

APPENDIX

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Appendix Table S1. Primer sequence for Sanger sequencing, RT-qPCR and ChIP-qPCR

Gene	Usage	Forward (5' - 3')	Reverse (5' - 3')
<i>SPOP</i> (Q165P)	Sequencing	TTTGCCCAGGTTTGTAGTCC	TCATCATCCATGCCTTGAAA
<i>SPOP</i> (Exon 6)	Sequencing	ACCCATAGCTTTGGTTTCTTCTCC C	TATCTGTTTTGGACAGGTGTTTGC G
<i>SPOP</i> (Exon 7)	Sequencing	ACTCATCAGATCTGGGAACTGC	AGTTGTGGCTTTGATCTGGTT
<i>GAPDH</i>	RT-qPCR	GAAGGTGAAGGTCGGAGTC	GAAGATGGTGATGGGATTC
<i>PSA</i>	RT-qPCR	AGGCCTTCCCTGTACACCAA	GTCTTGGCCTGGTCATTTC
<i>NKX3.1</i>	RT-qPCR	GTACCTGTGCGCCCCTGAAC	GGAGAGCTGCTTTCGCTTAG
<i>TMPRSS2</i>	RT-qPCR	TGGAGGTTGCTCAGGACTTC	GAGTTCAAAGCCATCTTGCTG
<i>RAC1</i> promoter	ChIP-qPCR	CCAAAGTGTTGGGATTACGG	CGGAGTTTCTCTGGACTTCG
<i>c-MYC</i> enhancer	ChIP-qPCR	GGCTTACAGGATACCCCCAACT	GGGCTATCACACCTCGCCC

Appendix Table S2. Patient-derived xenograft (PDX)

Name	Origin	Mutation status	Usage in this manuscript	Reference
LTL313HR (SPOP WT)	Primary prostate cancer	PTEN loss	Used in xenograft and organoid culture	First reported in this manuscript
LTL573R (SPOP Q165P)	Liver metastases tissue	SPOP mutation (Q165P), PTEN loss	Used in xenograft and organoid culture	First reported in this manuscript
V2-Met (SPOP WT)	Castrate-resistant prostate cancer (CRPC) metastases tissue	SPOP WT, <i>TMPRSS2-ETV4</i> fusion	Used in xenograft and organoid culture	(Kohli et al, 2015)

Appendix Table S3. Patient-derived organoids

Name	Origin	Mutation status	Collaboration	Reference
LTL313HR	PDX originally derived from primary prostate cancer	SPOP WT, PTEN loss	BC Cancer Research Centre, Canada	First reported in this manuscript
LTL573R	PDX originally derived from liver metastases tissue	SPOP mutation (Q165P), PTEN loss	BC Cancer Research Centre, Canada	First reported in this manuscript
MSK-PCa1 (BM1)	L2 vertebral body	SPOP WT, PTEN loss	Memorial Sloan Kettering Cancer Center, New York, USA	(Gao et al, 2014; Zhang et al, 2017)
MSK-PCa2 (BM5)	Acetabulum	SPOP WT, PTEN loss	Memorial Sloan Kettering Cancer Center, New York, USA	(Gao et al, 2014; Zhang et al, 2017)
MSK-PCa3 (ST1)	Retroperitoneal lymph node	SPOP WT, PTEN loss	Memorial Sloan Kettering Cancer Center, New York, USA	(Gao et al, 2014; Zhang et al, 2017)
MSK-PCa15 (ASC1)	Primary prostate cancer	SPOP mutation (W131R)	Memorial Sloan Kettering Cancer Center, New York, USA	(Gao et al, 2014; Zhang et al, 2017)

Appendix Table S4. Detailed *P* values and sample number (n)

Figure	Compared groups	Symbol	<i>P</i> Value
Fig 1E	SPOP WT (n = 85) vs. SPOP MUT (n = 12)	**	0.0012
Fig 1G	SPOP WT (n = 85) vs. SPOP MUT (n = 12)	***	0.0006
Fig 4B	In lenti-EV groups:		
	DMSO (n = 15) vs. JQ1 (n = 5)	***	1.59E-06
	DMSO (n = 15) vs. CPI-637 (n = 5)	***	8.69E-10
	DMSO (n = 15) vs. JQ1 + CPI-637 (n = 5)	***	1.89E-11
	DMSO (n = 15) vs. NEO2734 (n = 5)	***	9.22E-15
	In lenti-HA-SPOP-Q165P groups:		
	DMSO (n = 15) vs. JQ1 (n = 5)	*	0.049
	DMSO (n = 15) vs. CPI-637 (n = 5)	***	1.74E-5
	DMSO (n = 15) vs. JQ1 + CPI-637 (n = 5)	***	6.55E-13
	DMSO (n = 15) vs. NEO2734 (n = 5)	***	1.01E-13
	lenti-EV (DMSO, n = 15) vs. Lenti-HA-SPOP-Q165P (DMSO, n = 15)	*	0.018
Fig 4E	Lenti-EV (DMSO, n = 4) vs. Lenti-EV (NEO2734, n = 4)	**	0.008
	Lenti-EV (DMSO, n = 4) vs. Lenti-HA-SPOP-Q165P (DMSO, n = 4)	*	0.047
	Lenti-HA-SPOP-Q165P (DMSO, n = 4) vs. Lenti-HA-SPOP-Q165P (NEO2734, n = 4)	**	0.003
Fig 4F	BRD4 enrichment at the enhancer of <i>c-MYC</i> :		
	DMSO (n = 3) vs. JQ1 (n = 3)	**	0.0048
	JQ1 + CPI-637 (n = 3) vs. NEO2734 (n = 3)	n.s.	0.440
	BRD4 enrichment at the promoter of <i>RAC1</i> :		
	DMSO (n = 3) vs. JQ1 (n = 3)	*	0.012
	JQ1 + CPI-637 (n = 3) vs. NEO2734 (n = 3)	n.s.	0.305
Fig 4G	Ac-H3 level at the enhancer of <i>c-MYC</i> :		
	DMSO (n = 3) vs. CPI-637 (n = 3)	***	0.0067
	JQ1 + CPI-637 (n = 3) vs. NEO2734 (n = 3)	***	0.0097
	Ac-H3 level at the promoter of <i>RAC1</i> :		
	DMSO (n = 3) vs. CPI-637 (n = 3)	**	0.0014
	JQ1 + CPI-637 (n = 3) vs. NEO2734 (n = 3)	**	0.0020
Fig 5C	SPOP WT (Vehicle, n = 10) vs. Q165P (Vehicle, n = 10)	***	1.69E-05
	SPOP WT (Vehicle, n = 10) vs. SPOP WT (JQ1, n = 10)	***	9.44E-09
	SPOP Q165P (Vehicle, n = 10) vs. SPOP Q165P (JQ1, n = 10)	***	2.10E-09
	SPOP Q165P (JQ1, n = 10) vs. SPOP Q165P (NEO2734, n = 7)	***	2.17E-05
	SPOP Q165P (CPI-637, n = 9) vs. SPOP Q165P (NEO2734, n = 7)	***	2.53E-08
Fig 6D	BM1 (DMSO, n = 49) vs. BM1 (JQ1, n = 48)	***	0.00012
	BM1 (JQ1 + CPI-637, n = 52) vs. BM1 (NEO2734, n = 42)	**	0.0049
	BM5 (DMSO, n = 52) vs. BM5 (JQ1, n = 50)	***	1.21E-07
	BM5 (JQ1 + CPI-637, n = 49) vs. BM5 (NEO2734, n = 43)	*	0.044
	ST1 (DMSO, n = 52) vs. ST1 (JQ1, n = 45)	*	0.019
	ST1 (JQ1 + CPI-637, n = 52) vs. ST1 (NEO2734, n = 42)	**	0.0014
	313HR (DMSO, n = 50) vs. 313HR (JQ1, n = 48)	***	9.54E-07
	313HR (JQ1 + CPI-637, n = 50) vs. 313HR (NEO2734, n = 44)	***	3.24E-11
	ASC1 (DMSO, n = 50) vs. ASC1 (JQ1, n = 52)	n.s.	0.699
	ASC1 (JQ1 + CPI637, n = 50) vs. ASC1 (NEO2734, n = 38)	***	6.11E-07
	573R (DMSO, n = 52) vs. 573R (JQ1, n = 52)	*	0.022
	573R (JQ1 + CPI-637, n = 53) vs. 573R (NEO2734, n = 45)	***	5.43E-17

Figure	Compared groups	Symbol	P Value
Fig 6F	SPOP WT groups (313HR):		
	DMSO (n = 10) vs. JQ1 (n = 10)	***	6.88E-07
	DMSO (n = 10) vs. CPI-637 (n = 10)	***	0.0006
	DMSO (n = 10) vs. JQ1 + CPI-637 (n = 10)	***	7.79E-07
	DMSO (n = 10) vs. NEO2734 (n = 10)	***	2.39E-10
	SPOP MUT groups (573R):		
	DMSO (n = 10) vs. JQ1 (n = 10)	*	0.025
	DMSO (n = 10) vs. CPI-637 (n = 10)	***	4.32E-06
Fig 7B	DMSO (n = 10) vs. JQ1 + CPI-637 (n = 10)	***	3.07E-09
	DMSO (n = 10) vs. NEO2734 (n = 10)	***	7.31E-08
	EV (DMSO, n = 7) vs. EV (JQ1, n = 7)	***	2.13E-08
	EV (JQ1 + CPI-637, n = 7) vs. EV (NEO2734, n = 7)	***	6.92E-07
	Q165P (DMSO, n = 7) vs. Q165P (JQ1, n = 7)	*	0.015
	Q165P (JQ1 + CPI-637, n = 7) vs. Q165P (NEO2734, n = 7)	***	3.85E-07
	F133V (DMSO, n = 7) vs. F133V (JQ1, n = 7)	n.s.	0.055
	F133V (JQ1 + CPI-637, n = 7) vs. F133V (NEO2734, n = 7)	***	1.40E-13
Fig 7E	EV (DMSO, n = 7) vs. Q165P (DMSO, n = 7)	***	0.0002
	EV (DMSO, n = 7) vs. F133V (DMSO, n = 7)	***	1.78E-06
	EV (DMSO, n = 4) vs. EV (NEO2734, n = 4)	***	6.12E-05
	Q165P (DMSO, n = 4) vs. Q165P (NEO2734, n = 4)	***	5.52E-05
	F133V (DMSO, n = 4) vs. F133V (NEO2734, n = 4)	***	4.71E-05
Fig 7H	EV (DMSO, n = 4) vs. Q165P (DMSO, n = 4)	*	0.044
	EV (DMSO, n = 4) vs. F133V (DMSO, n = 4)	*	0.032
	EV (Vehicle, n = 6) vs. EV (JQ1, n = 6)	***	1.90E-05
	Q165P (Vehicle, n = 6) vs. Q165P (JQ1, n = 6)	**	0.005
	F133V (Vehicle, n = 6) vs. F133V (JQ1, n = 6)	*	0.017
	EV (Vehicle, n = 6) vs. EV (NEO2734, n = 6)	**	0.0047
	Q165P (Vehicle, n = 6) vs. Q165P (NEO2734, n = 6)	***	1.65E-06
Fig EV2A	F133V (Vehicle, n = 6) vs. F133V (NEO2734, n = 6)	***	7.13E-07
	BRD4 enrichment at the enhancer of <i>c-MYC</i> :		
	DMSO (n = 3) vs. JQ1 (n = 3)	**	0.0017
	JQ1 + CPI-637 (n = 3) vs. NEO2734 (n = 3)	n.s.	0.416
Fig EV2B	BRD4 enrichment at the promoter of <i>RAC1</i> :		
	DMSO (n = 3) vs. JQ1 (n = 3)	**	0.0021
	JQ1 + CPI-637 (n = 3) vs. NEO2734 (n = 3)	n.s.	0.263
	Ac-H3 level at the enhancer of <i>c-MYC</i> :		
Fig EV2B	DMSO (n = 3) vs. CPI-637 (n = 3)	**	0.0093
	JQ1 + CPI-637 (n = 3) vs. NEO2734 (n = 3)	***	3.05E-05
	Ac-H3 level at the promoter of <i>RAC1</i> :		
	DMSO (n = 3) vs. CPI-637 (n = 3)	**	0.0018
Fig EV2B	JQ1 + CPI-637 (n = 3) vs. NEO2734 (n = 3)	***	0.0002
Fig EV4B	313HR (WT, n = 12) vs. 573R (MUT, n = 14)	n.s.	0.133
Fig EV4D	313HR (WT, n = 3) vs. 573R (MUT, n = 3)	n.s.	0.445
Fig EV5D	SPOP WT (n = 60) vs. SPOP Q165P (n = 52)	**	0.0013
Fig EV5F	313HR (DMSO, n = 10) vs. 573R (DMSO, n = 10)	*	0.0412
	All 313HR treatment groups (n = 10)	n.s.	0.855
	All 573R treatment groups (n = 10)	n.s.	0.296