Supplemental Methods

RNA isolation and RT-qPCR

RNA was prepared by collecting cells or tissue in TRIzol reagent regent and isolated using a Direct-zol RNA kit (Zymo research) using manufacturer's recommendations. For qRT-PCR experiments, RNA was reverse transcribed using iScript cDNA synthesis Kit (Bio-Rad), and iTaq Universal SYBR Green Supermix (Bio-Rad) was used. Reactions were carried out on a CFX96 Touch Real-Time PCR Detection System (Bio-Rad). Primers used were designed using Primer3 and sequences were as follows:

Primer name	Sequence 5' to 3'
PRANCR-Fwd	GAGCTTGTGCGCGTACTTC
PRANCR-Rev	TGGTTTCATCAGAGGGGAAC
CNOT2-Fwd	TGGGTTTCTACTTCCGCAGG
CNOT2-Rev	CACAGTACCGGAGGCAATCA
KRT1-Fwd	GAAGTCTCGAGAAAGGGAGCA
KRT1-Rev	ATGGGTTCTAGTGGAGGTATCTA
KRT10-Fwd	GCAAATTGAGAGCCTGACTG
KRT10-Rev	CAGTGGACACATTTCGAAGG
FLG-Fwd	AAAGAGCTGAAGGAACTTCTGG
FLG-Rev	AACCATATCTGGGTCATCTGG
IVL-Fwd	TGCCTGAGCAAGAATGTGAG
IVL-Rev	TGCTCTGGGTTTTCTGCTTT
NEAT1-Fwd	GACGGAGGTTGAGATGAAGC
NEAT1-Rev	ATTCGGGGCTCTGTAGTCCT
MALAT1-Fwd	TCGGGTATGCTGTTGTGAAA
MALAT1-Rev	TGACGTAACAGAATTAGTTCTTACCA
ACTB-Fwd	AGGCACCAGGGCGTGAT
ACTB-Rev	GCCCACATAGGAATCCTTCTGAC
GAPDH-Fwd	TCGACAGTCAGCCGCATCT
GAPDH-Rev	AGTTAAAAGCAGCCCTGGTGA
L32-Fwd	AGGCATTGACAACAGGGTTC
L32-Rev	GTTGCACATCAGCAGCACTT

Short hairpin design and selection

For knockdown of *PRANCR*, six independent short hairpin RNAs (shRNA) were initially designed and produced as described in the Methods section. The shRNA sequences are:

PRANCR-shA: 5'-TTCCACCCAAGCCACAATAAT-3' (selected as shLNC3)

PRANCR-shB: 5'-ACGACACGACCGTGCTTTAAA-3'

PRANCR-shC: 5'-GCAGATACTTCACTCCTTTAA-3'

PRANCR-shD: 5'-CCAGCTGGTCACTCTTGTTTA-3'

PRANCR-shE: 5'-CACTTTGAATGACAACGATTT-3' (selected as shLNC1)

PRANCR-shF: 5'- TACTTCACTCCTTTAAGTTTC -3' (selected as shLNC2)

SCR1: 5'-CCTAAGGTTAAGTCGCCCTCG-3'

SCR2: 5'-GCAAGCTGACCCTGAAGTTCA-3'

Immunofluorescence staining

Slides with tissue were fixed 10 minutes using either 4% paraformaldehyde (PFA), ice-cold methanol or ice-cold aceton (see table below), then permeabilized in 0.1% PBS-Tween for 3 minutes. Blocking was performed in 0.1% PBS-T supplemented with 5% goat serum for 1 hour at room temperature. Primary antibodies (see below) were incubated in 0.1% PBS-T supplemented with 2% goat serum overnight at 4°C. Secondary antibodies were incubated in 0.1% PBS-T supplemented with 2% goat serum for 45 minutes at room temperature. Afterwards, slides were incubated with Hoechst stain for 2 minutes. Immunofluorescence was performed using the following antibodies, fixatives and dilutions:

Target (host)	Company (Catalog #)	Fixative used	Dilution used
KRT10 (Rabbit)	Abcam (76318)	4% PFA	1:500
FLG (Rabbit)	Santa Cruz (66192)	Methanol	1:500
MKI67 (Mouse)	Invitrogen (MA5-14520)	Acetone	1:100
IRDye 680CW anti-Rabbit (Goat)	Li-Cor Biosciences (925-68071)	No	1:10,000
IRDye 680CW anti- Mouse (Donkey)	Li-Cor Biosciences (926-68072)	No	1:10,000

Apoptosis analysis

Apoptosis was analyzed using the Annexin V FITC Assay Kit (Cayman Chemical), according to manufacturer's instructions. In short, 1 x 10^5 cells puromycin-selected cells were collected in V-shaped wells of a 96-well plate. After staining for Annexin V-FITC/Propidium Iodide, cells were quantified by flow cytometry using the Guava Easycyte 8HT (Millipore). Apoptotic cells were defined as cells positive for Annexin V-FITC.

Western blot

Protein lysates were loaded onto 4-12% Bis-Tris gels (Invitrogen) and resolved by electrophoresis. Wet transfer was performed onto PVDF membranes, and primary antibodies were incubated overnight at 4°C (dilutions shown below). Membranes were washed 3 times in PBS-0.1% Tween, then incubated with fluorescent secondary antibodies according to manufacturer's recommendations (Li-Cor), washed, and visualized. Blots were imaged and quantitated on an Odyssey imager (Li-Cor). Western blot was performed using the following antibodies:

Target (host)	Company (Catalog #)	Dilution used
CNOT2 (Rabbit)	Cell Signaling Technologies (34214S)	1:1,000
TP53 (Mouse)	Cell Signaling Technologies (18032S)	1:1,000
CDKN1A (p21; Rabbit)	Cell Signaling Technologies (2947T)	1:1,000
E2F4 (Rabbit)	Cell Signaling Technologies (40291S)	1:1,000
TUBB (Mouse)	Development Studies Hybridoma Bank (DSHB) (E7)	1:1,000
GAPDH (Mouse)	Santa Cruz (47724)	1:200
LMNA/C (Mouse)	Cell Signaling Technologies (4777S)	1:1,000
IRDye 680RD anti-mouse (Donkey)	LI-COR Biosciences (926-68072)	1:10,000
IRDye 800CW anti-rabbit (Goat)	LI-COR Biosciences (926-32211)	1:10,000