Plasmid	Source	Protocol Specifics	
Triple Reporter ERK kinase translocation mTurquoise (ERK-KTR), H2B-Venus and Geminin-mCherry	Gift from Dr. Luca Gerosa and Dr. Peter Sorger at Harvard Medical School (30-31)	Co-transfection of TBP3743 with piggybac transposase vector at 1:1 ratio with lipofectamine, selecting with 5 µg/ml puromycin (Gibco) and sorted by FACS	
pHAGE-BRAFV600E	Addgene plasmid no. 116204, a gift from Gordon Mills & Kenneth Scott	5000 Nhy-ori-3-1 or TPC1 cells were seeded into each well of 96- well image plates (Ibidi). After overnight incubation, fresh media containing 0.25 ng/μl of each plasmid DNA was added for 72 h	
pHAGE-BRAF <sup>wT</sup>	Addgene plasmid no. 116719, a gift from Gordon Mills & Kenneth Scott		
pHAGE_puro	Addgene plasmid no. 118692, a gift from Christopher Vakoc		
pBabe-KRASG12D	Addgene #58902, a gift from Christopher Vakoc		
pBabe-KRAS <sup>w7</sup>	Addgene #75282, a gift from Christopher Vakoc		
IGF1R siRNA SMARTPool	Dharmacon	7000 8505c cells or 6000 Nthy-ori-3-1 cells were seeded into	
PTEN siRNA SMARTPool	Dharmacon	each well of 96-well image plates (Ibidi) or 0.5 million 8505c cel were seeded into 10 cm tissue culture plates overnight for IGF1	
non-targeting siRNA control pool	Dharmacon	siRNA transfection. Media was replaced with growth media containing 25 nM siRNA in transfection reagent (Dharmacon) ar incubated for another 72 h prior to treatment with albumin or dextran	

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Cell Line	Source	RRID
8505c	Purchased from DSMZ	CVCL_1054
THJ-21t	abmgood	CVCL_W921
TPC1	Dr. F. Frasca (University of Catania, Italy)	CVCL_6298
BCPAP	Dr. G. Damante (University of Udine, Italy)	CVCL_0153
Nthy-ori-3-1	Dr. Raj Gopal (MGH)	CVCL_2659
FTC133	European Collection of	CVCL_1219
FTC236	Authenticated Cell Culture	CVCL_2446

Antibody	Source	Category #	RRID
p-AMPK	CST	#2535	AB_331250
p-IGF1R	CST	#3918	AB_10548764
p-ERK1/2	CST	#4370	AB_2315112
IGF1R	CST	#9750	AB_10950969
AMPK	CST	#2603	AB_490795
ERK	CST	#4695	AB_390779
PTEN	CST	#9559	AB_390810
β-actin	CST	#3700	AB_2242334
anti-rabbit IgG antibody AF647	Invitrogen	#A-21245	NA
rat anti-mouse CD16/CD32 antibody	BD Biosciences	#553141	AB_394656
CD45	BioLegend	#103151	AB_2565884
CD11b	BioLegend	#101210	AB_312793
F4/80	BioLegend	#123118	AB_893477
CD206	BioLegend	#141727	AB_2565822
CD80	BioLegend	#104729	AB_11126141
CD86	BioLegend	#105115	AB_493601

**Supplementary Table S1. Biological and chemical reagents and their sources.** This table reports detailed information of plasmids, siRNA and transfection protocols (A), human cell lines (B), and antibodies (C).