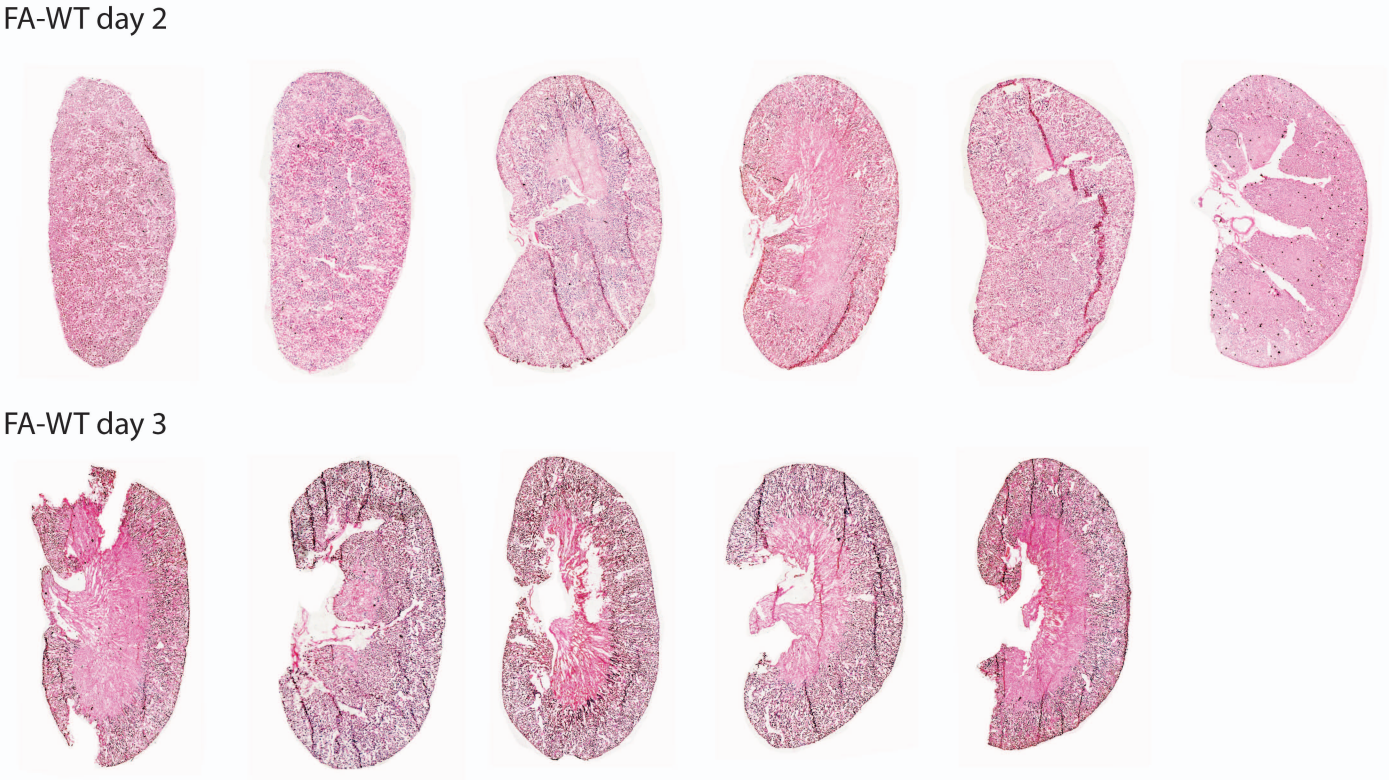
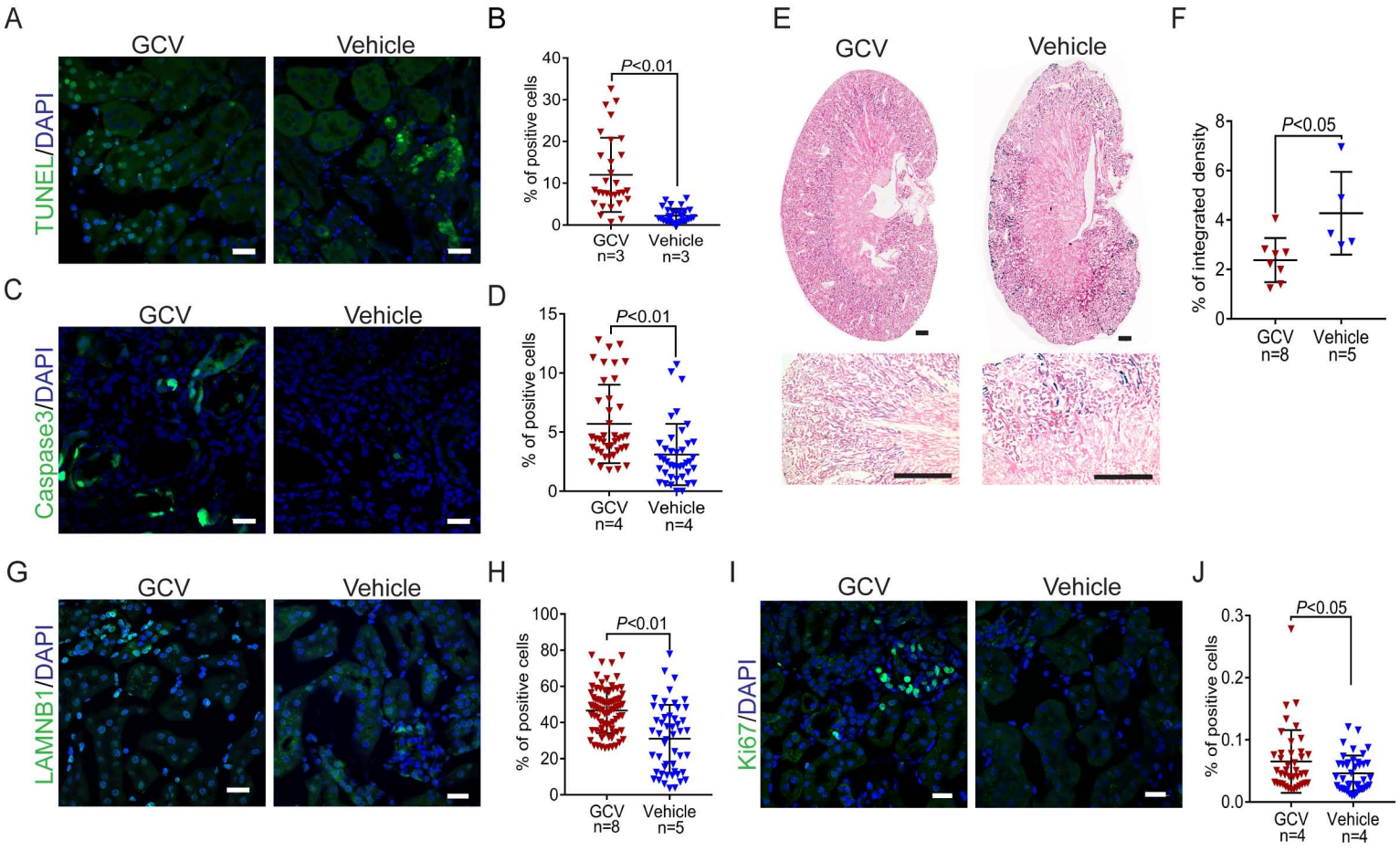
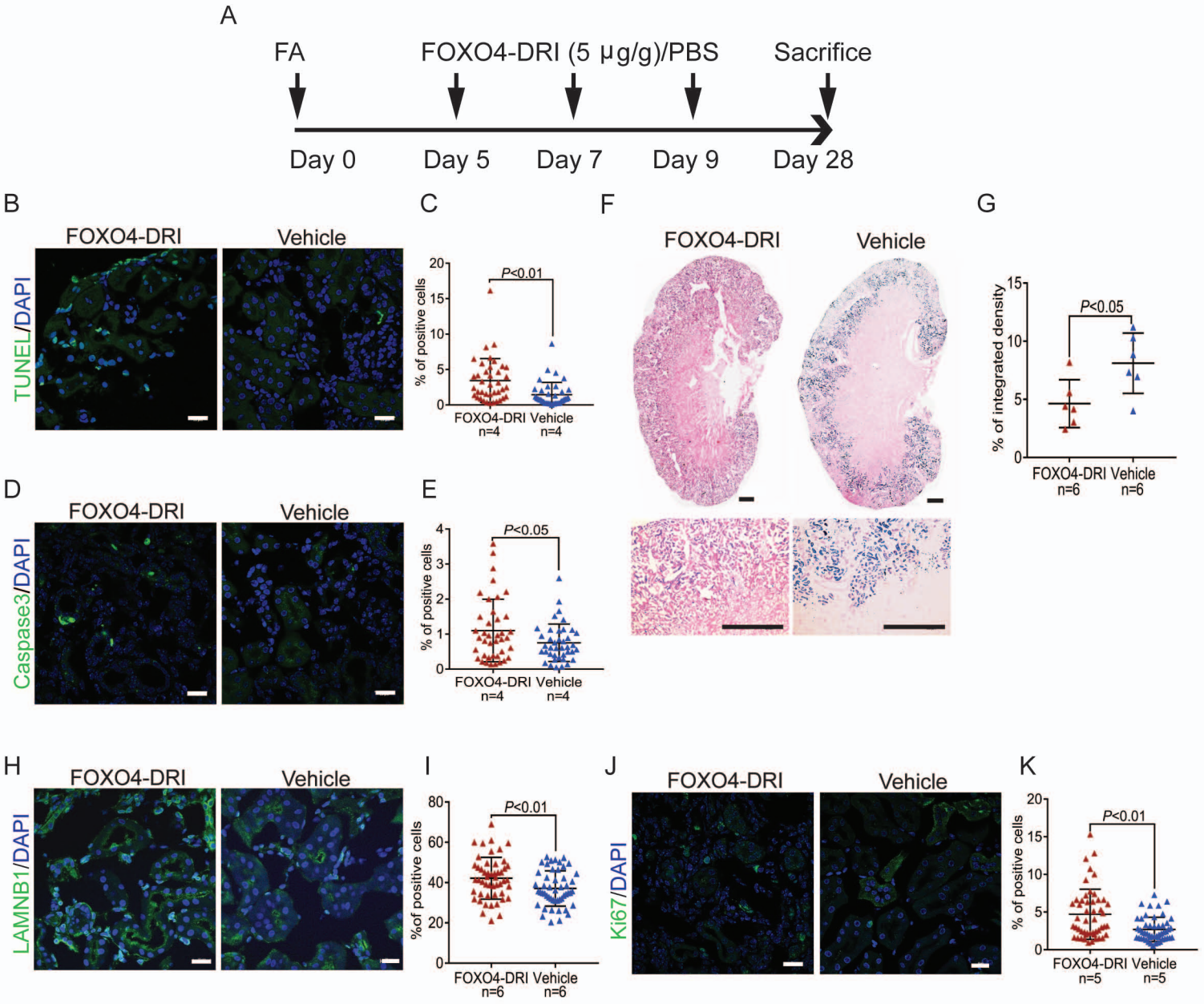


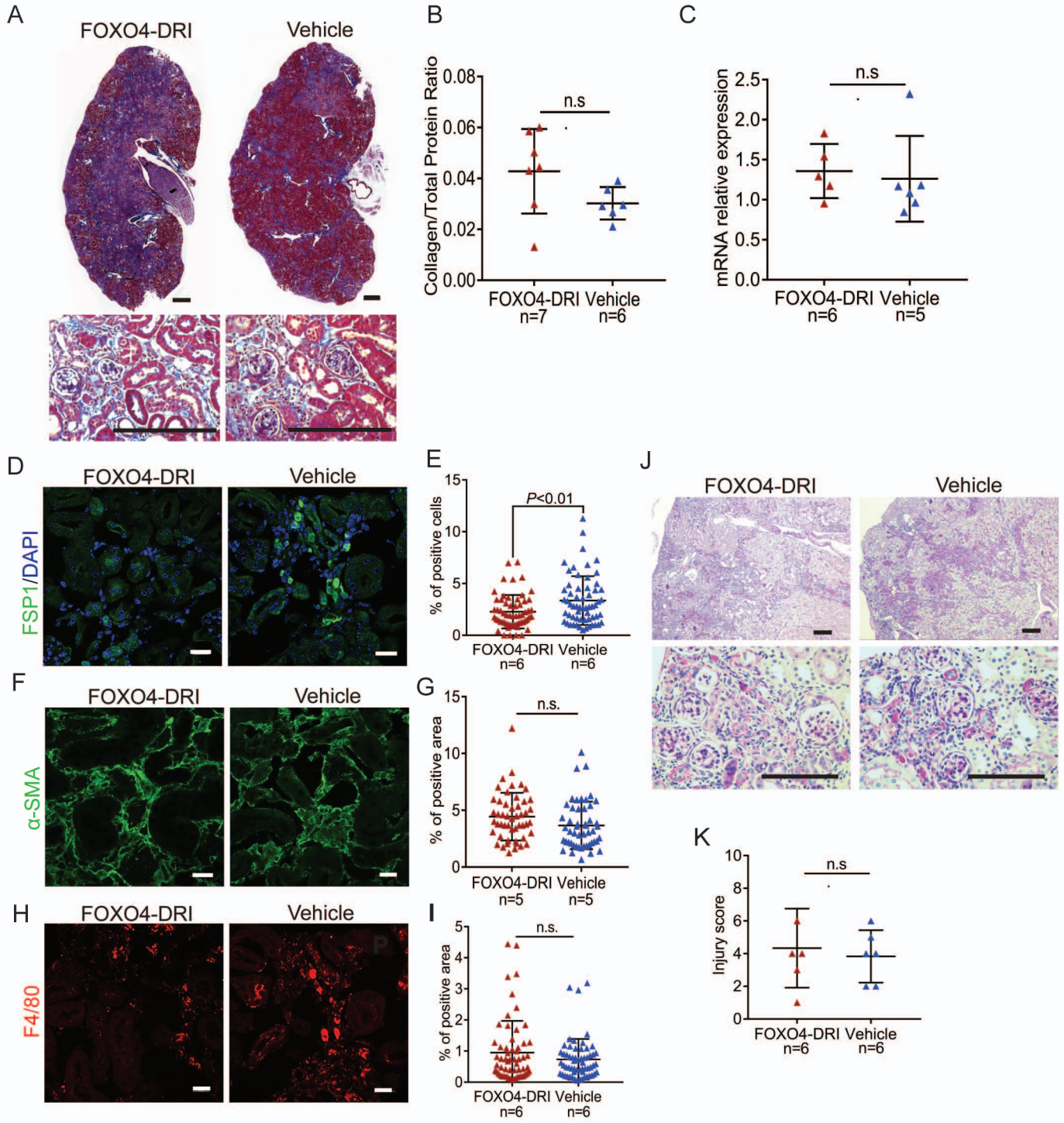
Supplementary Figure 1. Appearence of LacZ staining of SA-β-Gal activity in WT kidneys 2 and 3 days after FA injury.



Supplementary Figure 2. Ganciclovir treatment of p16-3MR mice induces tubular apoptosis and reduces senescence after FA injury. (**A**) Representative immunofluorescence confocal images of TUNEL-stained GCV-treated mice kidneys with correspondent digital image analysis quantification (**B**), and activated caspase 3 (**C-D**) compared to controls 28 days after FA injury. (**E**) Representative images of kidneys stained for SA-β-Gal activity at low (upper panels) and high (lower panels) magnification of GCV-treated mice compared to vehicle-treated controls 28 days after FA injury, and (**F**) correspondent quantification by digital image analysis. Scale bars are 500 μm in the upper and 200 μm in the lower panels. (**G**) Representative immunofluorescence confocal images of GCV-treated mice kidneys probed with an antibody against LAMNB1 compared to controls 28 days after FA injury, and (**H**) correspondent quantification. Scale bars are 20 μm. (**I**) Representative immunofluorescence confocal images of GCV-treated mice kidneys probed with an antibody against the proliferation marker Ki67 compared to controls 28 days after FA injury, and (**J**) correspondent quantification. Data are presented as mean ± SD. P values were calculated with two-tailed Student's t-test.



Supplementary Figure 3. FOXO4-DRI treatment increases tubular apoptosis and reduces kidney senescence after FA injury. (**A**) Schematic representation of the protocol for inducing clearance of senescent cells by FOXO4-DRI administration to FA-injured mice. PBS: phosphate-buffered saline. (**B**) Representative immunofluorescence confocal images of TUNEL-stained FOXO4-DRI-treated mice kidneys with correspondent digital image analysis quantification (**C**), and activated caspase 3 (**D-E**) compared to controls 28 days after FA injury. (**F**) Representative images of kidneys stained for SA-β-Gal activity at low (upper panels) and high (lower panels) magnification of FOXO4-DRI-treated mice compared to vehicle-treated controls 28 days after FA injury, and (**G**) correspondent quantification by digital image analysis. (**H**) Representative immunofluorescence confocal images of FOXO4-DRI-treated mice kidneys probed with an antibody against LAMNB1 compared to controls 28 days after FA injury, and (**I**) correspondent quantification. Scale bars are 20 µm. (**J**) Representative immunofluorescence confocal images of FOXO4-DRI-treated mice kidneys probed with an antibody against the proliferation marker Ki67 compared to controls 28 days after FA injury, and (**K**) correspondent quantification. Data are presented as mean ± SD. P values were calculated with two-tailed Student's t-test.



Supplementary Figure 4. FOXO4-DRI treatment does not affect kidney damage and fibrosis after FA injury. (**A**) Representative images of trichrome-stained kidneys at low (upper panels) and high (lower panels) magnification of FOXO4-DRI-treated mice compared to controls 28 days after FA injury. Scale bars are 500 µm in the upper and 200 µm in the lower panels. (**B**) Collagen/total protein content ratios and (**C**) real-time quantitative PCR of the Collagen 1 mRNA levels in kidney cortexes of FOXO4-DRI-treated and vehicle-treated mice 28 days after FA injury. (**D**) Representative immunofluorescence confocal images of FOXO4-DRI-treated mice kidneys immunostained for the fibroblast marker FSP1 compared to controls 28 days after FA injury, and (**E**) correspondent quantification by digital image analysis. Scale bars are 20 µm. (**F**) Representative immunofluorescence confocal images of FOXO4-DRI-treated mice kidneys immunostained for the myofibroblast marker α-SMA compared to controls 28 days after FA injury, and (**G**) correspondent quantification by digital image analysis. Scale bars are 20 µm. (**H**) Representative immunofluorescence confocal images of FOXO4-DRI-treated mice kidneys immunostained for the macrophage marker F4/80 compared to controls 28 days after FA injury, and (**I**) correspondent quantification by digital image analysis. Scale bars are 20 µm. (**J**) Representative images of PAS-stained kidneys at low (upper panels) and high (lower panels) magnification of FOXO4-DRI-treated mice compared to controls 28 days after FA injury. Scale bars are 500 µm in the upper and 200 µm in the lower panels. (**K**) Tubular injury scores of FOXO4-DRI-treated mice compared to controls 28 days after FA injury. Experimental numbers are reported in each panel. Data are presented as mean ± SD. P values were calculated with two-tailed Student's t-test.

Supplementary Figure 1. Appearance of LacZ staining of SA-β-Gal activity in WT kidneys 2 and 3 days after FA injury.

Supplementary Figure 2. Ganciclovir treatment of p16-3MR mice leads to an increase in apoptosis of TECs and reduced senescence after FA injury. (**A**) Representative immunofluorescence confocal images of TUNEL-stained GCV-treated mice kidneys with correspondent digital image analysis quantification (**B**), and activated caspase 3 (**C**-**D**) compared to controls 28 days after FA injury. (**E**) Representative images of kidneys stained for SA-β-Gal activity at low (upper panels) and high (lower panels) magnification of GCV-treated mice compared to vehicle-treated controls 28 days after FA injury, and (**F**) correspondent quantification by digital image analysis. Scale bars are 500 μm in the upper and 200 μm in the lower panels. (**G**) Representative immunofluorescence confocal images of GCV-treated mice kidneys probed with an antibody against LAMNB1 compared to controls 28 days after FA injury, and (**H**) correspondent quantification. Scale bars are 20 μm. (**I**) Representative immunofluorescence confocal images of GCV-treated mice kidneys probed with an antibody against the proliferation marker Ki67 compared to controls 28 days after FA injury, and (**J**) correspondent quantification. Data are presented as mean ± SD. P values were calculated with two-tailed Student's t-test.

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Supplementary Table 1. Primer pairs used in the study.

Primers	Forward	Reverse
Actin	GTACCACCATGTACCCAGGC	AACGCAGCTCAGTAACAGTC
IL-1α	CGAAGACTACAGTTCTGCCATT	GACGTTTCAGAGGTTCTCAGAG

IL-1β	GCAACTGTTCCTGAACTCAACT	ATCTTTTGGGGTCCGTCAACT
IL-6	GAGGATACCACTCCCAACAGACC	AAGTGCATCATCGTTGTTCATACA
TNF-α	GCCTCTTCTCATTCCTGCTTG	CTGATGAGAGGGAGGCCATT
MCP-1	TTAAAAACCTGGATCGGAACCAA	GCATTAGCTTCAGATTTACGGGT
Collagen1	CCTGGTAAAGATGGTGCC	CACCAGGTTCACCTTTCGCACC
Ihh	CTACAATCCCGACATCATCTTCAAG	CAGAGATGGCCAGTGAGTTCAGA
Shh	AAAGCTGACCCCTTTAGCCTA	TTCGGAGTTTCTTGTGATCTTCC