Supplementary Figure Captions

Supplementary Figure S1. Kidney chemokines in the UUO model

A) Gene expression of the chemokines MCP-1 and RANTES was increased in UUO kidneys. TWEAK KO mice showed a milder upregulation of these genes than WT mice. * p<0.05 TWEAK KO vs. WT. B) Kidney MCP-1 protein, as assessed by ELISA, was lower in TWEAK KO than in WT mice at 7 and 14 d. * p<0.05 vs. Sham 7d. ** p<0.05 TWEAK KO obstructed 7d. vs. WT 7d. # p<0.05 vs. Sham 14d. ## p<0.05 TWEAK KO obstructed 14d. vs. WT 14d.

Supplementary Figure S2. ECM gene expression in the UUO model

Collagen type I and fibronectin gene expression was lower in TWEAK deficient obstructed kidneys. * p<0.05 TWEAK KO vs. WT.

Supplementary Figure S3. Injury localization in mice overexpressing TWEAK.

Immunodetection of the tubular damage marker KIM-1, the macrophage marker F4/80 and the Masson’s trichrome staining revealed colocalization (arrows) of tubular damage, macrophage infiltration and fibrosis in the kidney cortex from mice infected with a TWEAK-overexpressing plasmid (Adeno-TWEAK). Magnification x80, scale bar 250 μm.

Supplementary Figure S4. Expression of Fn14 in cultured kidney interstitial fibroblasts:

Proliferative and antiapoptotic effects of TWEAK

A) Cultured murine kidney interstitial fibroblasts express Fn14 as assessed by Western Blot of total protein and by flow cytometry of proteins present in the cell surface. B) Fluorescence microscopy confirmed an increased number of mitotic nuclei (arrows) present in permeabilized, propidium iodide-stained cells treated with 200 ng/ml TWEAK for 24h. Insets show representative flow cytometry diagrams of DNA content and the black horizontal line indicates cells with increased cell DNA content. C) A mild antiapoptotic effect of 200 ng/ml TWEAK was observed in kidney interstitial fibroblasts deprived of serum for 48h, as assessed by flow cytometry of DNA content. Magnification x400, scale bar 30 μm.

Supplementary Figure S5. Cultured kidney interstitial fibroblasts: intracellular pathways of TWEAK-induced cell proliferation

A) ERK inhibition prevented the increased expression of the proliferation-related protein Cyclin D1 in response to TWEAK in kidney interstitial fibroblasts. *p<0.05 vs. control. # p<0.05 vs. TWEAK treated. B) NFκB inhibition by 3 ng/mL Parthenolide or 10 μM BAY11-7082 did not prevent TWEAK-induced
proliferation of TFB renal fibroblasts. C) ELISA assay of RasGTPase activity: TWEAK-induced Ras activation at 1 minute is absent in MEF cells lacking Fn14 (Fn14 -/-). *p<0.05 vs. control. Fn14 -/- MEF cells do not express Fn14 on the surface. D) Preincubation with the Ras inhibitor FTS prevented TWEAK-induced phosphorylation of ERK MAP kinase (pERK 1/2) at 15 minutes and 24 h. *p<0.05 vs. control. # p<0.05 vs. TWEAK-treated.

**Supplementary Figure S6. Cultured kidney interstitial fibroblasts: TWEAK-induced intracellular pathways regulating ECM synthesis**

A) Preincubation with the Ras inhibitor FTS prevented TWEAK-induced phosphorylation of p38 MAP kinase (pp38) at 15 minutes and 24 h. * p<0.05 vs. control. # p<0.05 vs. TWEAK-treated. B) TWEAK decreases cell-associated and secreted collagen type I and fibronectin, following 72h of incubation in renal fibroblasts (TFBs cells). C-D) Quantification showed that pretreatment with p38 inhibitor SB203580 partially reversed this TWEAK effect. * p<0.05 vs. control.