Supporting Information

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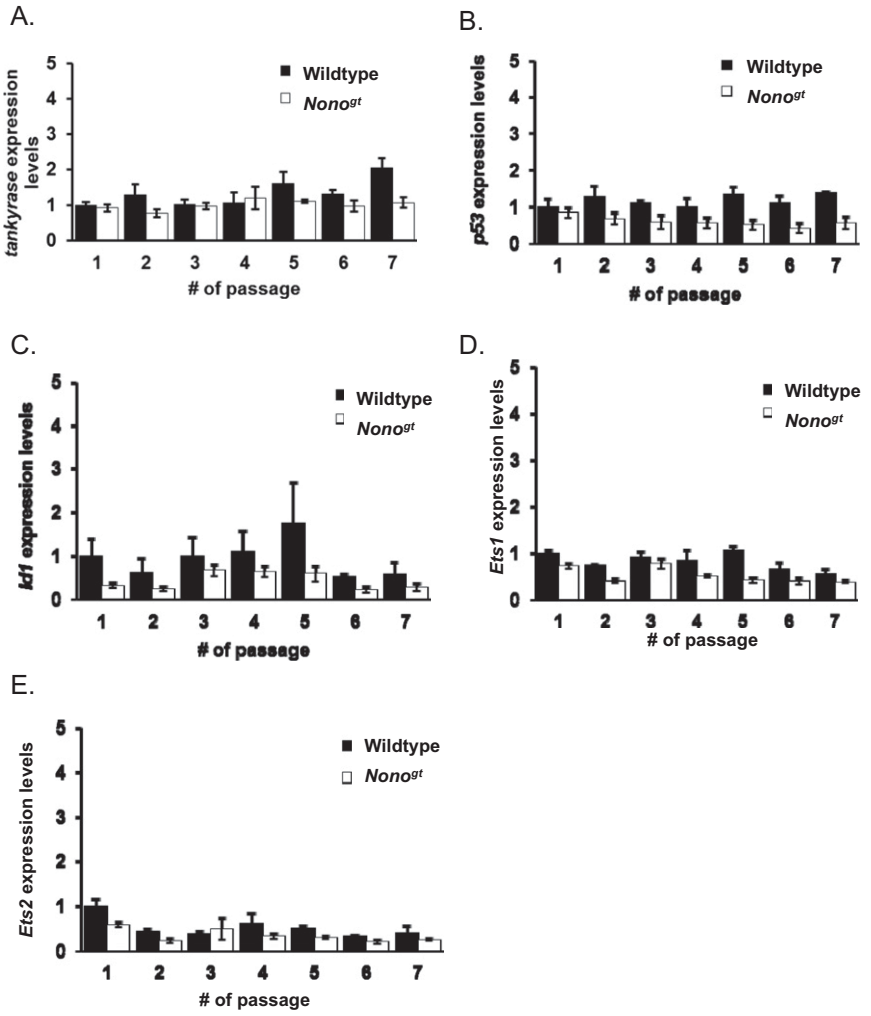

Fig. S1. Transcription of senescence-implicated genes in serially passaged WT and *Nono*^{gt} primary fibroblasts. WT and *Nono*^{gt} primary fibroblasts were counted and passaged every 2 d and a constant number of cells plated to a new dish. Total RNA was harvested from cells in each passage, and quantitative PCR (qPCR) was used to quantify the transcript levels of senescence-implicated genes *tankyrase* (*A*) and *p53* (*B*), as well as upstream regulators of *p16-Ink4A*, the genes *Id1* (*C*), *Ets1* (*D*), and *Ets2* (*E*). Values are plotted in arbitrary units relative to WT levels at passage 1.

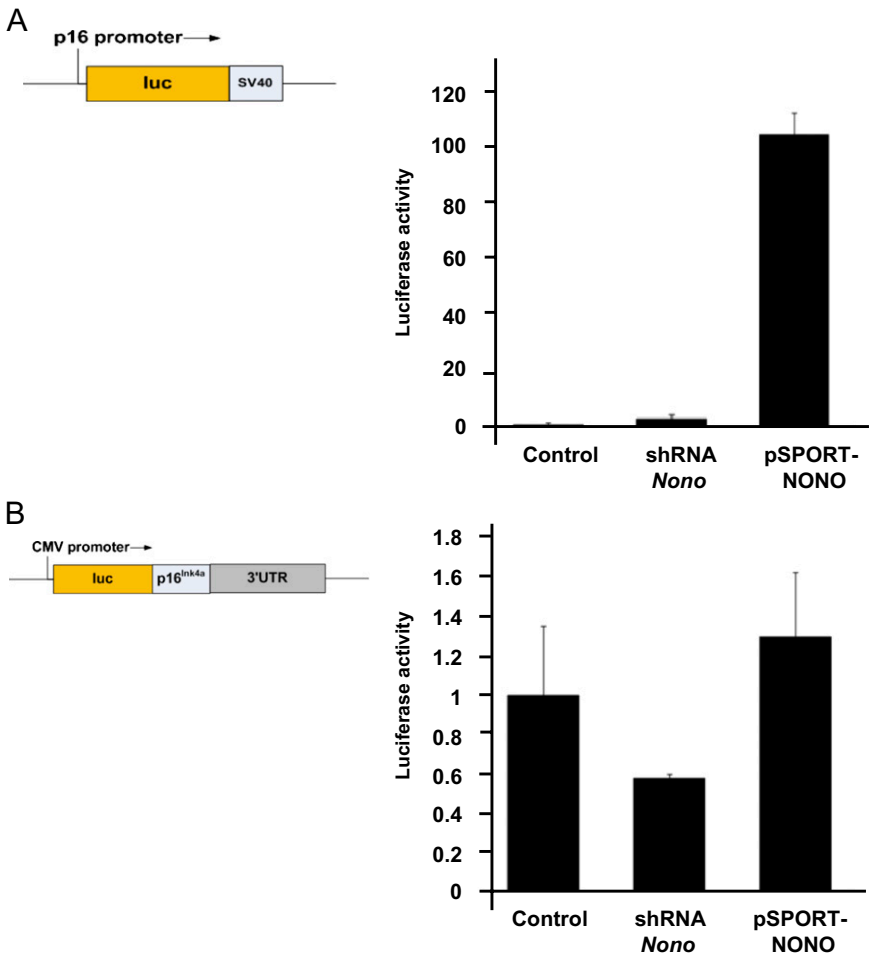

Fig. S2. NONO activates transcription of *p16-Ink4A* promoter reporters. (*A*) Relative expression levels of the diagrammed *p16-luc* promoter construct alone, in the presence of a NONO-targeting RNAi hairpin that reduces NONO levels 10-fold, and in the presence of a NONO-overexpressing vector. (*B*) Similar experiments using the diagrammed construct containing the *p16-Ink4A* 3′ UTR.

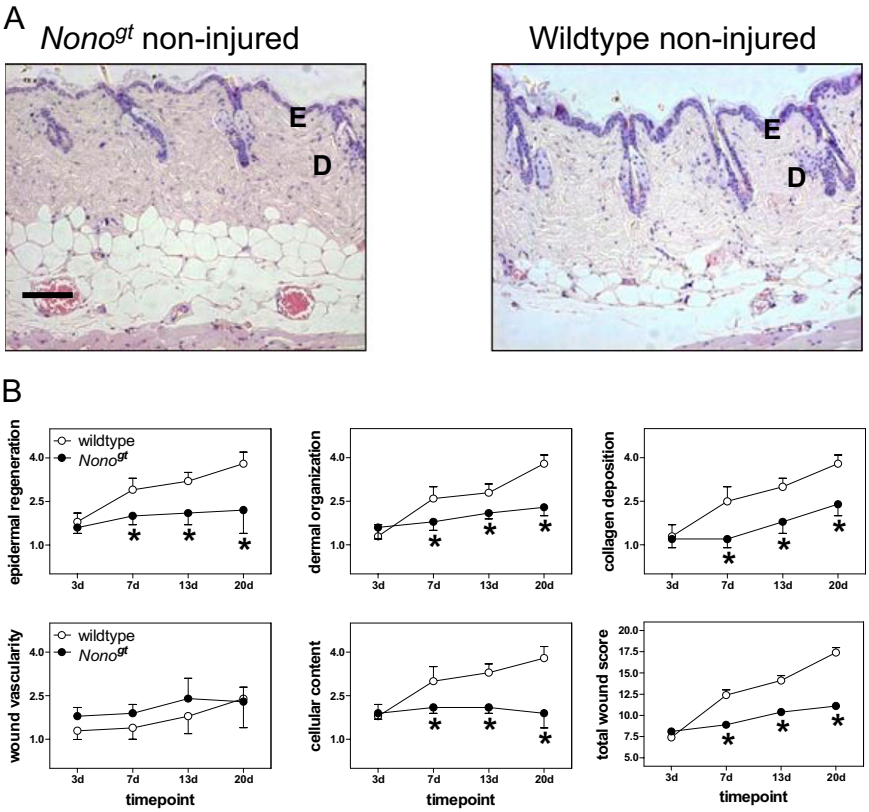

Fig. S3. Dermal structure and incisional wound healing in WT and *Nono*^{gt} mice. (*A*) H&E-stained paraffin sections from uninjured dorsal skin. Normal skin morphogenesis is not affected in *Nono*^{gt} mice compared with WT littermates (10–11 wk of age, 24 g body weight). (*B*) Full wound healing subscores of normal healing WT mice compared with *Nono*^{gt} mice on day 3, 7, 13, and 20 after incisional wounding in the dorsal skinfold. Data represent means ± SD (n = 5).

Table S1. Regulation of cell cycle genes in WT and *Nono*^{gt} fibroblasts

Gene	Fold difference, *gt*/WT
Abl1	2.11
Ak1	3.90
Apbb1	1.91
Atm	2.14
Brca1	3.09
Brca2	3.56
Camk2a	2.18
Camk2b	0.37
Casp3	2.67
Ccna1	0.37
Ccna2	19.68
Ccnb1	27.08
Ccnb2	10.26
Ccnc	5.27
Ccnd1	6.05
Ccne1	2.83
Ccnf	5.21
Cdc25a	2.58
Cdk2	12.98
Cdk4	4.51
Cdk5rap1	2.78
Cdkn1a	1.57
Cdkn1b	3.44
Cdkn2arf	1.85
Chek1	3.31
Cks1b	2.37
Ddit3	3.07
Dnajc2	1.73
Dst	1.12
E2f1	1.64
E2f2	0.37
E2f3	6.78
E2f4	1.70
Gadd45a	3.13
Gpr132	0.37
Hus1	3.04
Inha	0.82
Itgb1	1.81
Macf1	2.72
Mad2l1	2.93
Mcm2	7.62
Mcm3	9.82
Mcm4	5.67
Mdm2	2.94
Mki67	5.58
Mre11a	1.16
Msh2	1.57
Mtbp	4.46
Myb	0.17
Nek2	3.11
Nfatc1	2.82
Notch2	4.04
Npm2	1.06
Pcna	3.95
Pes1	2.48
Pkd1	1.93
Pmp22	1.74
Ppm1d	2.03
Ppp2r3a	0.90
Ppp3ca	1.86
Prm1	0.37
Rad17	3.17

Table S1. Cont.

Gene	Fold difference, *gt*/WT
Rad21	2.38
Rad51	0.43
Rad9	2.66
Ran	3.18
Rbl1	0.94
Rbl2	1.04
Sesn2	1.53
Sfn	2.05
Shc1	5.39
Skp2	3.24
Slfn1	0.37
Smc1a	5.86
Stag1	3.45
Sumo1	3.45
Taf10	3.08
Terf1	2.62
Tfdp1	3.53
Psmg2	2.74
Trp53	3.18
Trp63	0.15
Tsg101	1.25
Wee1	1.23
Gusb	5.23
Hprt1	0.01
Hsp90ab1	3.04
Gapdh	2.53
Actb	2.77

Total RNA was harvested from dividing cultures of WT and *Nono*^{gt} primary fibroblasts and subjected to qPCR array analysis. All array targets are shown, with fold-regulation of *Nono*^{gt} vs. WT fibroblasts. Note that the p16-*Ink4A* transcript itself was not probed on this commercial array. Independent qPCR analysis using the primers in Table S2 confirmed fivefold reduction in expression of *p16-Ink4A* in *Nono*^{gt} vs. WT fibroblasts in both replicates of the cellular RNA used for this array.

Table S2. Primer sequences

Gene	Orientation	Sequence (5′–3′)
Ets1	Sense	CGG CAT CAT AGC ACA GTT CAA G
Ets1	Antisense	CCC ATG CAA ACG GCT TTT AT
Ets1	Probe	FAM-AAC CGC TAC CCG AAA CAT GGA AGA CTC AG-TAMRA
Id1	Primer Set	1) Assay ID: Mm00775963_g1
Ets2	Primer Set	1) Assay ID: Mm00468972_m1
NONO	Sense	TGC GCT TCG CCT GTC A
NONO	Antisense	GCA GTT CGT TCG ACA GTA CTG
NONO	Probe	FAM-AGT GCA CCC TTA CAG TCC GCA ACC TT-TAMRA
qPCR		
p16-Ink4A	Sense	CCC AAC GCC CCG AAC T
p16-Ink4A	Antisense	GTG AAC GTT GCC CAT CAT CA
p16-Ink4A	Probe	FAM-TTT CGG TCG TAC CCC GAT TCA GG-TAMRA
ChIP		
p16-Ink4A	Sense	TTT CGC CCA ACG CCC CGA A
p16-Ink4A	Antisense	ACC CGA CTG CAG ATG GGA CAC
p16-Ink4A	Probe	FAM- CGA ACT CTT TCG GTC GTA CCC CGA TTC-TAMRA
p53	Sense	GCA TCC CGT CCC CAT CA
p53	Antisense	GGA TTG TGT CTC AGC CCT GAA G
p53	Probe	FAM-CAG CCT CCC CCT CTC CTT GCT GTC TTA-TAMRA
Tankyrase	Sense	CGG CAG CAG AGC AGA AGA C
Tankyrase	Antisense	TGT ACT CCA GTT GCA GGT TTG AAT
Tankyrase	Probe	TAG TGA CCA CCC CTG GTA AAG GCC AGA-TAMRA
GAPDH	Sense	CAT GGC CTT CCG TGT TCC TA
GAPDH	Antisense	CCT GCT TCA CCA CCT TCT TGA
GAPDH	Probe	YAK-CCG CCT GGA GAA ACC TGC CAA GTA TG-TAMRA

TaqMan Gene Expression Assays from Applied Biosystems are tested, but sequences are not provided. Assay consists of primer forward, primer reverse, and probe, as usual.

Table S3. Histological wound healing scores

Score	Dermal organization	Epidermal regeneration	Collagen deposition	Cellular content	Wound vascularity
1	25% thickness of granulation tissuecompared with healthy tissue	No epithelial closure	Gap without ingrowing collagen fibrils	Low cell proliferation, mainly inflammatory cells	1–3 capillaries per visual field
2	50% thickness of granulation tissuecompared with healthy tissue	Strong hyperproliferative epithelium	Gap with ingrowing collagen fibrils	Predominantly inflammatory cells or dysfunctional fibroblasts, hyper-proliferation	4–6 capillaries per visual field
3	75% thickness of granulation tissuecompared with healthy tissue	Moderate hyperproliferative epithelium	No gap, but unstable adhesion	Predominantly normal fibroblasts	7–9 capillaries per visual field
4	Thickness of granulation tissue equal to healthy tissue	Thickness and structure equal to normal epithelium	No gap, stable adhesion	Low cell proliferation, mainly fibroblasts	>9 capillaries per visual field