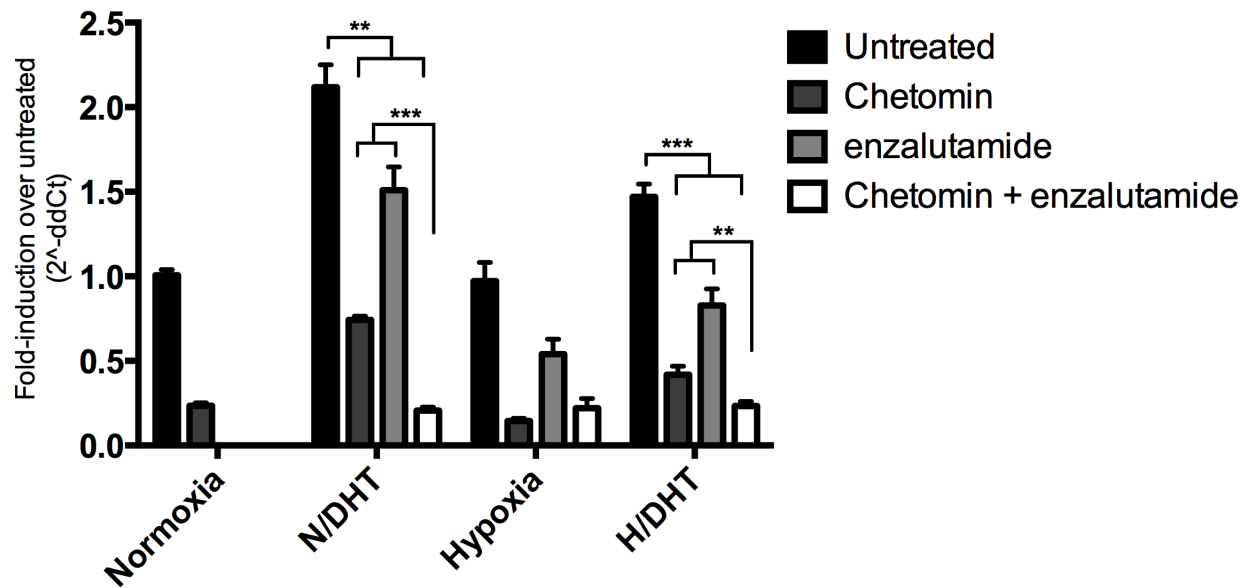


SUPPLEMENTAL DATA

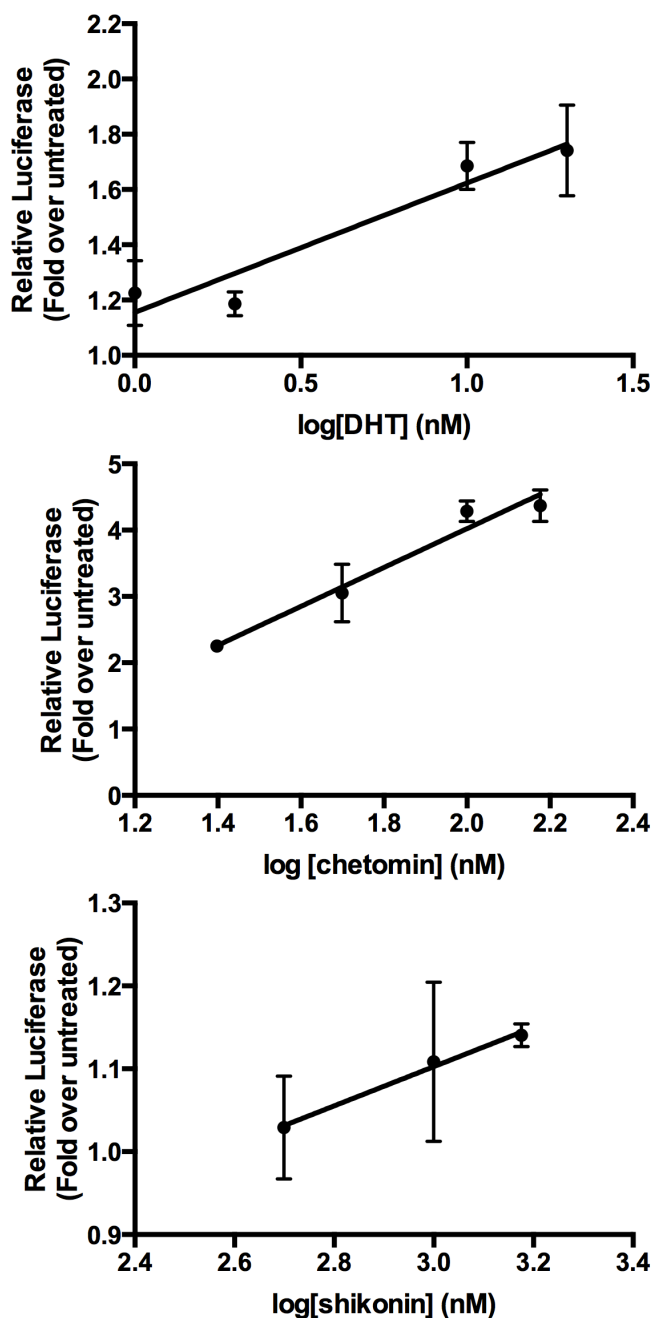
Article title: **Dual Targeting of the Androgen Receptor and Hypoxia-inducible Factor 1 α Pathways Synergistically Inhibits Castration-Resistant Prostate Cancer Cells**

Authors: Elena V. Fernandez, Kelie M. Reece, Ariel M. Ley, Sarah M. Troutman, Tristan M. Sissung, Douglas K. Price, Cindy H. Chau, and William D. Figg

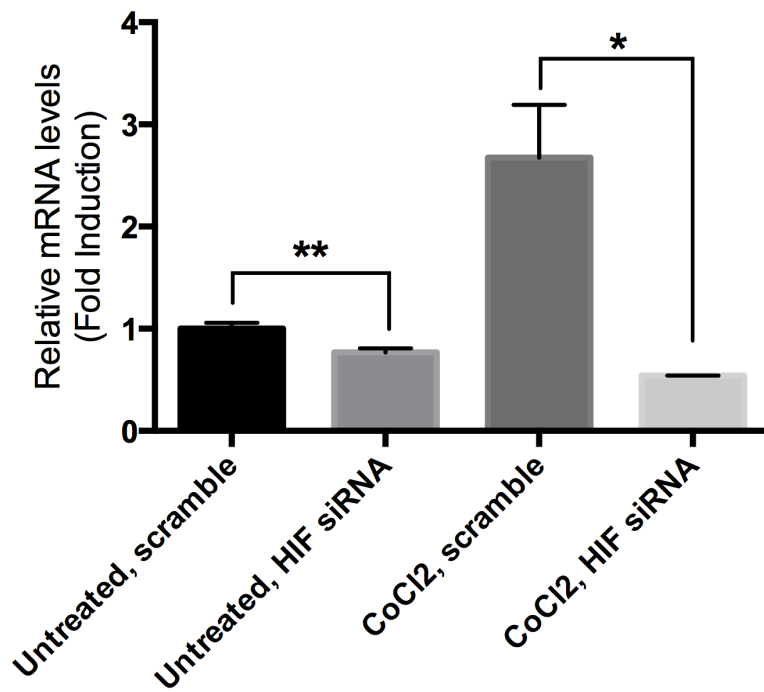
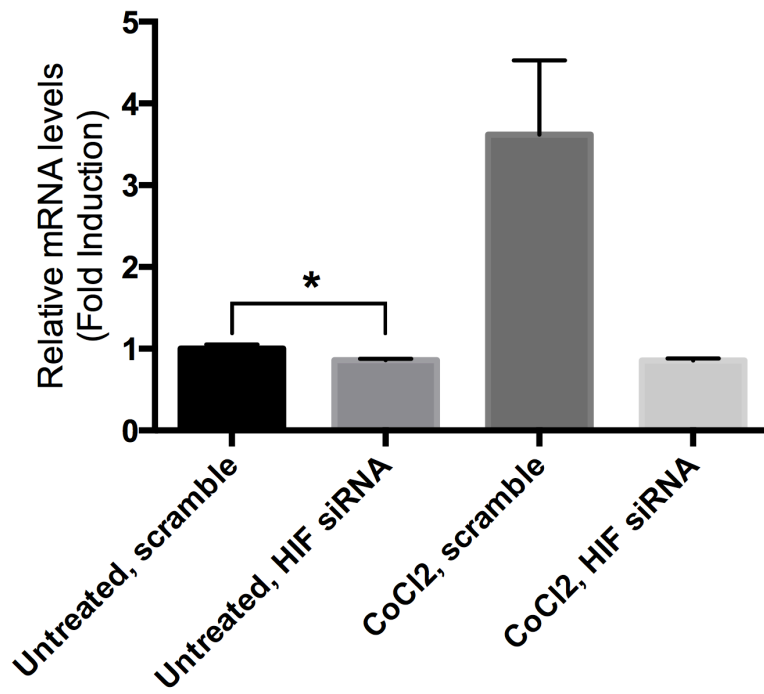
Journal Title: Molecular Pharmacology



Supplementary Figure 1. Effects of chetomin and enzalutamide on *KLK3* in 22Rv1 cells. 22Rv1 cells were cultured in the presence or absence of DHT (1 nM) under normoxic (N) or hypoxic (150 μ M CoCl₂) conditions for 18 h. Total RNA was extracted and qPCR analyses were performed for target gene, *KLK3*. Relative mRNA levels of each target gene expression are normalized by β -actin expression, and the results are indicated as fold change from those in the absence of DHT in normoxia. The result is representative of three independent experiments. ** $P < 0.01$, *** $P < 0.001$ on Figure.



Supplementary Figure 2. Reporter gene assay showing DHT and HIF-1 α inhibitors increasing AR transactivation. LNCaP or 22Rv1 cells were co-transfected with the ARE-luciferase construct and the pRL-TK construct, and the activity of the firefly luciferase was normalized by that of the *Renilla* luciferase. (A) DHT ((ARE-luc fold-change)/log[nM] = 0.47, $R^2=0.92$, $P=0.042$); (B) chetomin ((ARE-luc fold-change)/log[nM] = 2.93, $R^2=0.97$, $P=0.017$); (C) shikonin ((ARE-luc fold-change)/log[nM] = 0.24, $R^2=0.99$, $P=0.057$).



Supplementary Figure 3. HIF-1 α siRNA reduces transcription of two HIF-1 α targets: (A) ENO1 and (B) LDHA. * P <0.05, ** P <0.01 on Figure.