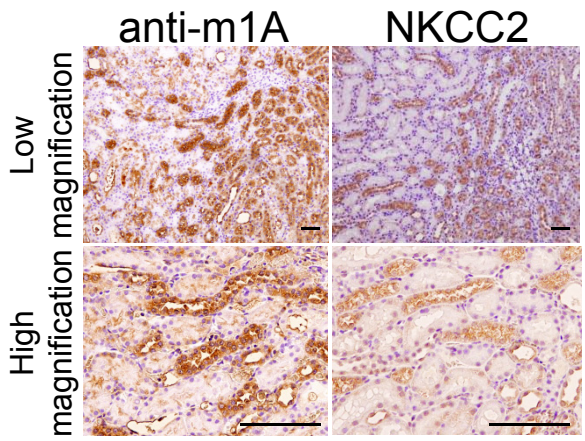
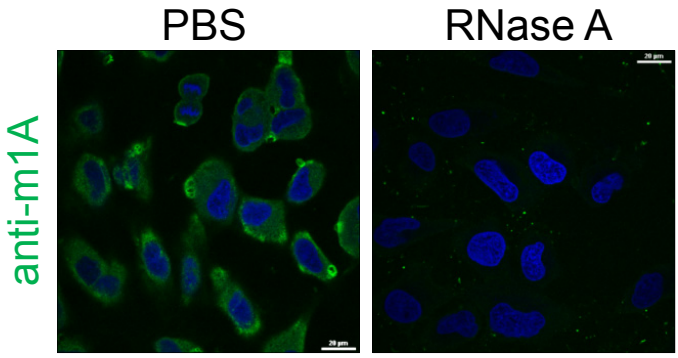
# Supplemental Figure 1




**Supplemental Figure 1. Anti m1A-Ab mainly stained renal medullary tubules after ischemic damage**

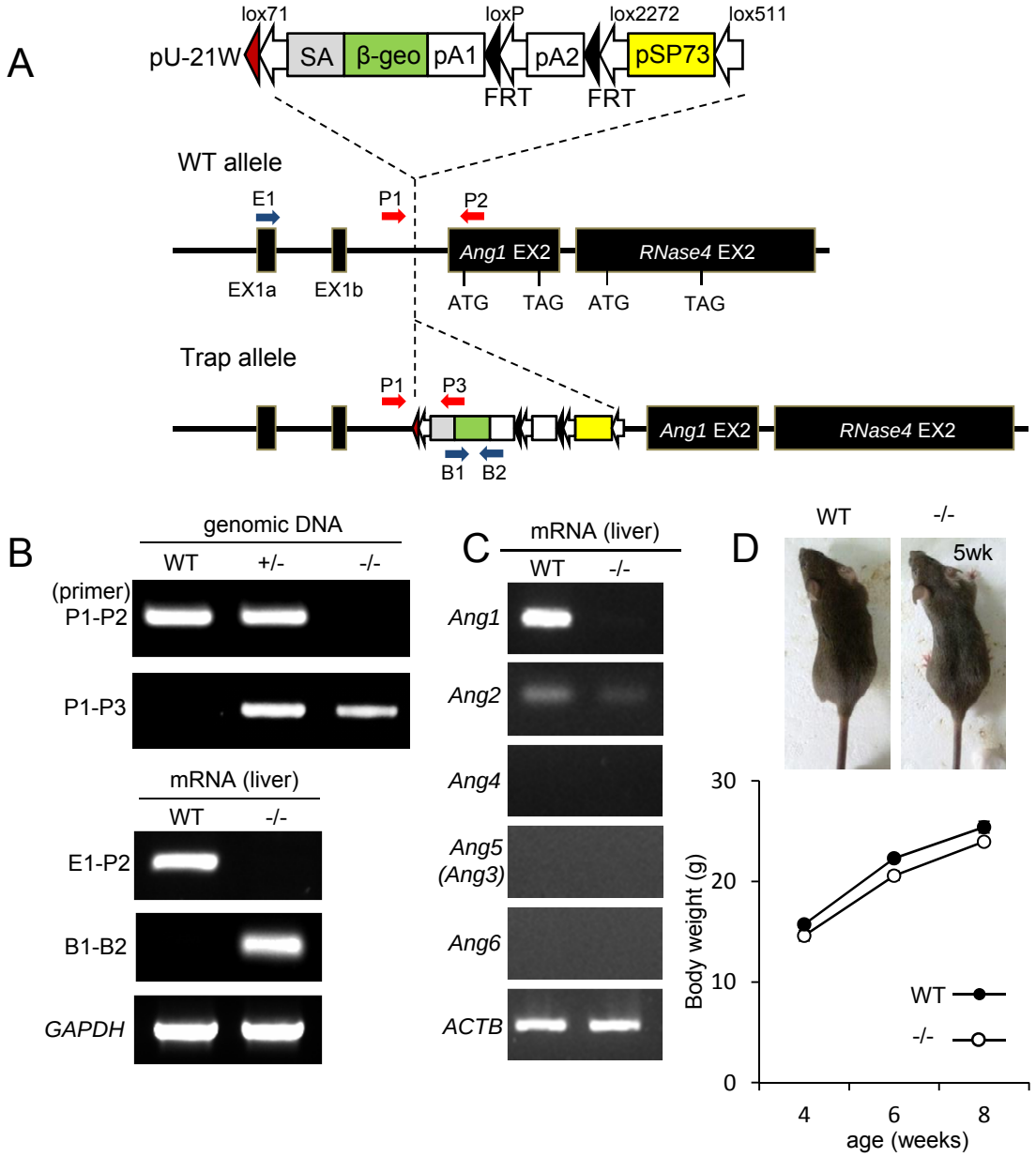
Immunostaining of rat kidney exposed to renal ischemia-reperfusion. Anti-m1A and anti-NKCC2 antibody were used. Scale bar, 100 μm.

# Supplemental Figure 2




**Supplemental Figure 2. Immunocytochemistry using m1A-Ab**
Human osteosarcoma U2OS cells were treated with RNase A or PBS (control) after fixation. DAPI nuclear staining is shown in blue. Scale bar, 20 μm.

# Supplemental Figure 3




**Supplemental Figure 3. Generation of *angiogenin1*-deficient mice and characterization of phenotype**

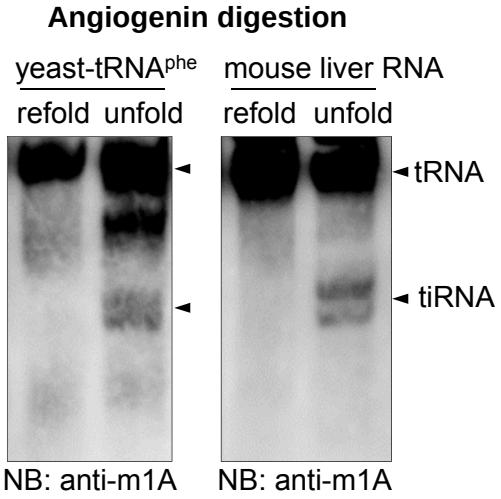
(A) The trap vector, pU-21W, was inserted into the upstream of *Ang1* exon2. P1-P2 and P1-P3 primer sets were used for genotyping. E1-P2 and B1-B2 primer sets were used for RT-PCR.

(B) PCR genotyping and RT-PCR. Genomic DNA and total RNA were extracted from mouse tail and liver tissue, respectively.

(C) RT-PCR analysis with each *Ang* family (*Ang1-Ang6*) specific primer sets. Primer sets of *Ang5* were designed to also amplify *Ang3*. Primers using for genotyping and RT-PCR was described in Table S2.

(D) Phenotype of WT ($Ang1^{+/+}$) and $Ang1^{-/-}$ mice. The sizes of 5-wk-old WT and $Ang1^{-/-}$ littermates are shown. The data of body weight represent the means ± SEM (n=4-5 per group).

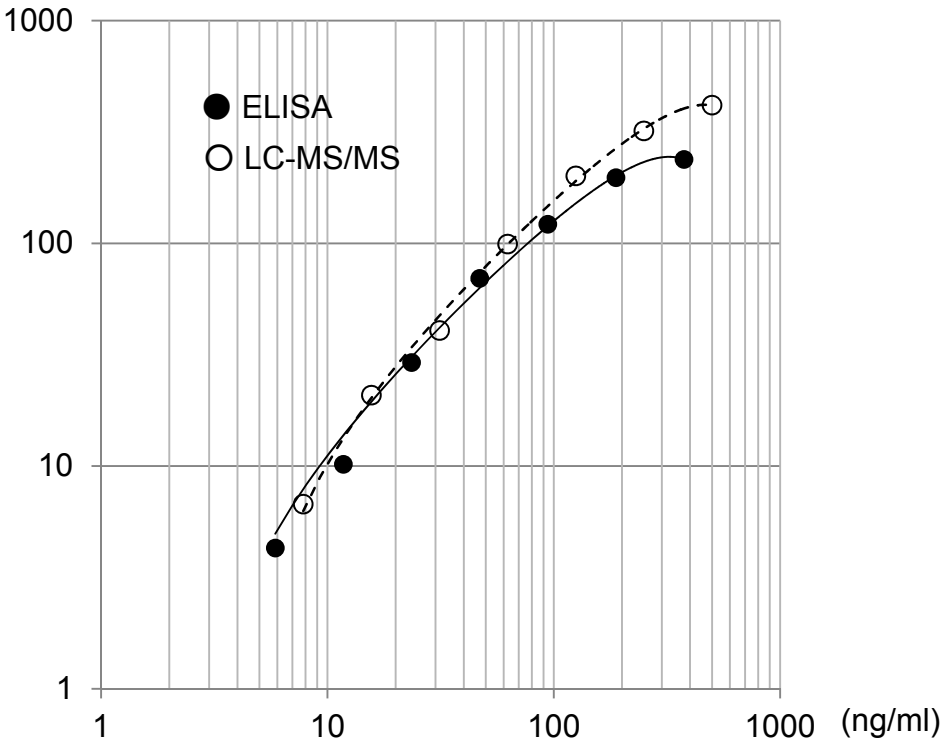
# Supplemental Figure 4




**Supplemental Figure 4. Unfolded tRNA is more likely to be cleaved by Angiogenin**

*In vitro* digestion of refolded or unfolded tRNA (yeast tRNA$^{phe}$ or mouse liver RNA) by angiogenin. RNAs were incubated with recombinant angiogenin (0.3 μg/ml) and analyzed by Northern blot using the anti-m1A antibody. Unfolded tRNA was prepared without the addition of $Mg^{2+}$ in the tRNA refolding process.

# Supplemental Figure 5




**Supplemental Figure 5. The calibration curve of m1A by ELISA and LC-MS/MS**
Diluted reagent of m1A was measured by ELISA or LC-MS/MS

# Supplemental Figure 6

A

measurement sample (10 ml)

↓ Addition,
$CH_3CN$ (200 ml)
IS (tubercidin 200 ng/ml, 50 µl)

↓ Mixing, 30 sec
Sonication, 1 min
Centrifugation, 16,400 g, 10 min, 4 °C

supernatant

↓ Purging, nitrogen, 60 °C (heating)

↓ Dissolution,
2 mmol/l $CH_3COONH_4$ (0.1% $CH_3COOH$) (50 ml)

↓ Filtration, 0.2 mm pore size
Centrifugation, 5,500 g, 5min, 4 °C

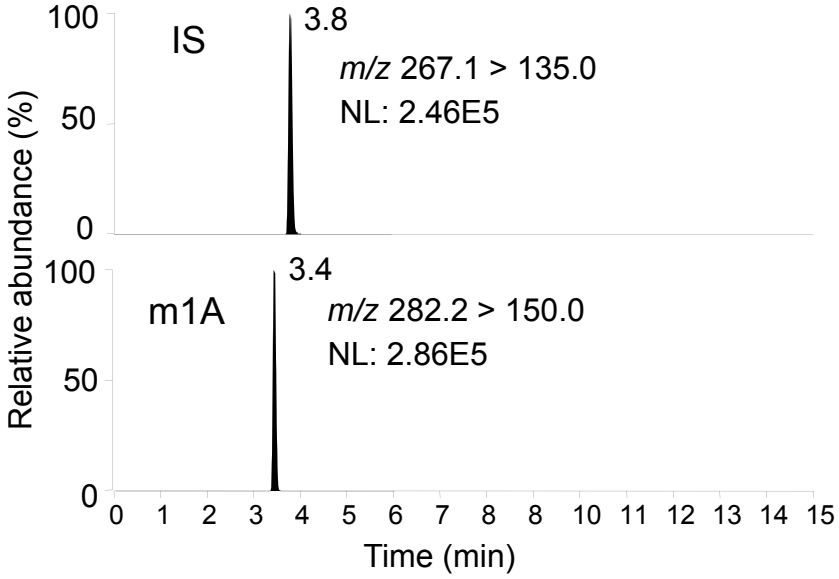
LC-MS/MS

B

| | | |
|---|---|---|
| **MS system** | Spray voltage | 3,000 V |
| | Vaporizer temperature | 450°C |
| | Sheath gas pressure | 50 psi |
| | Auxiliary gas pressure | 20 psi |
| | Capillary temperature | 300°C |
| | Collision gas pressure | 1.5 mTorr |
| | Tube lens offset | m1A: 84 V<br>Tubercidin (IS): 87 V |
| | Collision energy | m1A: 20 eV (*m/z* 282.1 > 150.0)<br>IS: 20 eV (*m/z* 267.1 > 135.0) |
| **LC system** | Mobile phase | A: 2 mM $CH_3COONH_4$ - $H_2O$ + 0.1% $CH_3COOH$<br>B: 2 mM $CH_3COONH_4$ - $CH_3OH$ + 0.1% $CH_3COOH$<br>C: 2 mM $CH_3COONH_4$ - $CH_3CN$ + 0.1% $CH_3COOH$ |
| | Gradient | 0.0 - 0.5 min: A/B/C = 100/0/0<br>0.5 - 4.0 min: A/B/C = 100/0/0 → 55/45/0<br>4.0 - 4.1 min: A/B/C = 55/45/0 → 0/100/0<br>4.1 - 6.0 min: A/B/C = 0/100/0<br>6.0 - 6.1 min: A/B/C = 0/100/0 → 0/0/100<br>6.1 - 9.0 min: A/B/C = 0/0/100<br>9.0 - 9.1 min: A/B/C = 0/0/100 → 0/100/0<br>9.0 - 12.0 min: A/B/C = 0/100/0<br>12.0 - 12.1 min: A/B/C = 0/100/0 → 100/0/0<br>12.1 - 15.0 min: A/B/C = 100/0/0 |
| | Flow rate | 0.0 - 5.0 min: 200 µl/min<br>5.0 - 11.1 min: 300 µl/min<br>11.1 - 15.0 min: 200 µl/min |
| | Oven temperature | 40°C |
| | Injection volume | 1 µl |

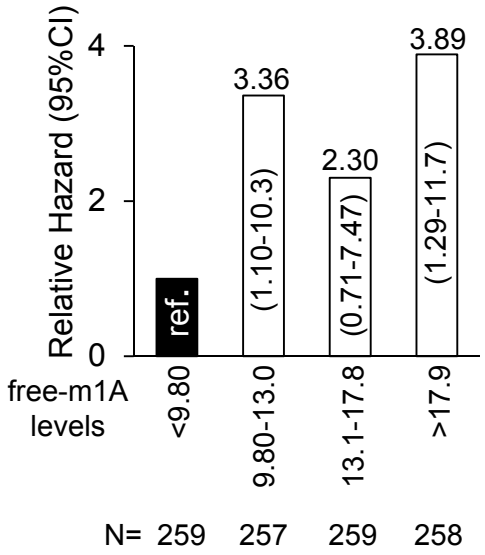
**Supplemental Figure 6. Measurement conditions of free-m1A by LC-MS/MS analysis**
(A) Sample preparation procedures.
(B) MS and LC condition for analysis of m1A.

# Supplemental Figure 7




**Supplemental Figure 7. SRM chromatograms of m1A and internal standard**
The selected reaction monitoring (SRM) transitions were *m/z* 282.2 > 150.0 for m1A and *m/z* 267.1 > 135.0 for internal standard (IS), and they were detected at 3.4 and 3.8 min, respectively. The sheath gas and collision gas were nitrogen and argon, respectively.

# Supplemental Figure 8



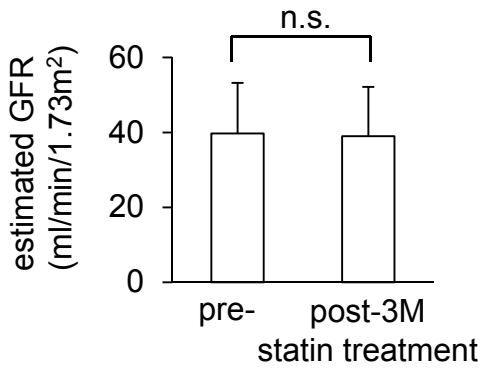

**Supplemental Figure 8. The univariate analysis between free-m1A levels and mortality.**
Association between the circulating free-m1A level and mortality in general population (n=1,033) analyzed with univariate analysis.

# Supplemental Figure 9

A

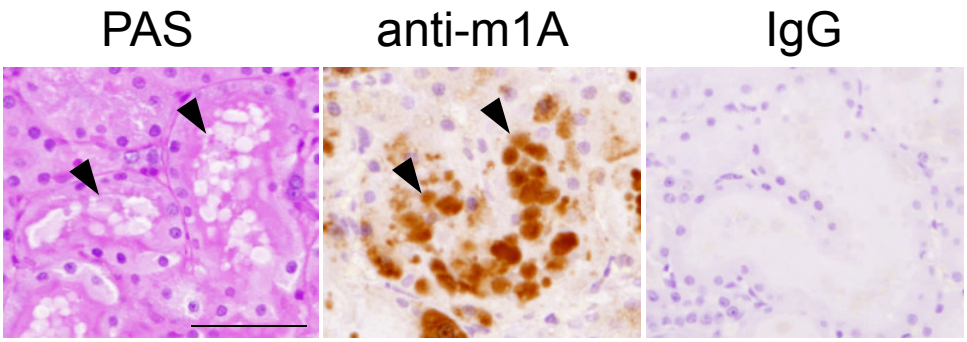
| | | |
|---|---|---|
| Number of participants | 29 | |
| Men | 13 | (66%) |
| Age (years) | 64.1 + 11.8 | |
| Systolic BP (mmHg) | 131.2 + 11.0 | |
| Diastolic BP (mmHg) | 74.8 + 6.26 | |
| Serum creatinine (mg/100ml) | 1.45 + 0.46 | |
| Estimated GFR (ml/min/1.73m$^2$) | 39.7 + 13.5 | |
| Urine protein (g/gCr) | 0.67 + 1.57 | |
| Total cholesterol (mg/100ml) | 213.4 + 29.9 | |
| *Baseline disease* | | |
| Antihypertensive medications (%) | 27 | (93%) |
| Cardiovascular disease (%) | 8 | (28%) |
| Diabetes (%) | 6 | (21%) |
| Current smoking (%) | 1 | (3%) |
| Body mass index >30 kgm$^2$ | 1 | (3%) |
| *Cause of CKD* | | |
| Glomeruloscrerosis | 8 | (28%) |
| IgA nephropathy | 6 | (21%) |
| Interstitial nephritis | 3 | (10%) |
| Diabetic nephropathy | 2 | (7%) |
| Lupus nephropathy | 1 | (3%) |
| Membranoproliferative glomerulonephritis | 1 | (3%) |
| Membranous nephropathy | 1 | (3%) |
| Polycystic kidney | 1 | (3%) |
| Microscopic polyangitis | 1 | (3%) |
| Renal cell carcinoma | 1 | (3%) |
| Unknown | 4 | (14%) |

B



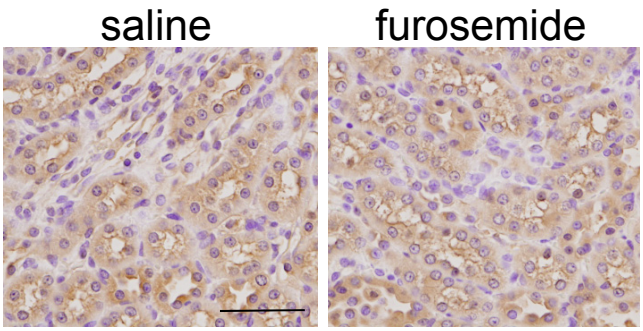

**Supplemental Figure 9. Characteristics of participants of statin treatment**
(A) Baseline characteristics of CKD patients.
(B) Estimated GFR did not change significantly after 3-month statin treatments.
Data are shown as mean ± SD. *GFR*, glomerular filtration rate.

# Supplemental Figure 10



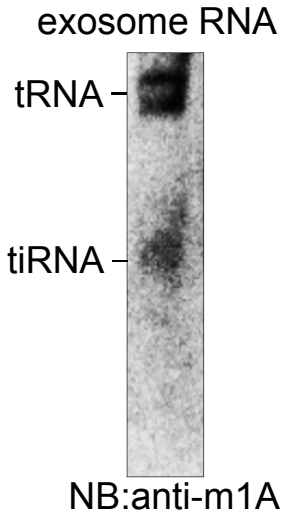

**Supplemental Figure 10. Blebs in proximal tubules contains damaged tRNAs** Immunohistochemistry by anti-m1A antibody in S3 segments of rat kidney after I/R (60-min renal ischemia and 60-min reperfusion). Blebs (indicated by arrow heads) showed strong immunopositive signals. Isotype IgG were used to control. Tissues were fixed with 2% glutaraldehyde and 2% paraformaldehyde to maintain blebs within sections. Scale, 50 μm.

# Supplemental Figure 11



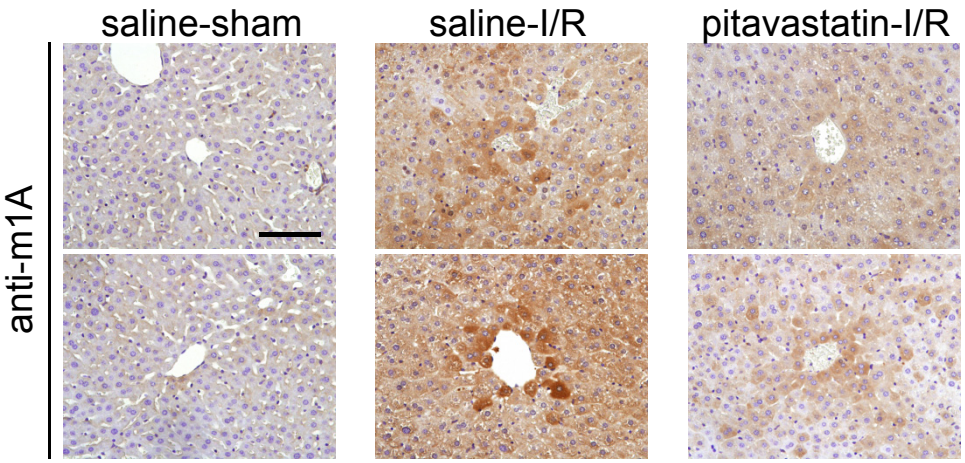

**Supplemental Figure 11. Furosemide does not change the immunopositive signal by anti-m1A antibody**
Immunohistochemistry using anti-m1A antibody. Furosemide (10mg/kg) or saline was injected intravenously to rats (n = each 3). Three hours after injection, kidneys were collected. Scale bar, 100 μm.

# Supplemental Figure 12




**Supplemental Figure 12. tRNA and tiRNA are present in plasma exosomes**
Total RNA isolated from rat plasma exosomes was analyzed by Northern blot using the anti-m1A antibody.

# Supplemental Figure 13




**Supplemental Figure 13. Statin treatment reduced tRNA damage**
Immunostaining of mouse liver by the anti-m1A antibody. One hour-hepatic ischemia and 1 h-reperfusion were performed after intraperitoneal administration of pitavastatin (3mg/kg) or saline for 7 days. Each n=3. Representative data are shown. Scale bar, 100 μm.

# Supplemental Table 1

| | Total | Quartile1 | Quartile2 | Quartile3 | Quartile4 | |
|---|---|---|---|---|---|---|
| Serum m1A levels (ng/ml) | | <9.80 | 9.80-13.0 | 13.1-17.8 | >17.9 | *P* |
| Number of participants | 1033 | 259 | 257 | 259 | 258 | |
| Men (%) | 32.3 | 29.3 | 30.7 | 32.4 | 36.8 | 0.29 |
| Age (years) | 61.1 ± 10.9 | 59.3 ± 10.7 | 60.9 ± 11.3 | 61.4 ± 10.7 | 62.8 ± 10.5 | <0.01 |
| Systolic BP (mmHg) | 131.0 ± 13.7 | 129.6 ± 14.5 | 130.7 ± 13.7 | 131.5 ± 13.2 | 132.1 ± 13.4 | 0.17 |
| Diastolic BP (mmHg) | 73.5 ± 9.0 | 73.0 ± 9.5 | 73.3 ± 8.8 | 73.5 ± 8.6 | 74.2 ± 9.2 | 0.50 |
| Estimated GFR ($ml/min/1.73m^2$) | 85.3 ± 17.5 | 88.1 ± 18.0 | 85.2 ± 17.3 | 84.7 ± 17.9 | 83.2 ± 16.7 | <0.05 |
| Diabetes (%) | 8.6 | 7.7 | 9.3 | 7.0 | 10.5 | 0.48 |
| Hyperlipidemia (%) | 26.4 | 23.9 | 26.1 | 29.7 | 26 | 0.51 |
| Cardiovascular disease (%) | 8.6 | 6.6 | 8.2 | 8.5 | 11.2 | 0.29 |
| Antihypertensive medications (%) | 26.5 | 23.9 | 26.9 | 26.3 | 29.1 | 0.62 |
| Smoker (%) | 23.3 | 20.1 | 19.8 | 28.2 | 25.2 | 0.066 |

**Supplemental Table 1. Baseline characteristics of participants**
Value are shown as mean ± SD. BP, blood pressure; GFR, Glomerular filtration rate.

# Supplemental Table 2

| | | |
|---|---|---|
| P1 | | 5'-AGTTTCTGGGCCCAATAGGAC |
| P2 | | 5'-CATCGAAGTGGACAGGCAAAC |
| P3 | | 5'-CACATCCATGCTGAGGATGAG |
| E1 | | 5'-ATTACCAGCCTGTGAGGAGC |
| B1 | | 5'-CCAACTTAATCGCCTTGCAGC |
| B2 | | 5'-GAAGATCGCACTCCAGCCAG |
| *ACTB* | Forward | 5'-AGCCATGTACGTAGCCATCCA |
| *ACTB* | Reverse | 5'-TCTCCGGAGTCCATCACAATG |
| *Ang1* | Forward | 5'-AAGAAGCCTAACCTCACCCT |
| *Ang1* | Reverse | 5'-CAACATGTCTGAACCCTGCA |
| *Ang2* | Forward | 5'-TCCTTTGTTCTTGGTCTTCCT |
| *Ang2* | Reverse | 5'-TGTTGACATCTTTGCAGAAAG |
| *Ang4* | Forward | 5'-GCTCAGAATGAAAGGTACGAA |
| *Ang4* | Reverse | 5'-CTTTAAAGGCTCGGTACCCG |
| *Ang5* and *3* | Forward | 5'-AGCCAACTGGCCGGGATTA |
| *Ang5* and *3* | Reverse | 5'-GCTTGGGAGACCCTCCTTTG |
| *Ang6* | Forward | 5'-TTCCTTGATGTTGGTCTTTGT |
| *Ang6* | Reverse | 5'-TGCATTTCAAGGTTTCTTGGAT |

**Supplemental Table 2. Using primer sequences**