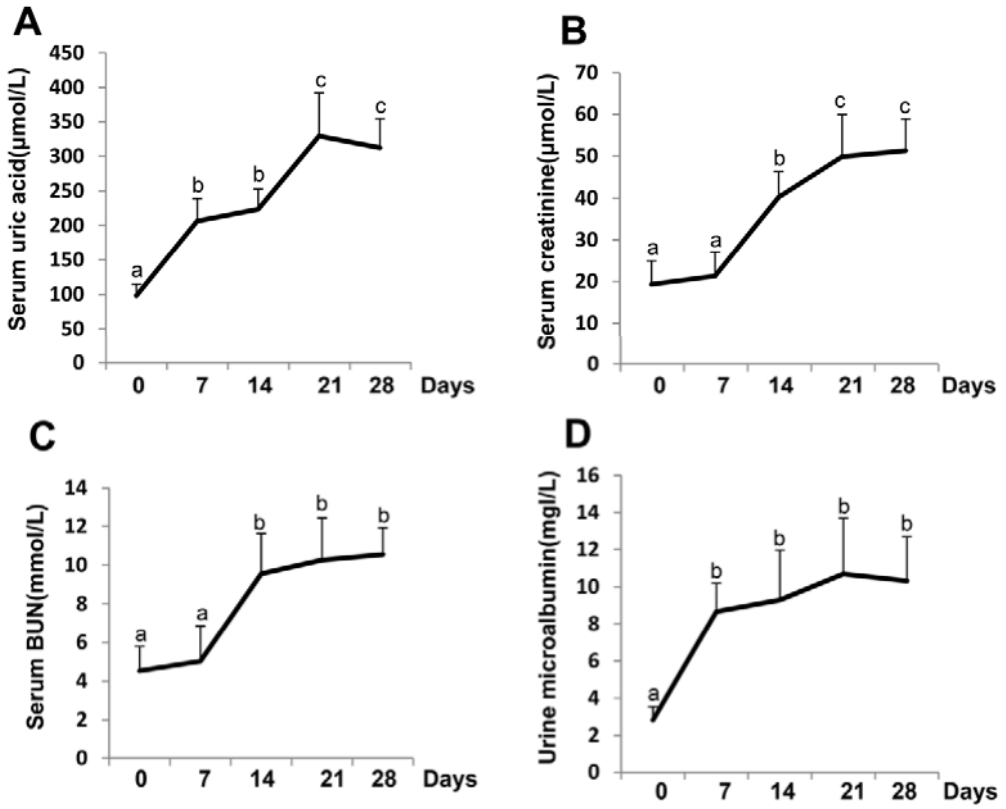
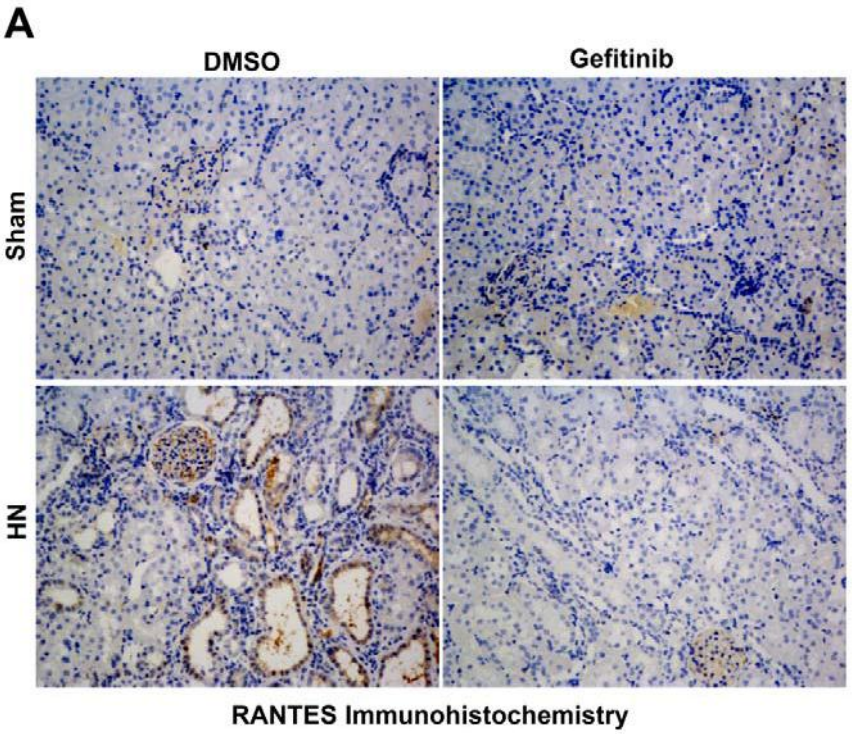
Supplemental Figure 1



Supplemental Figure 1. The onset and duration of HN after daily feeding of the mixture of adenine and potassium oxonate. Levels of serum uric acid (A), serum creatinine (B) and blood urea nitrogen (BUN) (C) as well as urine microalbumin (D). Data are represented as the mean ± S.E.M (n = 6). Means with different superscript letters are significantly different from one another ($P< 0.05$).

Supplemental Figure 2

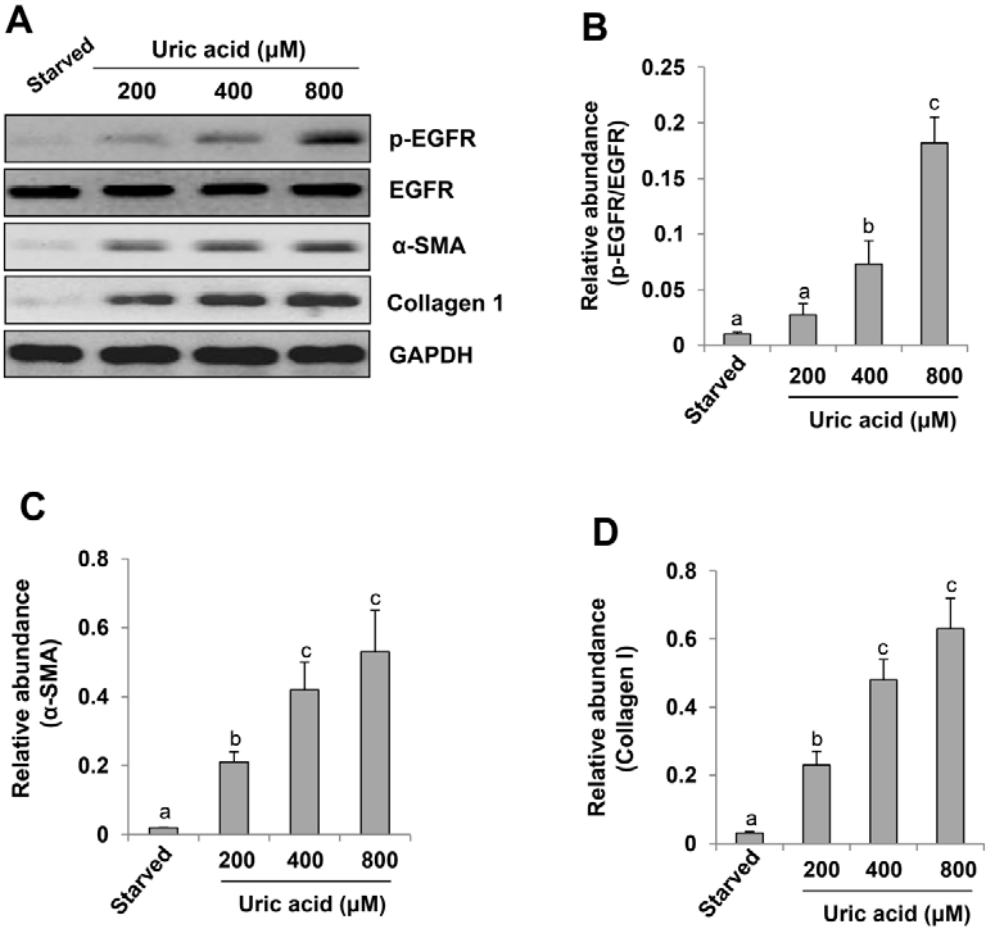


Supplemental Figure 2. EGFR activation is required for RANTES expression.

A: Photomicrographs illustrating RANTES immunochemistry staining of kidney tissue collected at day 21 after feeding of the mixture of adenine and potassium oxonate

with/without gefitinib. B: RANTES staining graphic presentation of quantitative data. Data are represented as the mean ± S.E.M (n = 6). Means with different superscript letters are significantly different from one another ($P< 0.05$).

Supplemental Figure 3

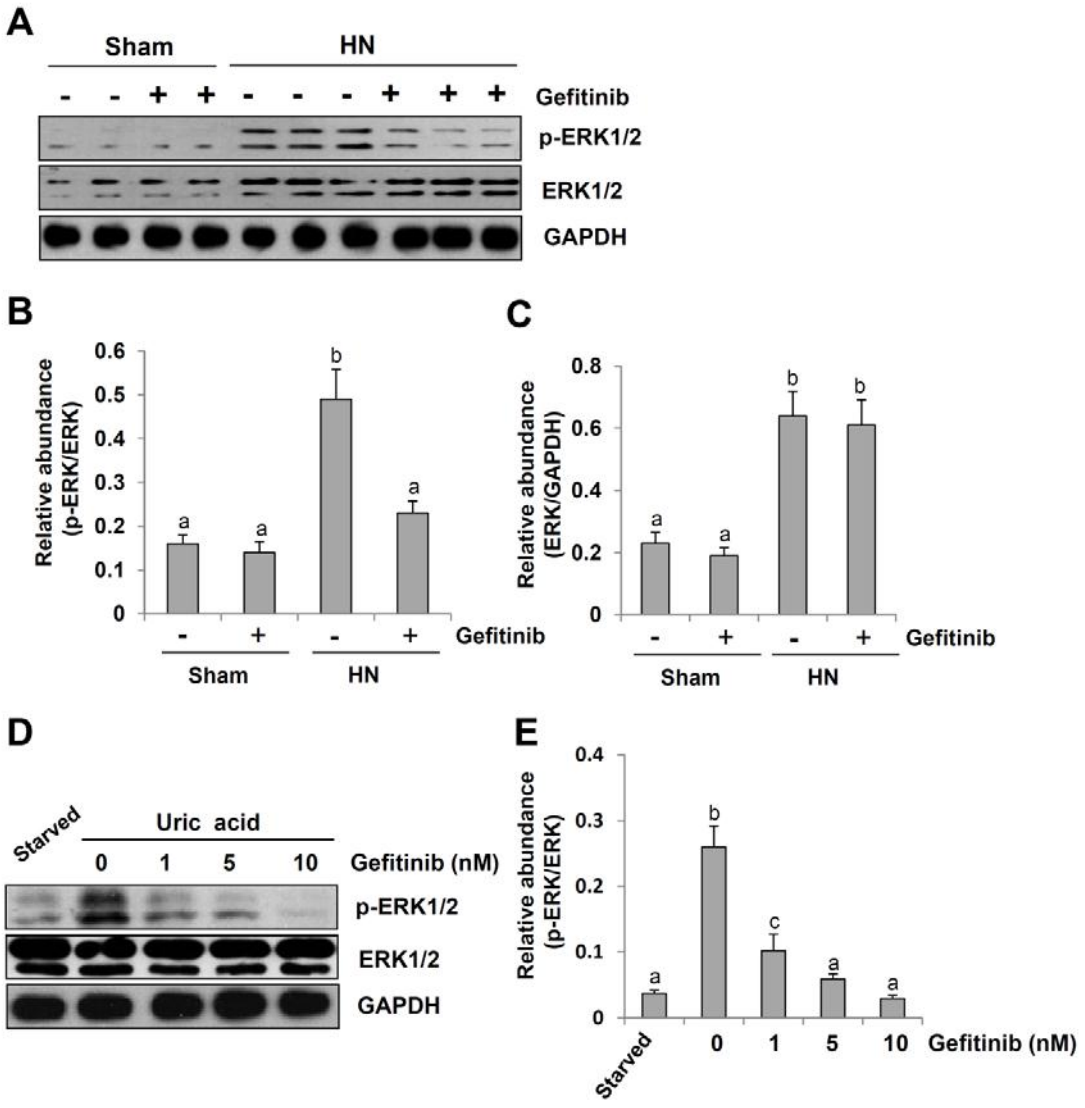


Supplemental Figure 3. Uric acid induces EGFR phosphorylation and renal interstitial fibroblast activation in dose-dependant manner

Serum-starved NRK-49F cells were incubated with various concentrations of uric acid from 0-800 μM. **A:** Cell lysates were prepared and subject to immunoblot analysis with antibodies to p-EGFR, EGFR, α-SMA, collagen 1 or GAPDH. **B:** Expression levels of p-EGFR and EGFR were calculated by densitometry and the ratio between p-EGFR and total EGFR was determined; **C:** α-SMA levels were normalized with GAPDH; **D:**

Collagen 1 levels were normalized with GAPDH. Data are represented as the mean ± S.E.M (n = 6). Means with different superscript letters are significantly different from one another ($P< 0.05$).

Supplemental Figure 4

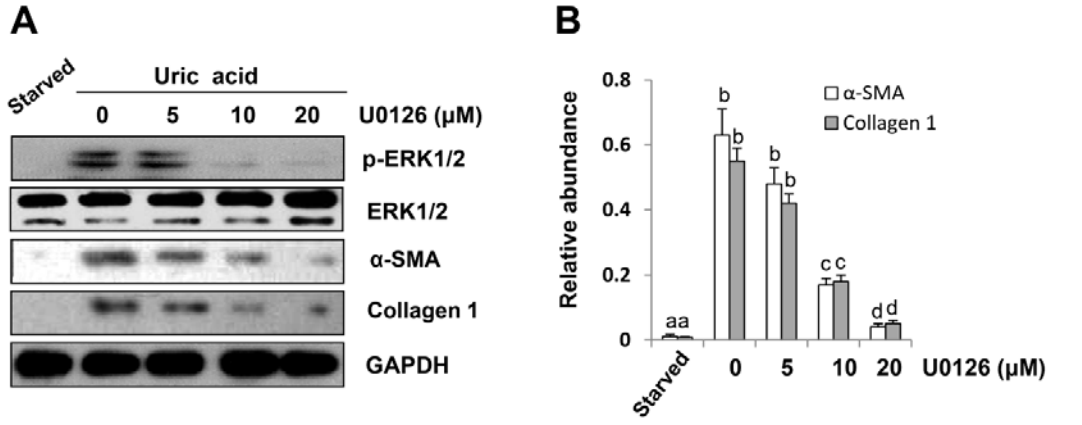


Supplemental Figure 4. EGFR activation is required for uric acid-induced ERK1/2 phosphorylation

A: The kidneys were taken for immunoblot analysis of p-ERK1/2, ERK1/2 or GAPDH.

B: Expression levels of p-ERK1/2 and ERK1/2 were calculated by densitometry and the ratio between p-ERK1/2 and total ERK1/2 was determined. **C:** Total ERK1/2 levels were normalized with GAPDH. **D:** Cultured NRK-49F cells were starved for 24 h and then exposed to 800 μM of uric acid for 36 h in the absence or presence of Gefitinib (0-10 nM). Cell lysates were subjected to immunoblot analysis using antibodies to p-ERK1/2, ERK1/2 or GAPDH. Representative immunoblots from three experiments are shown. **E:** Expression levels of p-ERK1/2 and ERK1/2 were calculated by densitometry and the ratio between p-ERK1/2 and total ERK1/2 was determined. Data are represented as the mean ± S.E.M . Means with different superscript letters are significantly different from one another ($P< 0.05$).

Supplemental Figure 5



Supplemental Figure 5. Effect of ERK inhibitor on uric acid induced activation of cultured renal interstitial fibroblasts.

Cultured NRK-49F cells were starved for 24 h and then exposed to 800 μM of uric acid for 36 h in the absence or presence of U0126 (0-20 μM). Cell lysates were subjected to immunoblot analysis using antibodies to α-SMA, Collagen 1, p-ERK1/2, ERK1/2, or GAPDH. Representative immunoblots from three experiments are shown (A). Expression levels of all these proteins were quantified by densitometry and expressed as means ± SEM. α-SMA and Collagen 1(B) were normalized with GAPDH. Means with different superscript letters are significantly different from one another ($P< 0.05$).