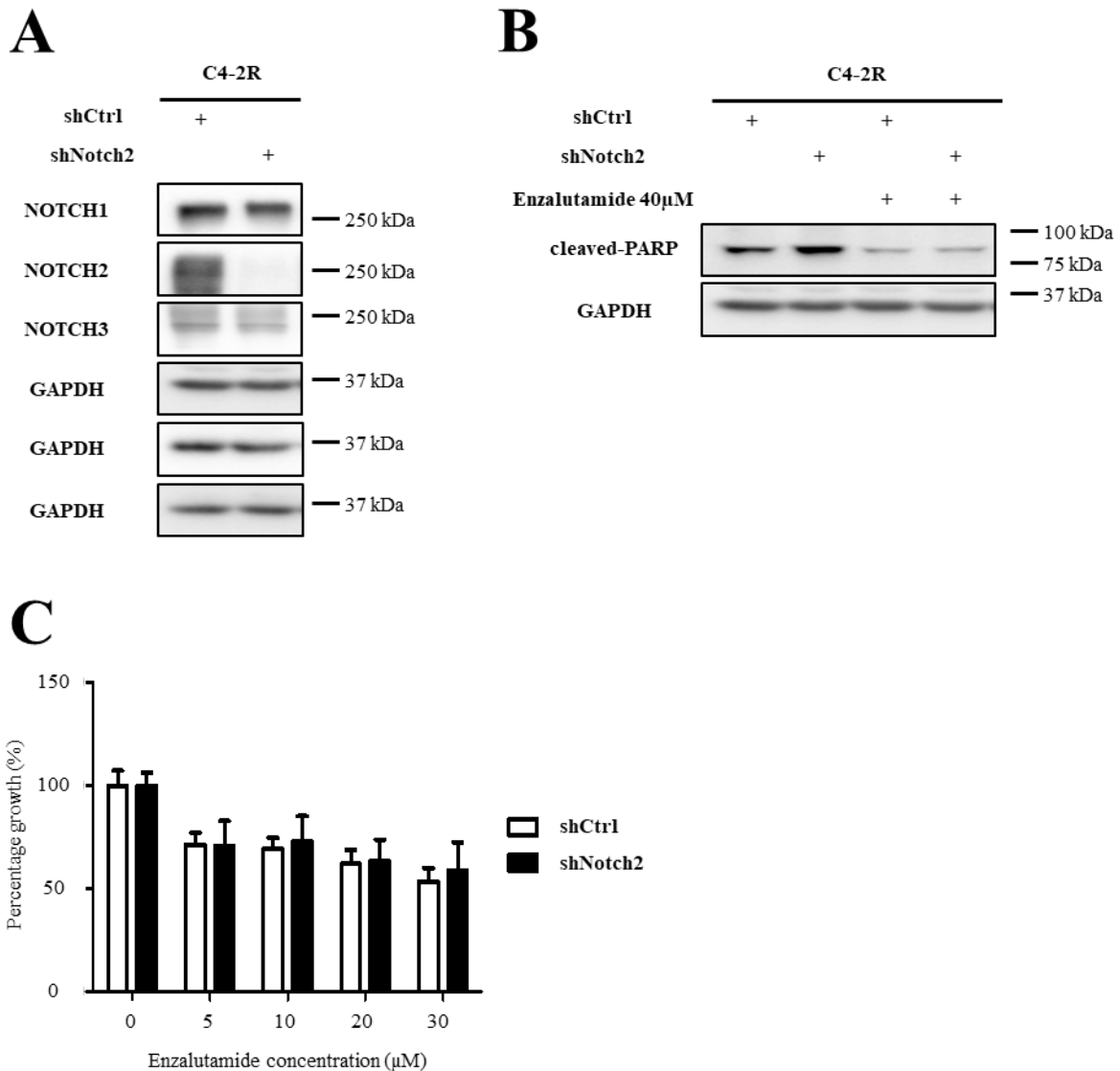


LNcaP vs. MR49F	C4-2 vs. C4-2R
SEL1L	UBB
FOXA1	RPS19
RPS27A	MYC
RBPJ	GALNT11
SNW1	APH1A
ADAM10	MIB2
IFT74	NCSTN
MIB1	APH1B
WDR12	MAML3
MAML1	PSEN1
RPS19	EPN1
PSEN2	PSEN2
NCSTN	SEL1L
UBB	CREBBP
SUSD5	POFUT1
MYC	ADAM17
APH1A	RBPJ
DTX4	ITCH
IFT172	NKAP
ADAM17	EP300
GMDS	MAML1
DTX3	IFT74
NEURL1B	SNW1
UBC	KAT2B
GALNT11	RBM15
APH1B	NOTCH2
CDKN1B	SPEN
NKAP	APP
ITGB1BP1	NOTCH3
KAT2B	IFT172
KRT19	ITGB1BP1
S1PR3	JAG2
GOT1	WDR12
MIB2	JAG1
NLE1	HES1
POFUT1	SUSD5
JAG2	DTX3
NOTCH2	KRT19
PSEN1	DTX4
PERP	HNF1B
NOTCH1	RPS27A
SPEN	MDK
CREBBP	FOXA1
EP300	ADAM10
APP	GOT1
MDK	NOTCH1
NOTCH3	UBC
SOX9	GMDS
MAML3	CEBPA
JAG1	PERP
UBA52	CDKN1B
ANXA4	S1PR3
EPN1	SOX9

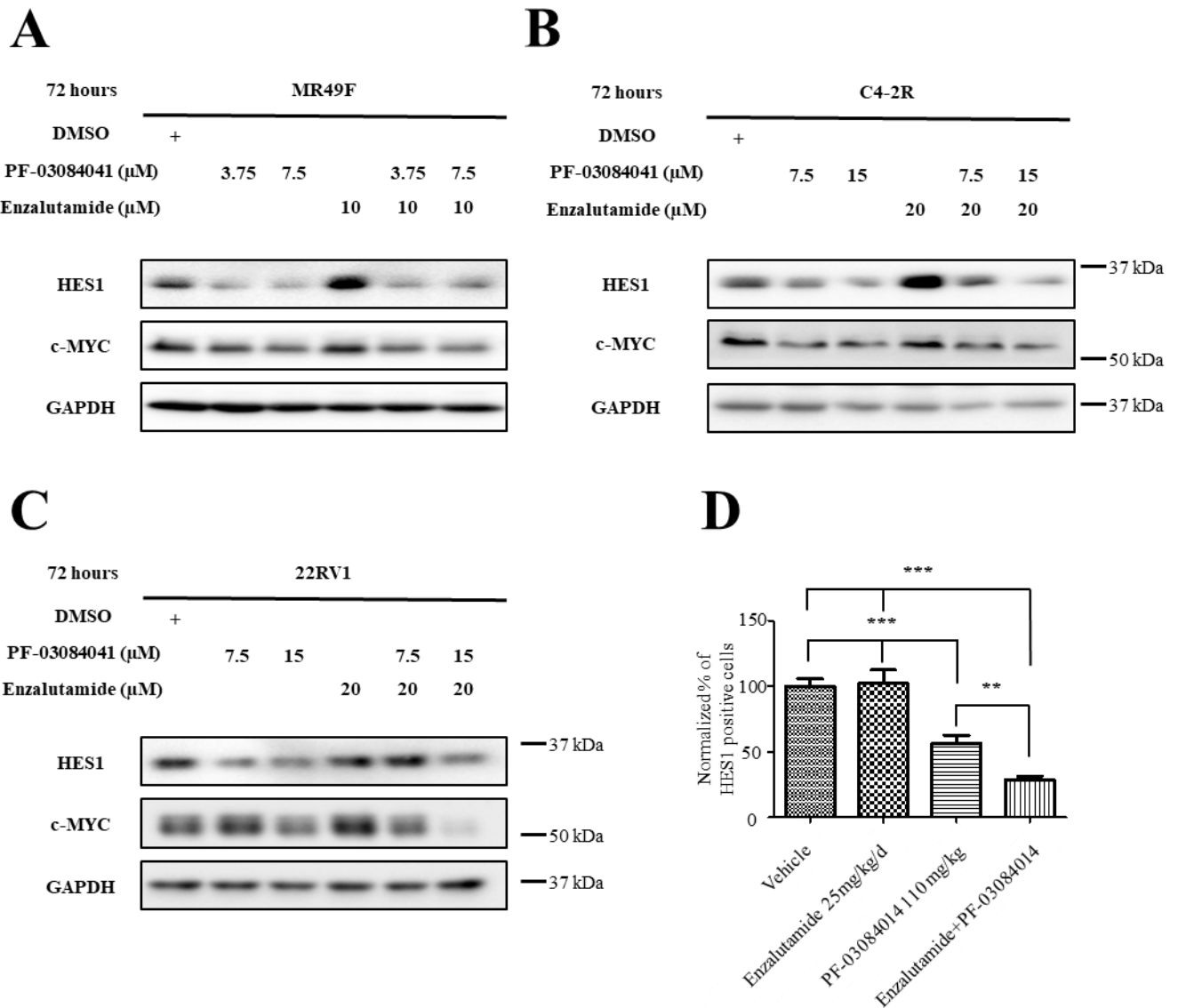
DTX2	NEURL1B
CEBPA	UBA52
ITCH	PSENEN
PSENEN	DTX2
HNF1B	NLE1
RBM15	MIB1
HES1	ANXA4

Supplemental Table S1. List of differentially expressed genes in LNCaP vs. MR49F and C4-2 vs. C4-2R. The list of genes corresponds to the heatmaps represented in Figures 3A and 3B. Genes are listed in an order matching the representative heatmap.



Supplemental Figure S1. Knockdown of Notch2 induces no changes in cleaved-PARP expression and in cell proliferation. **A**, C4-2R cells were infected with shCtrl or shNotch2 virus particles and selected with

puromycin. Cells were collected and subjected to western blot analysis with indicated antibodies. **B**, Stable C4-2R shCtrl and shNotch2 cells were treated with DMSO or 40 μ M enzalutamide for 72 hours and subjected to western blot analysis with indicated antibodies. **C**, Stable C4-2R shCtrl and shNotch2 cells were treated with DMSO or increasing concentrations of enzalutamide and subjected to MTT assay. Optical densities were measured and normalized to DMSO-treated samples.



Supplemental Figure S2. PF-03084014 reduces the expression of Notch signaling downstream targets in enzalutamide-resistant cell lines *in vitro* and *in vivo*. **A**, **B** and **C**, MR49F, C4-2R and 22RV1 cells were treated with DMSO, PF-03084014, enzalutamide or both at the indicated concentrations for 72 hours. Cells were collected and subjected to western blot. **D**, Quantification of HES1 positively stained cells (n=3). All groups were normalized to the vehicle control group. * indicates that p-value<0.05, ** indicates that p-value<0.01 and *** indicates that p-value<0.001.