

Supplementary Tables

Supplementary Table 1: Overview of experimental groups and timepoints

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|--|----------------------|----------------------|---|----|----|----|----|----|
| | Experimental groups | | Control groups (previously reported in [18]) | | | | | |
| Strain (<i>RASSF1A</i> -KO or WT) | KO | WT | KO | WT | KO | WT | KO | WT |
| Injected construct | NRAS ^{G12V} | NRAS ^{G12V} | | | | | | |
| 1x PBS injection | | | X | X | | | | |
| EV | | | | | X | X | | |
| untreated | | | | | | | X | X |
| Animals per timepoint (<i>N</i>) | | | | | | | | |
| 1 week | 10 | 10 | 5 | 5 | 5 | 5 | 5 | 5 |
| 1 month | 10 | 10 | 5 | 5 | 5 | 5 | 5 | 5 |
| 3 months | 10 | 10 | 5 | 5 | 5 | 5 | 5 | 5 |
| 6 months | 10 | 10 | 5 | 5 | 5 | 5 | 5 | 5 |
| 9 months | 10 | 10 | 5 | 5 | 5 | 5 | 5 | 5 |
| 12 months | 10 | 10 | 5 | 5 | 5 | 5 | 5 | 5 |
| Sum of animals per experimental group | 60 | 60 | 30 | 30 | 30 | 30 | 30 | 30 |
| Sum of all animals | 300 | | | | | | | |

Supplementary Table 2: Antibodies used for immunohistochemistry and Western blots

| Name | Dilution | Company | Catalogue number |
|---|---------------------------------------|--|------------------|
| Primary antibodies | | | |
| AKT (pan) (C67E7) Rabbit mAb | WB: 1:1000 | Cell Signaling Technology, Inc., Cambridge, UK | 4691S |
| Anti-beta Actin antibody [mAbcam 8226] - Loading Control (HRP) | WB: 1:5000 | Abcam plc., Cambridge, UK | ab8226 |
| Anti-CD133 antibody – Stem Cell Marker | WB: 1:1000 IHC 1:100 | Abcam plc., Cambridge, UK | ab16518 |
| Anti-NRAS antibody | WB: 1:500 | Abcam plc., Cambridge, UK | ab77392 |
| Anti-phospho-mTOR (Ser2448) Antibody | WB: 1:333 | Merck KGaA, Darmstadt, Germany | 09-213 |
| C/EBP α (D56F10) XP $\text{\textcircled{R}}$ Rabbit mAb | WB: 1:1000 IHC: 1:100 | Cell Signaling Technology, Inc., Cambridge, UK | 8178S |
| Cyclin D1 (E3P5S) XP $\text{\textcircled{R}}$ Rabbit mAb | IHC: 1:100 | Cell Signaling Technology, Inc., Cambridge, UK | 55506S |
| Cyclin E1 Polyclonal Antibody | IHC: 1:100 | Proteintech Group, Inc., Rosemont, USA | 11554-1-AP |
| mTOR Antibody | WB: 1:333 | Merck KGaA, Darmstadt, Germany | 04-385 |
| N-Ras Antikörper (C-20) | WB: 1:50 IHC: 1:100 | Santa Cruz Biotechnology, Inc., Dallas, USA | sc-519 |
| NF- κ B p65 (D14E12) XP $\text{\textcircled{R}}$ Rabbit mAb | WB: 1:500 | Cell Signaling Technology, Inc., Cambridge, UK | 8242S |
| Osteopontin polyclonal Antibody | WB: 1:500 | Proteintech Group, Inc., Rosemont, USA | 22952-1-AP |
| p-Raf-1 (Ser259)-R | WB: 1:200 | Santa Cruz Biotechnology, Inc., Dallas, USA | sc-21833 |
| p44/42 MAPK (ERK 1/2) (137F5) Rabbit mAb | WB: 1:1000 | Cell Signaling Technology, Inc., Cambridge, UK | 4695S |
| Phospho-4E-BP1 (Thr37/46) (236B4) Rabbit mAb | WB: 1:1000 IHC: 1:300 | Cell Signaling Technology, Inc., Cambridge, UK | 2855 |
| Phospho-AKT (Ser473) (D9E) XP $\text{\textcircled{R}}$ Rabbit mAb | WB: 1:1000 IHC: 1:50 | Cell Signaling Technology, Inc., Cambridge, UK | 4060 |
| Phospho-c-Jun (Ser63) II Antibody | WB: 1:1000 | Cell Signaling Technology, Inc., Cambridge, UK | 9261S |
| Phospho-c-Jun (Ser73) (D47G9) XP $\text{\textcircled{R}}$ Rabbit mAb | WB: 1:1000 | Cell Signaling Technology, Inc., Cambridge, UK | 3270S |
| Phospho-MEK1/2 (Ser217/221) (E4M5C) Rabbit mAb | WB: 1:1000 WB: 1:500 IHC: 1:100 | Cell Signaling Technology, Inc., Cambridge, UK | 86128S |
| Phospho-NDRG1 (Thr346) (D98G11) XP $\text{\textcircled{R}}$ Rabbit mAb | WB: 1:500 IHC: 1:500 | Cell Signaling Technology, Inc., Cambridge, UK | 5482S |
| Phospho-NF- κ B p65 (Ser276) Antibody | WB: 1:500 | Cell Signaling Technology, Inc., Cambridge, UK | 3037S |
| Phospho-p44/42 MAPK (ERK1/2) (Thr202/Tyr204) (D13.14.4E) XP $\text{\textcircled{R}}$ Rabbit mAb | WB: 1:1000 IHC: 1:100 | Cell Signaling Technology, Inc., Cambridge, UK | 4370S |
| Phospho-S6 Ribosomal Protein (Ser235/236) (2F9) Rabbit mAb | WB: 1:1000 IHC: 1:100 | Cell Signaling Technology, Inc., Cambridge, UK | 4856S |
| Rabbit anti-FASN Antibody | WB: 1:100 IHC: 1:100 | Bethyl Laboratories, Inc., Montgomery, USA | A301-323A |
| Rabbit anti-Ki-67 IHC Antibody | IHC: 1:100 | Bethyl Laboratories, Inc., Montgomery, USA | ICH-00375 |
| RAF1 Antibody | WB: 1:500 | LifeSpan BioSciences, Inc, Seattle; USA | LS-C49537 |
| Ral B Antibody (R-19) | WB: 1:200 | Santa Cruz Biotechnology, Inc., Dallas, USA | sc-1531 |
| RALA Polyclonal Antibody | WB: 1:333 | Thermo Fisher Inc. Waltham, USA | OSR00268W |
| RAS (E8N8L) XP $\text{\textcircled{R}}$ Rabbit mAb | IHC: 1:100 | Cell Signaling Technology, Inc., Cambridge, UK | 67648S |

| | | | |
|--|--------------------------|--|------------|
| Recombinant Ant-CPS1 antibody [EPR7493-3] | IHC: 1:100 | Abcam plc., Cambridge, UK | ab129076 |
| Recombinant Anti-c-Myc antibody [Y69] | WB: 1:1000 | Abcam plc., Cambridge, UK | ab32072 |
| Recombinant Anti-CD133 antibody [EPR24348-38] | WB: 1:500 IHC: 1:200 | Abcam plc., Cambridge, UK | ab271092 |
| Recombinant Anti-Cytokeratin 7 antibody [EPR17078] – Cytoskeleton Marker | IHC: 1:400 | Abcam plc., Cambridge, UK | ab181598 |
| Recombinant Anti-DUSP4 antibody [EPR19881] | WB: 1:500 WB: 1:200 | Abcam plc., Cambridge, UK | ab216576 |
| Polyclonal Rabbit anti-Human DUSP4 / MKP2 Antibody | IHC: 1:100 | Lifespan Bioscience, Seattle, USA | LS-B14575 |
| Recombinant Anti-DUSP6 antibody [EPR129Y] | WB: 1:500 IHC: 1:100 | Abcam plc., Cambridge, UK | ab76310 |
| Recombinant Anti-EpCAM antibody [EPR20533-63] | IHC: 1:100 | Abcam plc., Cambridge, UK | ab221552 |
| Recombinant Anti-MEK1 + MEK2 antibody [EPR16667] | WB: 1:1000 | Abcam plc., Cambridge, UK | ab178876 |
| Recombinant Anti-Osteopontin antibody [RM1018] | WB: 1:1000 IHC: 1:200 | Abcam plc., Cambridge, UK | ab283656 |
| RICTOR Antibody | WB: 1:1000 | Bethyl Laboratories, Inc., Montgomery, USA | A300-459A |
| SCD1 (C12H5) Rabbit mAb | WB: 1:1000 IHC: 1:100 | Cell Signaling Technology, Inc., Cambridge, UK | 2794S |
| YAP/TAZ (D24E4) Rabbit mAb | WB: 1:1000 | Cell Signaling Technology, Inc., Cambridge, UK | 8418 |
| Secondary antibodies | | | |
| Anti-Goat IgG (whole molecule) – Peroxidase antibody produced in rabbit | 1:20000 | Sigma-Aldrich, Inc., St. Louis, USA | A4174 |
| HRP, Goat Anti-Mouse IgG | 1:20000 | Abbkine Scientific Co., Ltd., Wuhan, CN | A21010 |
| HRP, Goat Anti-Rabbit IgG | 1:20000 | Abbkine Scientific Co., Ltd., Wuhan, CN | A21020 |
| N-Histofine® Simple Stain Mouse MAX PO (Rat) Anti-Rat | 1:20000 | Nichirei Biosciences Inc., Tokyo, Japan | 414311F |
| ZytoChem Plus HRP-Polymer anti-Rabbit | 1:20000 | Zytomed Systems GmbH, Berlin, Germany | ZUC032-100 |

Supplementary Table 3: Taqman® probes

| Name | Company | Catalogue number |
|---------------------------------|---------------------------------|-------------------------|
| TaqMan™ Actb mouse VIC 20x Mix | Thermo Fisher Inc. Waltham, USA | Mm00607939_s1 |
| TaqMan™ DUSP4 human 20x Mix | Thermo Fisher Inc. Waltham, USA | Hs01027785_m1 |
| TaqMan™ DUSP4 mouse FAM 20x Mix | Thermo Fisher Inc. Waltham, USA | Mm00723761_m1 |
| TaqMan™ DUSP6 human 20x Mix | Thermo Fisher Inc. Waltham, USA | Hs04329643_s1 |
| TaqMan™ DUSP6 mouse FAM 20x Mix | Thermo Fisher Inc. Waltham, USA | Mm00518185_m1 |
| TaqMan™ GAPDH human VIC 60x Mix | Thermo Fisher Inc. Waltham, USA | Hs02786624_g1 |
| TaqMan™ NUPR1 mouse FAM 20x Mix | Thermo Fisher Inc. Waltham, USA | Mm00498104_m1 |