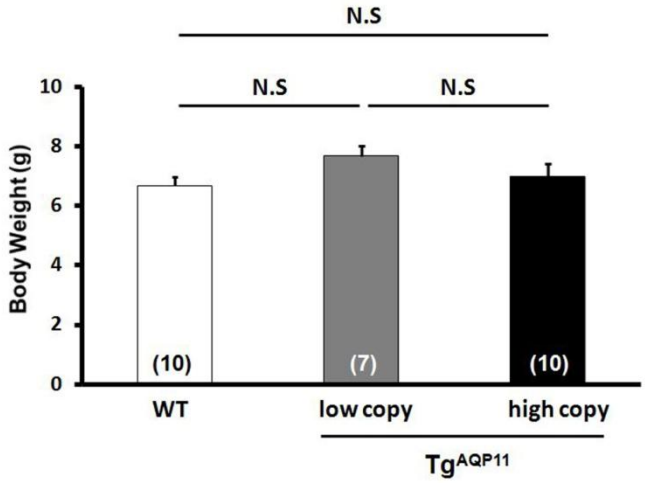
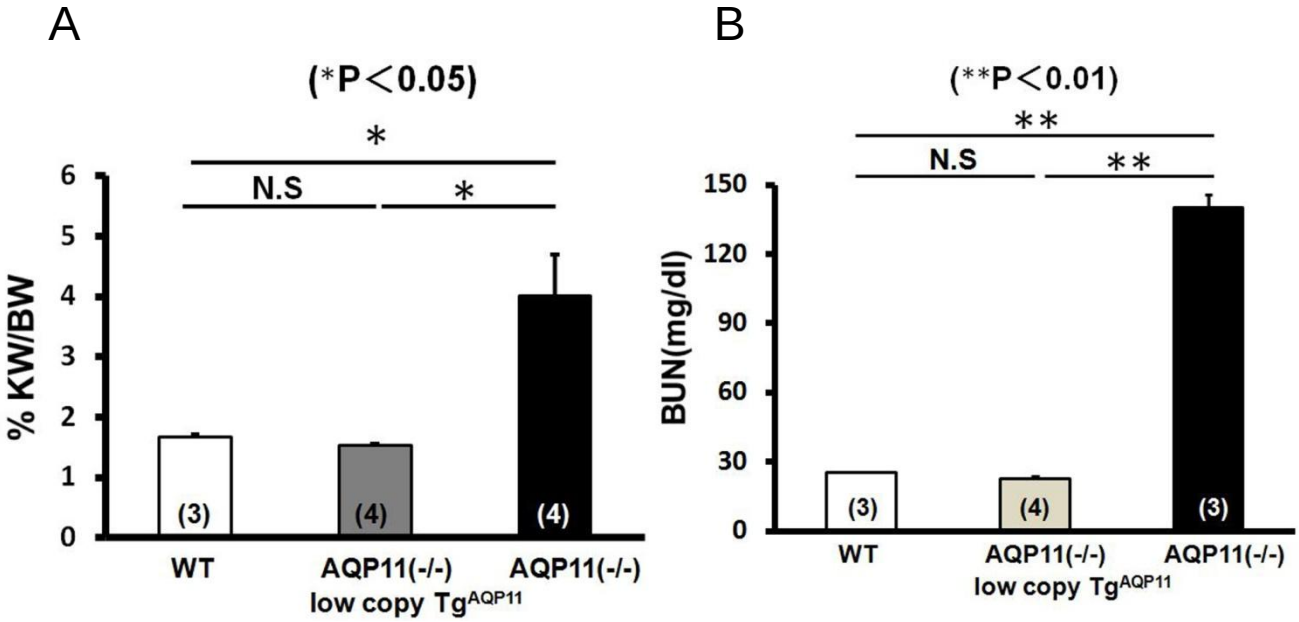
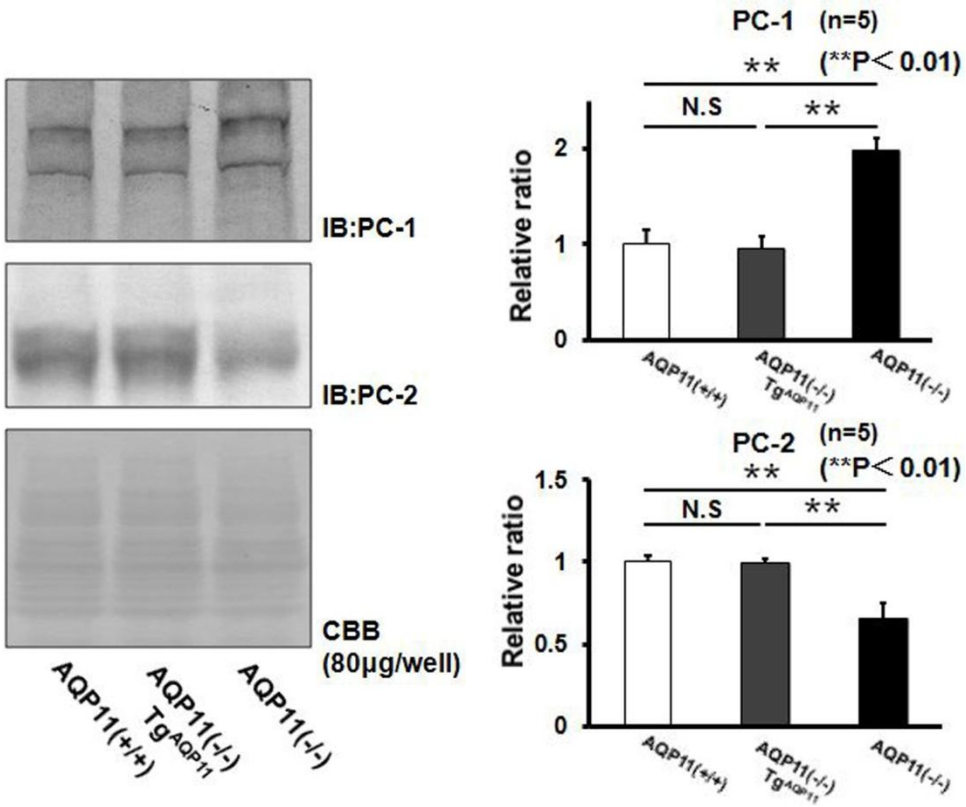


Supplementary Figure 1. Body Weight of Tg^{AQP11} and wild-type mice.
Analysis of the body weights of 3-week-old low and high copy Tg^{AQP11} and wild-type mice indicated that there were no significant differences between high copy Tg^{AQP11}, low copy Tg^{AQP11}, and wild-type mice.



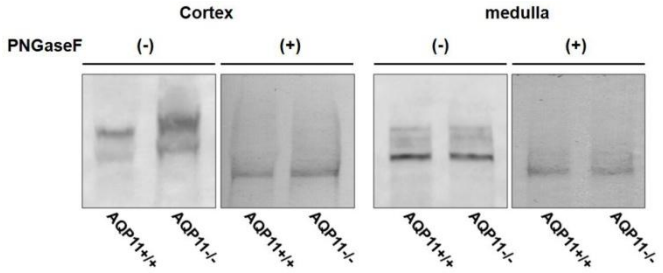
Supplementary Figure 2. 3×HA-tagged AQP11 transgene rescues renal cyst formation in AQP11(-/-) mice.

Kidney to body weight ratio (A) and blood urea nitrogen (B) showed no significant differences between wild-type and AQP11(-/-) low copy Tg^{AQP11} mice, indicating that the 3×HA-tagged AQP11 transgene completely rescues renal cyst formation in AQP11(-/-) mice.

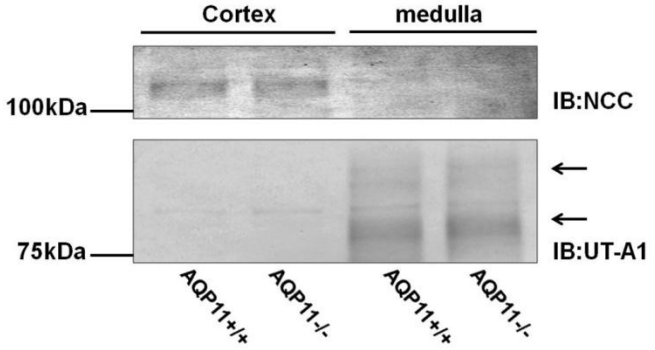


Supplementary Figure 3. PC-1 and PC-2 expression in AQP11(-/-)Tg^{AQP11} kidney.
Western blots of PC-1 and PC-2 in 2-week-old wild-type, AQP11(-/-)Tg^{AQP11}, and AQP11(-/-) mouse kidneys were conducted. The relative levels of PC-1 and PC-2 expression were determined by normalization to overall CBB staining in each lane. The expression levels and electrophoretic mobility of PC-1 are not different between wild-type and AQP11(-/-)Tg^{AQP11} kidneys. The PC-2 expression level does not differ between wild-type and AQP11(-/-)Tg^{AQP11} kidneys. These data clearly demonstrated that AQP11 transgene rescued PC-1 and PC-2 status in AQP11(-/-) kidney.

A

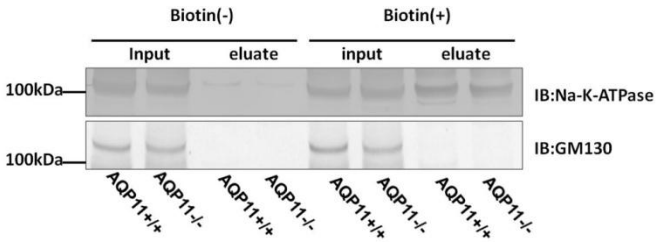


B

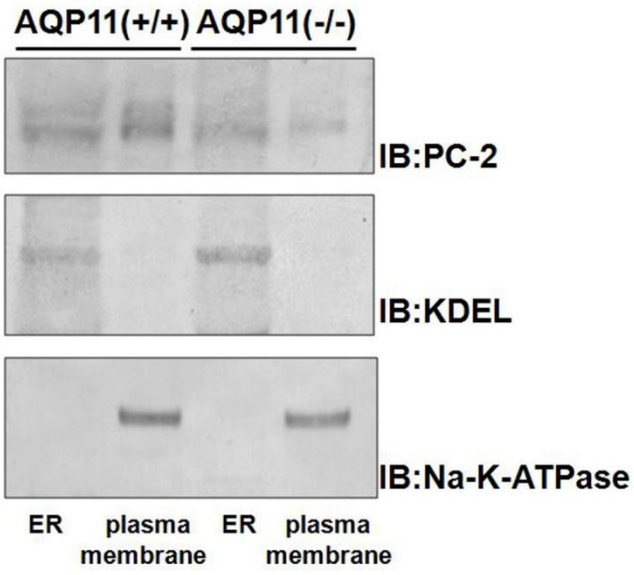


Supplementary Figure 4. Aberrant glycosylation of PC-1 was observed in the cortex, but not medulla of AQP11(-/-) kidney.

(A) PC-1 immunoblots in cortex and medulla of 2-week-old wild-type and AQP11(-/-) kidneys before and after PNGaseF treatment. Aberrant glycosylation of PC-1 was detected in the cortex only of AQP11(-/-) kidney. (B) NCC and UT-A1 immunoblots in cortex and medulla of 2-week-old wild-type and AQP11(-/-) kidneys. We confirmed that these samples represent cortex and medulla. The arrowheads show the UT-A1 bands.



Supplementary Figure 5. Confirmation of successful *in vivo* biotinylation assay.
Each lane was loaded with 20 μg of total input protein or 5 μl of eluate protein from the streptavidin beads. (Upper) Na-K-ATPase immunoblots of the eluates showed that Na-K-ATPase was biotinylated in both wild-type and AQP11(-/-) mice kidneys. These blots indicated that this *in vivo* biotinylation assay correctly labeled surface proteins. (Lower) GM130 immunoblots of the eluates showed that this *in vivo* biotinylation assay did not label intracellular proteins.



Supplementary Figure 6. Membrane trafficking of PC-2 in AQP11(-/-) kidneys.
ER and plasma membrane fractions were analyzed by immunoblotting with antibodies against PC-2, KDEL, and Na-K-ATPase. Membrane trafficking of PC-2 was still observed in AQP11(-/-) mice, although PC-2 levels in the membrane fraction were decreased. Control immunoblotting of plasma membrane (Na-K-ATPase) and ER (KDEL) fractions are same as Figure 7B.