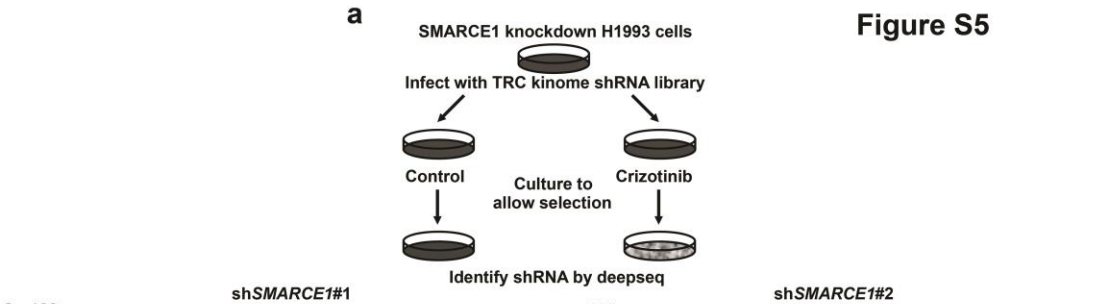
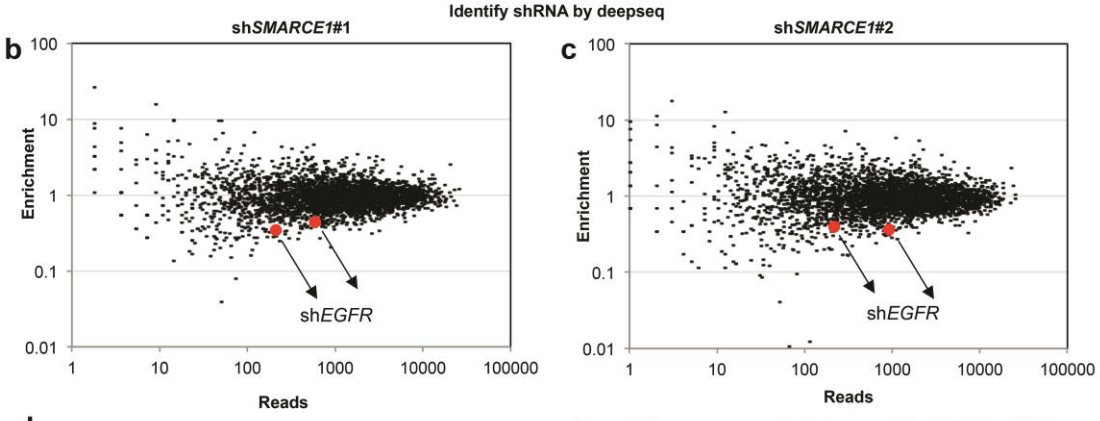
Figure S5





d

TRC#	Symbol	Crizotinib/UT	UT/T0
TRCN0000010075	*BLK*	0.26	1.24
TRCN0000057884	*CCL15*	0.27	1.23
TRCN0000002000	*PDGFRB*	0.29	0.81
TRCN0000010105	*LYN*	0.32	0.88
TRCN0000220129	*C7orf16*	0.33	1.22
TRCN0000038683	*GSK3A*	0.34	1.04
TRCN0000221545	*MTOR*	0.34	0.85
TRCN0000121071	*EGFR*	0.35	1.05
TRCN0000039615	*ATR*	0.36	0.86
TRCN0000010280	*MAPK9*	0.36	1.19
TRCN0000037507	*RIOK2*	0.38	1.22
TRCN0000036967	*SPHK1*	0.39	0.94
TRCN0000000733	*MAP3K14*	0.40	0.90
TRCN0000002139	*DYRK1B*	0.40	0.88
TRCN0000000805	*CSK*	0.40	0.80
TRCN0000021413	*NEK5*	0.41	1.04
TRCN0000000724	*CDKL2*	0.43	0.77
TRCN0000001793	*PRKCQ*	0.43	1.24
TRCN0000009819	*AKT2*	0.44	1.06
TRCN0000000758	*CLK1*	0.44	1.04
TRCN0000001751	*PAK6*	0.44	1.05
TRCN0000000921	*WNK1*	0.44	1.01
TRCN0000000893	*ULK2*	0.44	0.75
TRCN0000039635	*EGFR*	0.45	1.25
TRCN0000002094	*STK35*	0.46	1.08
TRCN0000010236	*VRK3*	0.46	0.92
TRCN0000003267	*ZAK*	0.46	1.23
TRCN0000037407	*TRIB3*	0.47	0.99
TRCN0000010313	*CHEK2*	0.48	1.19
TRCN0000010231	*EIF2AK1*	0.49	1.24
TRCN0000002410	*FLJ25006*	0.49	1.06
TRCN0000009951	*DGKG*	0.49	1.10
TRCN0000033269	*PIK3R5*	0.49	0.78
TRCN0000039945	*CHEK2*	0.49	0.94
TRCN0000221540	*PDPK1*	0.49	0.79
TRCN0000010268	*GCK*	0.49	1.24
TRCN0000009982	*TEC*	0.49	0.76

e

TRC#	Symbol	Crizotinib/UT	UT/T0
TRCN0000121183	*FGFR1*	0.24	0.85
TRCN0000000259	*PDK3*	0.30	0.87
TRCN0000010032	*PRKG1*	0.31	0.93
TRCN0000000630	*FGFR4*	0.33	1.08
TRCN0000039635	*EGFR*	0.36	1.24
TRCN0000000876	*IRAK3*	0.38	0.76
TRCN0000130981	*C18orf15*	0.38	1.11
TRCN0000009975	*MAP2K3*	0.40	1.24
TRCN0000002408	*GRK7*	0.40	1.17
TRCN0000000999	*MAP3K12*	0.40	1.12
TRCN0000001392	*MAP2K4*	0.41	1.17
TRCN0000121071	*EGFR*	0.42	0.94
TRCN0000006336	*PCTK3*	0.42	0.94
TRCN0000039881	*ERBB2*	0.43	1.18
TRCN0000003275	*STK31*	0.43	1.13
TRCN0000002042	*TNK2*	0.43	1.06
TRCN0000037522	*TP53RK*	0.43	0.79
TRCN0000001345	*EPHA8*	0.44	0.99
TRCN0000009960	*CAMK4*	0.44	1.01
TRCN0000040154	*BUB1*	0.44	0.87
TRCN0000037415	*PIM3*	0.44	1.23
TRCN0000012071	*Mef2c*	0.45	1.22
TRCN0000006038	*PRKCI*	0.45	0.75
TRCN0000039699	*INSR*	0.45	0.95
TRCN0000037405	*TRIB3*	0.46	0.98
TRCN0000021474	*ALPK1*	0.46	0.91
TRCN0000001436	*TESK2*	0.46	1.20
TRCN0000000440	*ZAP70*	0.46	1.10
TRCN0000000761	*PLK3*	0.47	0.96
TRCN0000005118	*IGF1R*	0.47	0.94
TRCN0000047596	*ARHGEF7*	0.47	1.06
TRCN0000007000	*HIPK4*	0.47	0.98
TRCN0000000858	*PRKAA1*	0.47	0.91
TRCN0000037586	*PI4K2B*	0.48	0.98
TRCN0000000921	*WNK1*	0.48	0.84
TRCN0000006323	*ICK*	0.48	0.84
TRCN0000121253	*MST1R*	0.48	1.15
TRCN0000007050	*STRADA*	0.49	1.04
TRCN0000001480	*PDPK1*	0.49	0.98
TRCN0000047174	*GOPC;ROS1*	0.49	1.22
TRCN0000006317	*CIT*	0.49	1.14
TRCN0000052395	*SERPINA2*	0.49	0.87

Supplementary information, Figure S5 Crizotinib re-sensitization Kinome screen in *SMARCE1* knockdown cells identifies *EGFR* as the top candidate required for drug resistance driving by *SMARCE1* knockdown.

(A) Schematic outline of the "drop out" RNAi screen for kinases whose inhibition restores sensitivity to crizotinib in *SMARCE1* knockdown cells. Human TRC kinome shRNA library polyclonal virus was produced to infect H1993 cells stably expressing sh*SMARCE1#*1 or sh*SMARCE1#*2, which were then left untreated (control) or treated with 300 nM crizotinib for 11 days. After selection, shRNA inserts from both populations were recovered by PCR and identified by next generation sequencing.
(B, C) Representation of the relative abundance of the shRNA bar code sequences from the shRNA screens experiment performed in H1993 cells stably expressing sh*SMARCE1#*1 (B) or sh*SMARCE1#*2 (C) as depicted in panel A. The y-axis is enrichment (relative abundance of crizotinib treated/untreated) and x-axis is the intensity (average sequence reads in untreated sample) of each shRNA. Among the top shRNA candidates (see selection criteria described below in Figure S4D and 4E), two independent sh*EGFR* vectors (in red) were identified from both screens.
(D, E) Lists of the top shRNA candidates from the screens performed in H1993 cells stably expressing sh*SMARCE1#*1 (D) or sh*SMARCE1#*2 (E). Candidates were selected based on the following criteria: more than 2-fold depleted by crizotinib treatment; more than 200 reads in the untreated pool; do not have significant impact on proliferation in the absence of crizotinib (UT/T0 > 0.75 and < 1.25). Only genes that are represented by 2 or more shRNAs are considered as hits. UT, untreated; T0, time point taken right after introduction of kinome shRNA library.