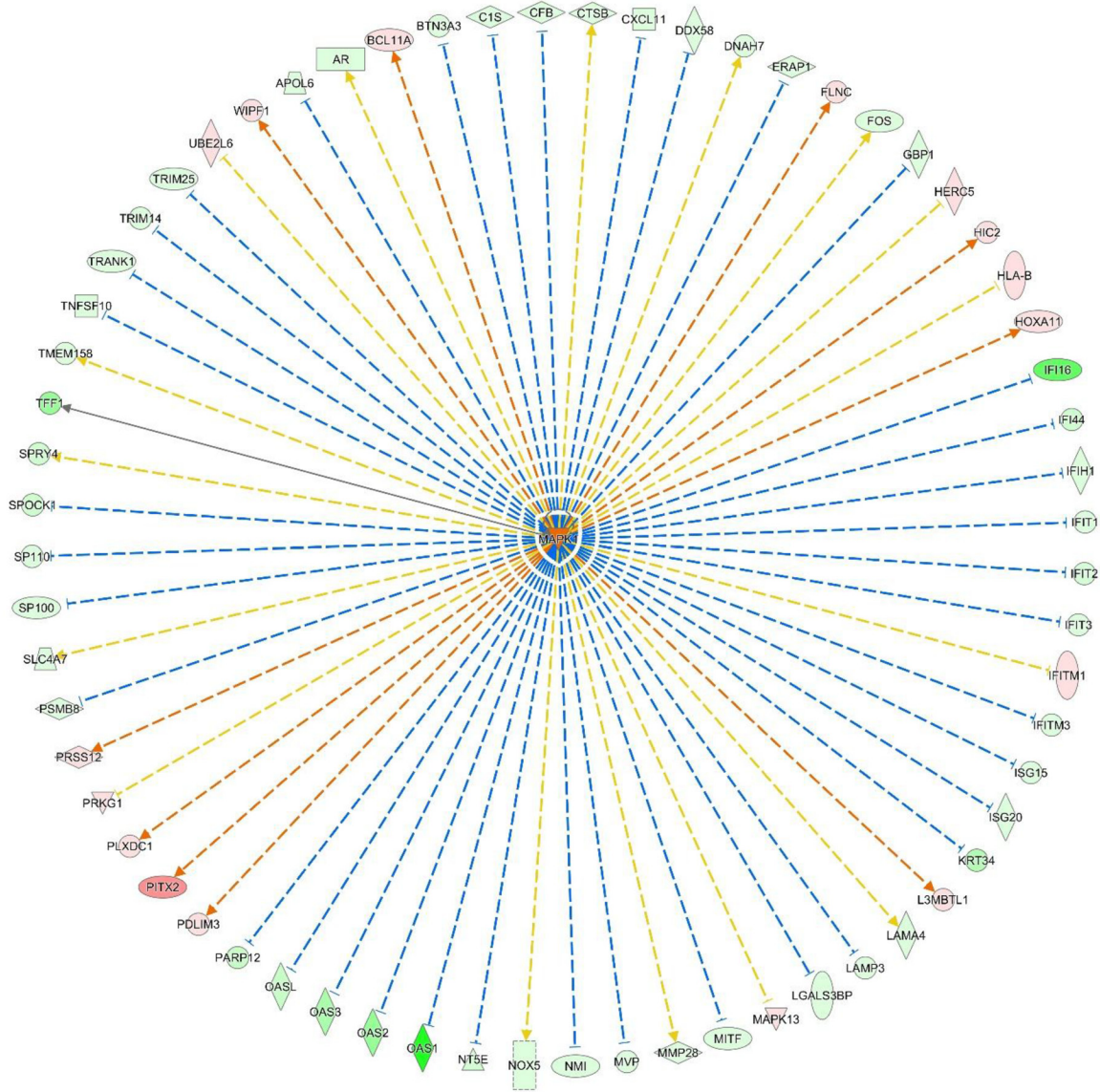


Supplementary Figure 1: Principal component analysis.

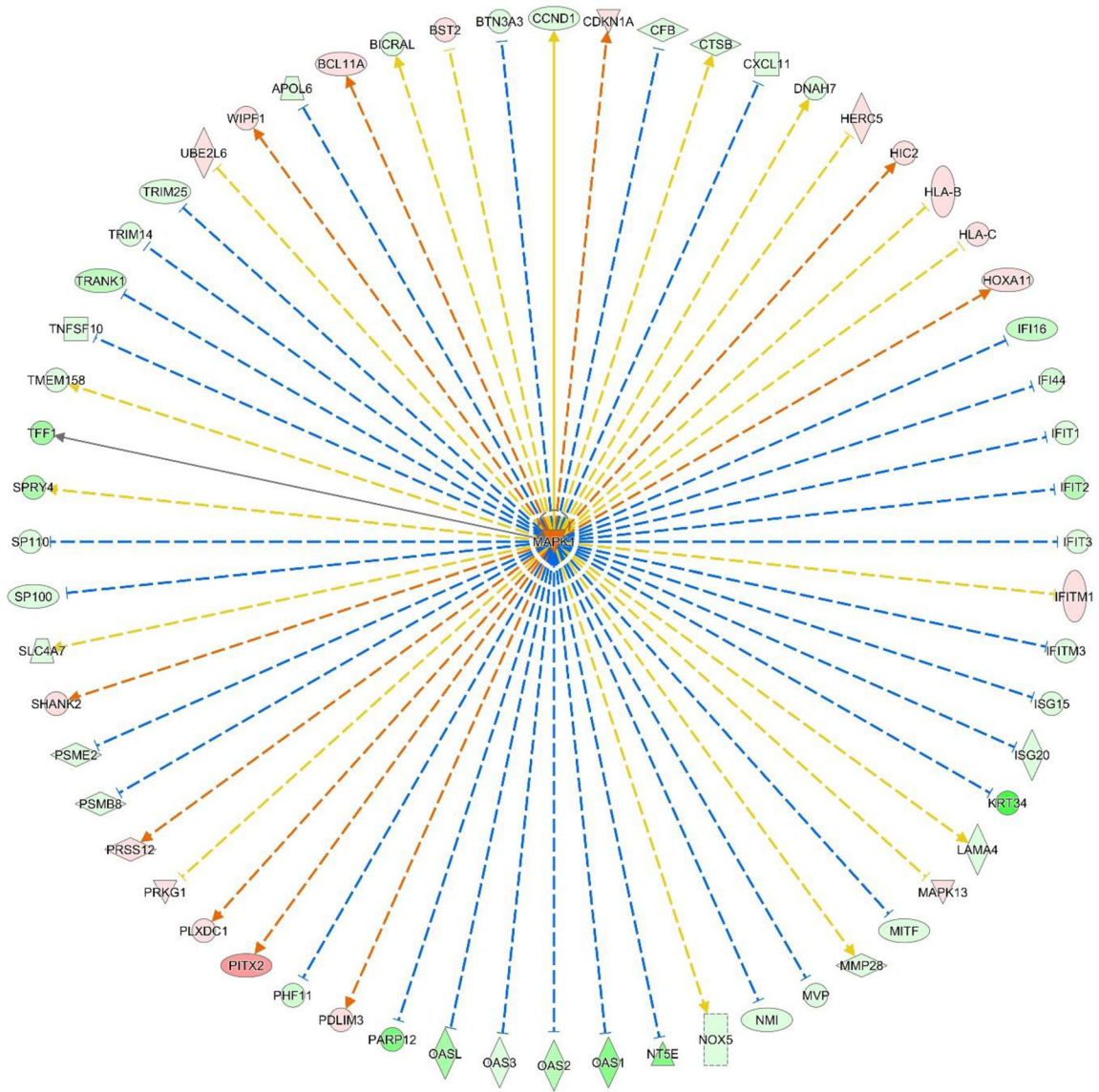


Supplementary Figure 2: Heatmap showing high similarity between repeat samples and big difference between controls and ERβ2/5 expressing cells.

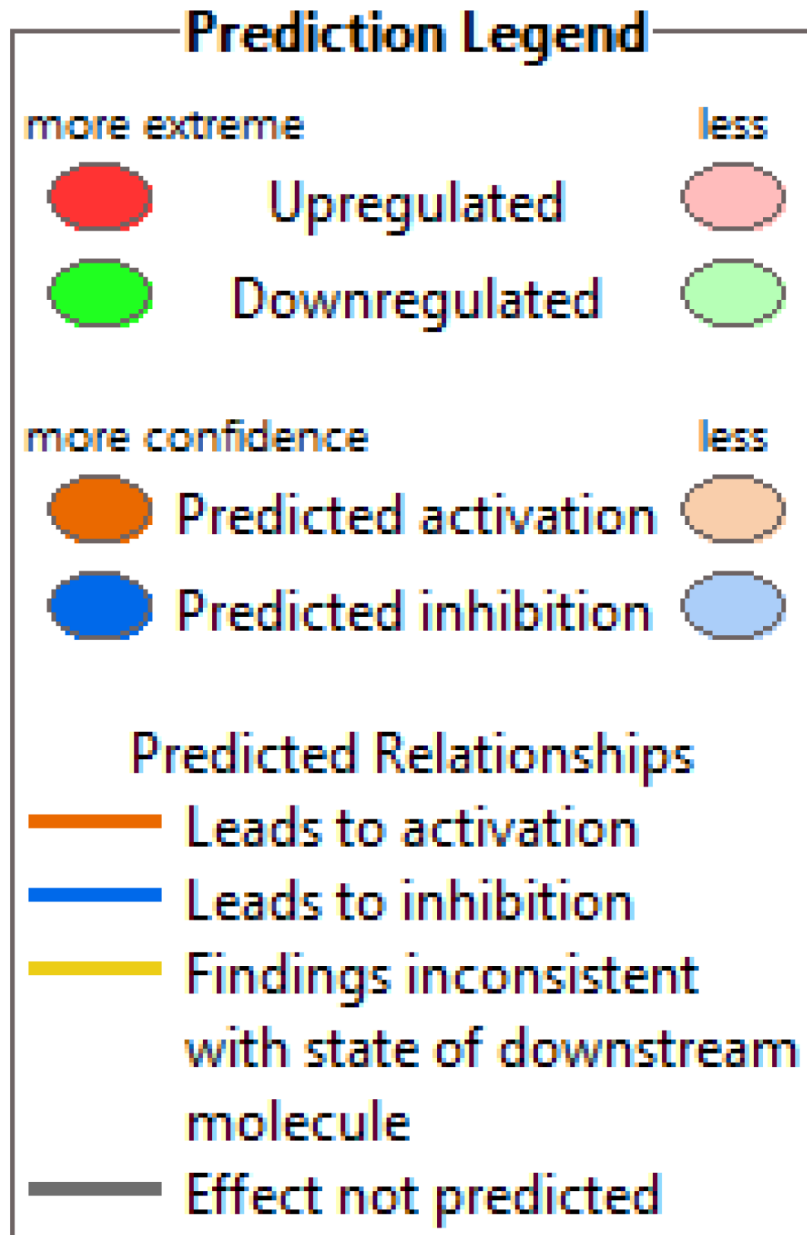
A



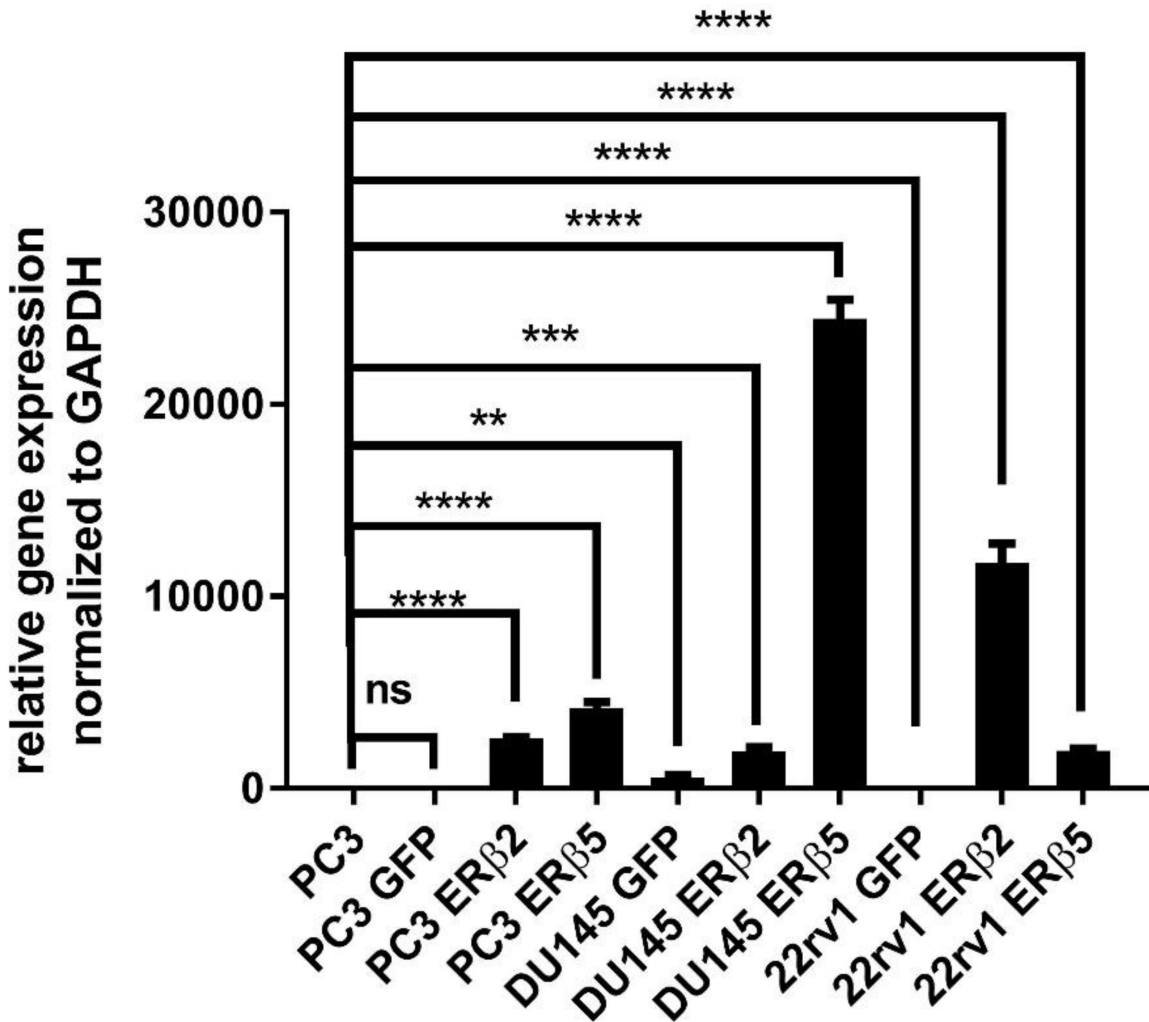
B



C



Supplementary Figure 3: (A) ER β 2 increases MAPK1 signaling. (B) ER β 5 increases MAPK1 signaling. (C) Color codes for (A) and (B).



Supplementary Figure 4: ERβ2 and ERβ5 expression in three different prostate cancer stable cell lines.

Supplementary Table 1A: Selected mutually up regulated transcripts. See Supplementary_Table_1A

Supplementary Table 1B: Top 30 mutually down regulated transcripts. See Supplementary_Table_1B

Supplementary Table 1C: Top 30 up regulated transcripts for ERβ2. See Supplementary_Table_1C

Supplementary Table 1D: Top 30 down regulated transcripts for ERβ2. See Supplementary_Table_1D

Supplementary Table 1E: Top 30 up regulated transcripts for ERβ5. See Supplementary_Table_1E

Supplementary Table 1F: Top 30 down regulated transcripts for ERβ5. See Supplementary_Table_1F

Supplementary Table 2: ER β expression in prostate cancer PDX from the MDA PCa PDX series (UT MD Anderson Cancer Center, Texas)

	PDX name: MDA PCa	Total ERβ FPKM	Diagnosis & Tumor site	Grade	Therapy	Clinical state	Survival from diagnosis (years)
1	118-b	0.722384	Metastatic adenocarcinoma, bone	N/A	HT, CT, RT	CRPC	2.9
2	133-4	0.232289	Metastatic carcinoma, bone	N/A	HT, CT, RT	CRPC	8.6
3	144-4	3.873795	Adenocarcinoma with NE differentiation and small cell carcinoma, prostate	N/A	HT, CT, RT	CRPC	4.8
4	149-1	0.714604	Adenocarcinoma, ureter	4+5	HT, CT, RT	CRPC	6.9
5	152-1	0	Metastatic adenocarcinoma (ductal), brain	N/A	HT, RT	CRPC	11.4
6	173-2	0.037032	Adenocarcinoma, prostate	3+4	None	N	4
7	178-11	0.389715	Adenocarcinoma, prostate	4+5	HT	Ar	3.4
8	183-A	0	Metastatic carcinoma, bone	N/A	None	N	2.3
9	230-A	0.282839	Metastatic Adenocarcinoma, chest wall	N/A	HT, CT, RT	CRPC	10.7
10	250-9	0.123058	Metastatic Adenocarcinoma, adrenal gland	N/A	HT	Ar	5.7
11	259-11	0	Adenocarcinoma, prostate	4+5	None	N	4
12	277-6	0.105902	Metastatic small cell carcinoma, lymph node	N/A	HT, CT, RT	CRPC	9.9

Abbreviations: HT = Hormone Therapy, CT = Chemotherapy, RT = Radiotherapy, CRPC = Castration-resistant prostate cancer, Ar = Androgen responsive, N = Naïve, FPKM = Fragments per Kilobase of Exon per Million Fragments Mapped.

Supplementary Table 3: List of antibodies and source and list of primers used in the study

Antibodies	Source	Order number
Cyclin D2	Santa Cruz	Sc-593
Notch3	Cell Signaling Technology	D11B8
WNT11	AbCam	Ab31962
ERR β	AbCam	Ab104804
HIF-1 α	Santa Cruz	Sc-10790
HIF-2 α	Santa Cruz	Sc-46691
SCF/Kit	AbCam	Ab52603
ABCG2	Santa Cruz	Sc-25822
IKK β	Cell Signaling Technology	D30C6
ER β	GeneTex	GTX70174 (14C8)
β -actin	Sigma	A-1978
ID4	Santa Cruz	Sc-365656

Primer	Forward	Reverse
ABCG2	5'AGGTGCAAGGAAAGATCCAA	5'TCCAGACACACCACGGATAA
GAPDH	5'TGACAACCTTGGTATCGTGG	5'AGGCAGGGATGATGTTCTGGA
MDR1	5'AGGAAGCCAATGCCTATGACT	5'CAACTGGGCCCCTCTCTCTC
LPXN	5'ACGCTCCACCCTTCAGGACA	5'GACATTGAGCTCCTGGATATTGG
PLAT	5'CCGGCTACGGCAAGCA	5'AGCGGCTGGATGGGTACA
CCDC74A	5'TCTAATTCAGGCAAGGCCAGG	5'AGTAGGGGCTCCTCTTCCAG
HS6ST2	5'GAAGCAGAAGTCAGGCAAGG	5'CCAATGAAGGAAGCAGGATGT
ITPR1	5'CTGCCACCAGTTCAAAAGCC	5'CCACCTCTGCTGCCAAGTAA
NEDD9	5'GAGCTGGATGGATGACTACGA	5'AGCTCTTTCTGTTGCCTCTCA
PLS3	5'ACAGAAGAAGACAAGCACAATAACG	5'CCCATCAAACAGGCAAACACG
SOS1	5'GACCAAGCGGGTTGTTATTGA	5'TGCCTTGTCGGTCATATTTTTCA
CAMK2N1	5'GACCAAGCGGGTTGTTATTGA	5'TGCCTTGTCGGTCATATTTTTCA
HOTAIR	5'GGCGGATGCAAGTTAATAAAA	5'TACGCTGAGTGTTTCACGAG
XIST	5'GCATAACTCGGCTTAGGGCT	5'TCCTCTGCCTGACCTGCTAT

Supplementary Table 4: A list of ER β 2 regulated transcripts. See Supplementary_Table_4

Supplementary Table 5: A list of ER β 5 regulated transcripts. See Supplementary_Table_5

Supplementary Table 6: A list of mutual regulated transcripts. See Supplementary_Table_6

Supplementary Table 7: A list of unique ER β 2 regulated transcripts. See Supplementary_Table_7

Supplementary Table 8: A list of unique ER β 5 regulated transcripts. See Supplementary_Table_8