

Table S1. Reagents and Tools

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Antibodies		
Extracellular domain of E-cadherin	Santa Cruz Biotechnology	Cat# sc-7870, RRID:AB_2076666
Intracellular domain of E-cadherin	BD Biosciences	Cat# 610182, RRID:AB_397581
Vimentin	Abcam	Cat# ab24525, RRID:AB_778824
HIF-1 α	BD Biosciences	Cat# 610958, RRID:AB_398271
HIF-2 α	Invitrogen	Cat# PA1-16510, RRID: AB_2098236
Goat anti-mouse IgG (H + L) cross-adsorbed secondary antibody, DyLight 488	Thermo Fisher Scientific	Cat# 35503, RRID: AB_1965946
Goat anti-rabbit IgG (H + L) cross-adsorbed secondary antibody, DyLight 550	Thermo Fisher Scientific	Cat# SA5-10033, RRID: AB_2556613
Goat anti-Chicken IgY (H+L) Cross-Adsorbed Secondary Antibody, DyLight™ 550.	Invitrogen	Cat# SA5-10071, RRID: AB_2556651
β -actin	GeneTex	Cat# GTX109639, RRID: AB_1949572
GAPDH	GeneTex	Cat# GTX627408, RRID: AB_11174761
Horseradish peroxidase-conjugated secondary antibodies	Abcam	Cat# ab6721, RRID: AB_955447
ECL reagent(1) SuperSignal™ West Femto Maximum Sensitivity Substrate	Thermo Fisher Scientific	Cat# 34096
ECL reagent(2) Immobilon Forte Western HRP substrate	MilliporeSigma™	Cat#WBLUF0500
ECL reagent(3) Immobilon Crescendo Western HRP Substrate	MilliporeSigma™	Cat#WBLUR0500
Hemotoxylin Gill II	Leica Surgipath	Cat#3801520

Eosin	Leica Surgipath	Cat#3801602
Cytokeratin Pan Polyclonal Antibody	Invitrogen	Cat# PA1-27114 AB 780038
DAPI (4',6-Diamidino-2-phenylindole dihydrochloride).	Millipore Sigma Aldrich	Cat# D9542
Donkey anti-Rabbit IgG (H+L) Cross-Adsorbed Secondary Antibody, DyLight™ 488	Thermo Fisher Scientific	Cat# SA5-10038, RRID:AB_2556618
Goat anti-Mouse IgG (H+L) Secondary Antibody, DyLight™ 633	Thermo Fisher Scientific	Cat# 35512, RRID:AB_1307538
Biological samples		
Human head and neck cancer samples	Department of Otolaryngology, National Taiwan University Hospital and College of Medicine, Taiwan	N/A
Chemicals, peptides, and recombinant proteins		
DMEM/F12	Gibco™	Cat# 12500062
DMEM	Gibco™	Cat# 12100046
RPMI	Gibco™	Cat# 31800089
Cobalt Chloride (coCl ₂)	Sigma Aldrich	Cat#255599
Puromycin	Merck	P9620
Rat tail type I collagen	Corning Life Sciences	Cat# 354236
TransIT-LT1	Mirus Bio	MR-MIR2300
Critical commercial assays		
RNeasy mini kit	QIAGEN	Cat#QIA74104
RevertAid First Strand cDNA Synthesis Kit	Thermo Fisher Scientific	Cat#K1621
Quick-RNA Miniprep Kit	Zymo Research	Biosite-R1054
BIO-RAD iQ™ SYBR® Green Supermix (real-time PCR)	BIO-RAD	Cat#1708882
Deposited data		

Raw and analyzed data	Public studies and this paper	GSE178537
Raw and analyzed data	Public studies and this paper	GSE18300
RNAseq for tumor satellites	This paper	See Table_RNAseq for details
Experimental models: Organisms/strains		
N/A	N/A	N/A
Oligonucleotides		
HIF-1 α knockout sgRNA sequence #1 (5'-CGG GGA CCG ATT CAC CAT GG-3') was used for SAS and SCC25 cells sgRNA sequence #3 (5'-GAA CTC ACA TTA TGT GGA AG-3') was employed for OECM1 cells.	This paper	N/A
HIF-2 α knockout sgRNA sequence #2 (5'-GCT GAT TGC CAG TCG CAT GA- 3' for SAS, OECM1 and SCC25 cells.	This paper	N/A
Target site-specific primers HIF-1 α (sgRNA #1: F: 5'-TTG CCG CCC GCT TCT CTC TAG T-3' and R: 5'-ACA AGA TCG CAT CCG ACC ACG C-3'; sgRNA#3: F: 5'-GGA GGA AAC ACC TGC TTC CGA CA-3' and R: 5'-CGC CCG GCC TGA GTC ATG TTT T-3')	This paper	N/A
Target site-specific HIF-2 α (sgRNA#2: F:5'-TCT GGC CTC CAC AGG GAA TGC A-3' and R: 5'- AGC CTC TGG GTG CCC ATG TTC T-3').	This paper	N/A
HIF-1 α (HIF1A) (NM_001530) Human Tagged ORF Clone	OriGene	Cat# RC202461
HIF-2 α (EPAS1) (NM_001430) Human Tagged ORF Clone	OriGene	Cat# RC208604

PX459 plasmid	addgene	Cat# 62988, RRID:Addgene_21745 5
HIF-1 α Primer for rtPCR Forward: 5'- GAACGTCGAAAAGAAAAGTCTCG- 3'.	This paper	N/A
HIF-1 α Primer for rtPCR Reverse: 5'- CCTTATCAAGATGCGAACTCACA-3'	This paper	N/A
HIF-2 α Primer for rtPCR Forward: 5'-TGACCCAAGACGGTGACATGA- 3'.	This paper	N/A
HIF-2 α Primer for rtPCR Reverse: 5'-CATGGTCGCAAGGATGAGTGA-3'	This paper	N/A
Software and algorithms		
Stata/IC 17.0	Stata	RRID:SCR_012763
ImageJ	Rasband, W.S., U. S. NIH, Bethesda, Maryland, USA	https://imagej.nih.gov/ij/ RRID:SCR_003070
GraphPad Prism9.3.1	Dotmatics	GraphPad Software, Inc. Accessed 15 December 2021. RRID:SCR_002798
Transcriptome Analysis Console (TAC) 4.0.2	Thermo Fisher Scientific	TAC, Accessed January 2019
Enrichr Datasets2Tools	Ma'ayan et al.	https://maayanlab.cloud/Enrichr/
Appyters	Ma'ayan et al. (62, 63)	https://appyters.maayanlab.cloud/#/Bulk_RNA_seq
GO pathway resource	The Gene Ontology Resource	http://geneontology.org/

NCI-Nature PID	The NCI-Nature Pathway Interaction Database	http://pid.nci.nih.gov
KEGG pathway resource	KEGG pathway resource	https://www.genome.jp/kegg
Gene Set Enrichment Analysis	MSigDB collections	https://www.gsea-msigdb.org/gsea/msigdb/human/collections.jsp
Leica TCS SP8 Software Modules	Leica Microsystems	N/A
Imaris microscopy image analysis software	Oxford Instruments	N/A
Photoshop CS6	Adobe	N/A
Other		
UCSC Xena for GTEx RNAseq data download	M. J. Goldman et al. (64)	http://xena.ucsc.edu