Supplemental material: This article contains the following supplemental material online at:

Figure S1.	There are no significant differences in systolic blood pressure between males and females within each group in stenosed mice.
Figure S2.	There are no significant differences in renin and prorenin expressions between males and females within each group in stenosed mice in chronic settings.
Figure S3.	There are no significant differences in renin and prorenin expression between males and females within each group in stenosed mice in acute settings.
Figure S4.	Knock out of Sox6 in renin expressing cells does not affect renin expression in the contralateral kidneys during renal artery stenosis.
Figure S5.	Knock out of Sox6 in renin expressing cells inhibits renin expression.
Figure S6.	There are no significant differences in co-localization of renin and Sox6 expression between males and females within each group in stenosed mice.
Figure S7.	Knock out of Sox6 in renin expressing cells does not affect mRNA levels of renin expression in the contralateral kidneys during renal artery stenosis.
Figure S8.	Knock out of Sox6 in renin expressing cells inhibits renin mRNA expression.
Figure S9.	There are no significant differences in JG cell recruitment/expansion between males and females within each group in stenosed mice.
Figure S10.	There are no significant differences in N-GAL expression between males and females within each group in stenosed mice.
Figure S11.	There are no significant differences in creatinine clearance between males and females within each group in stenosed mice.
Figure S12.	Competition assay with renin peptide, and recombinant prorenin and renin experiments using Western blot show the antibody specificity and positions of both bands of both proteins respectively.

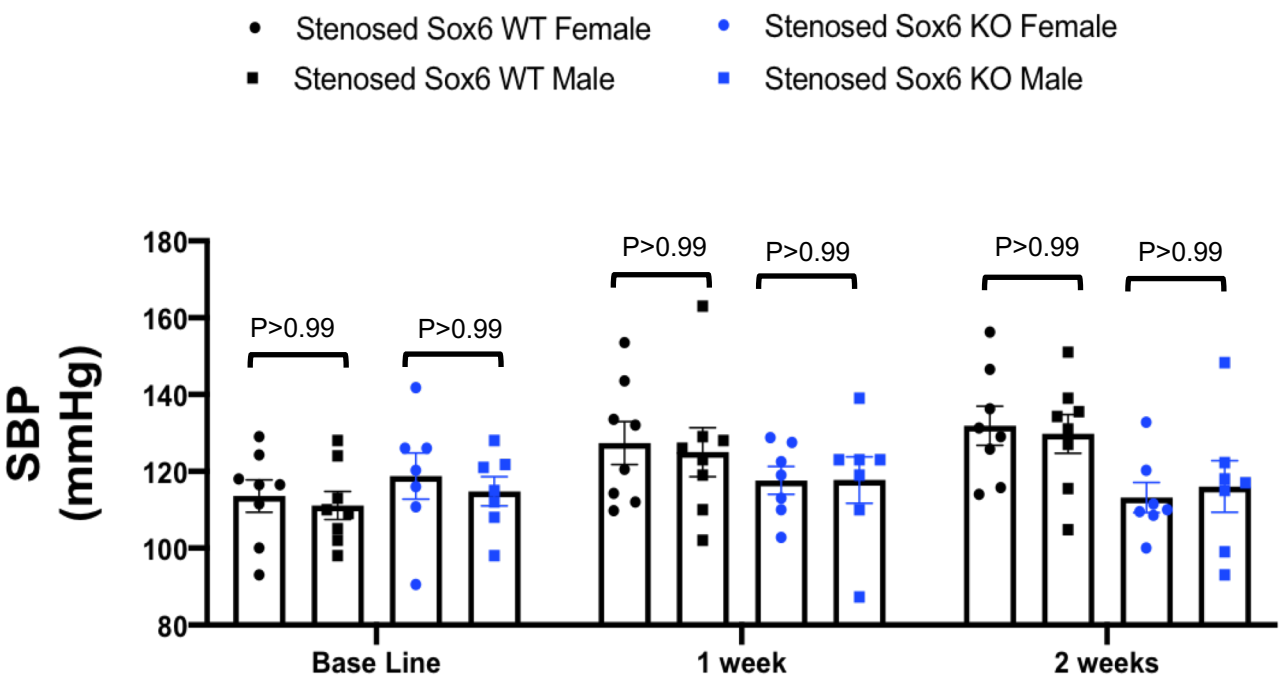
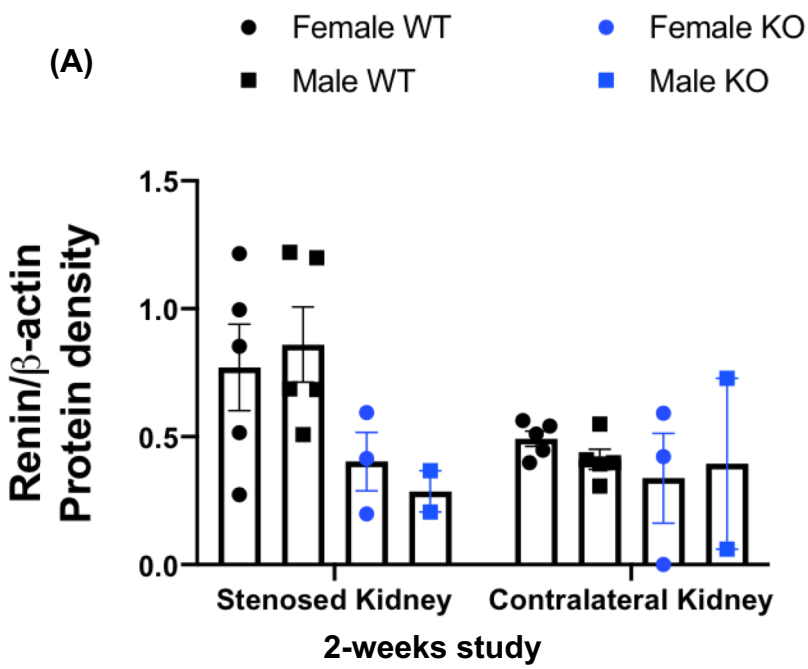


Figure S1. There are no significant differences in systolic blood pressure between males and females within each group in stenosed mice. Blood pressure was measured one week before and two weeks after the surgery by tail cuff method. Blood pressure was measured for 2 consecutive days each week. N= Female: Sox6 WT 8, Sox6 KO 7; Male: Sox6 WT 8, Sox6 KO 7. Data are presented as the mean ± SEM. P calculated with two-way ANOVA followed by Tukey post-hoc test. A p-value equal or less than 0.05 was considered significant.



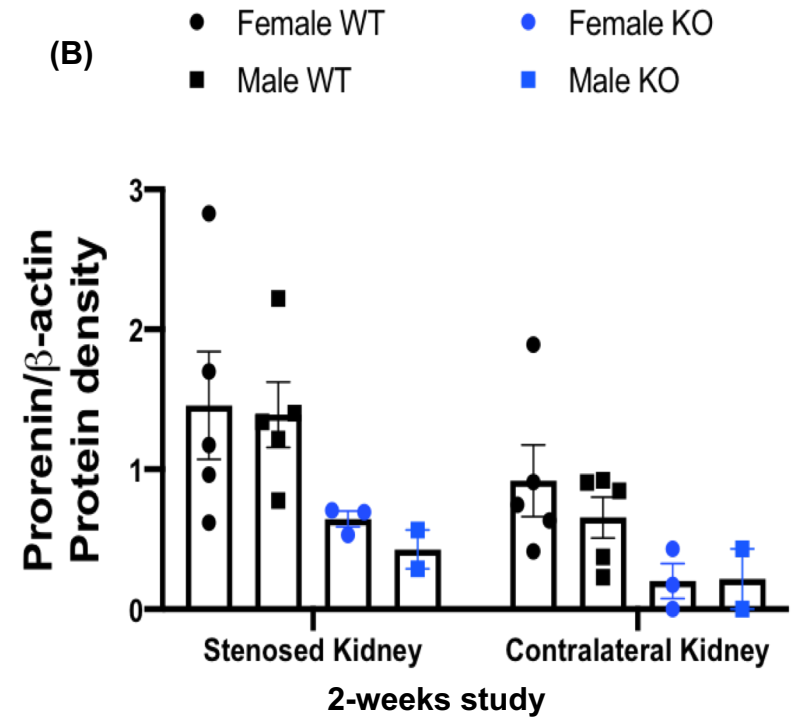


Figure S2. There are no significant differences in renin and prorenin expressions between males and females within each group in stenosed mice in chronic settings. Two weeks after surgery, kidneys were harvested, and Western blot was performed. (**A**) Densitometric analysis of renin protein bands. (**B**) Densitometric analysis of prorenin protein bands. N= Female: Sox6 WT 5, Sox6 KO 3; Male: Sox6 WT 5, Sox6 KO 2. Data are presented as the mean ± SEM. P calculated with two-way ANOVA followed by Tukey post-hoc test. A p-value equal or less than 0.05 was considered significant.

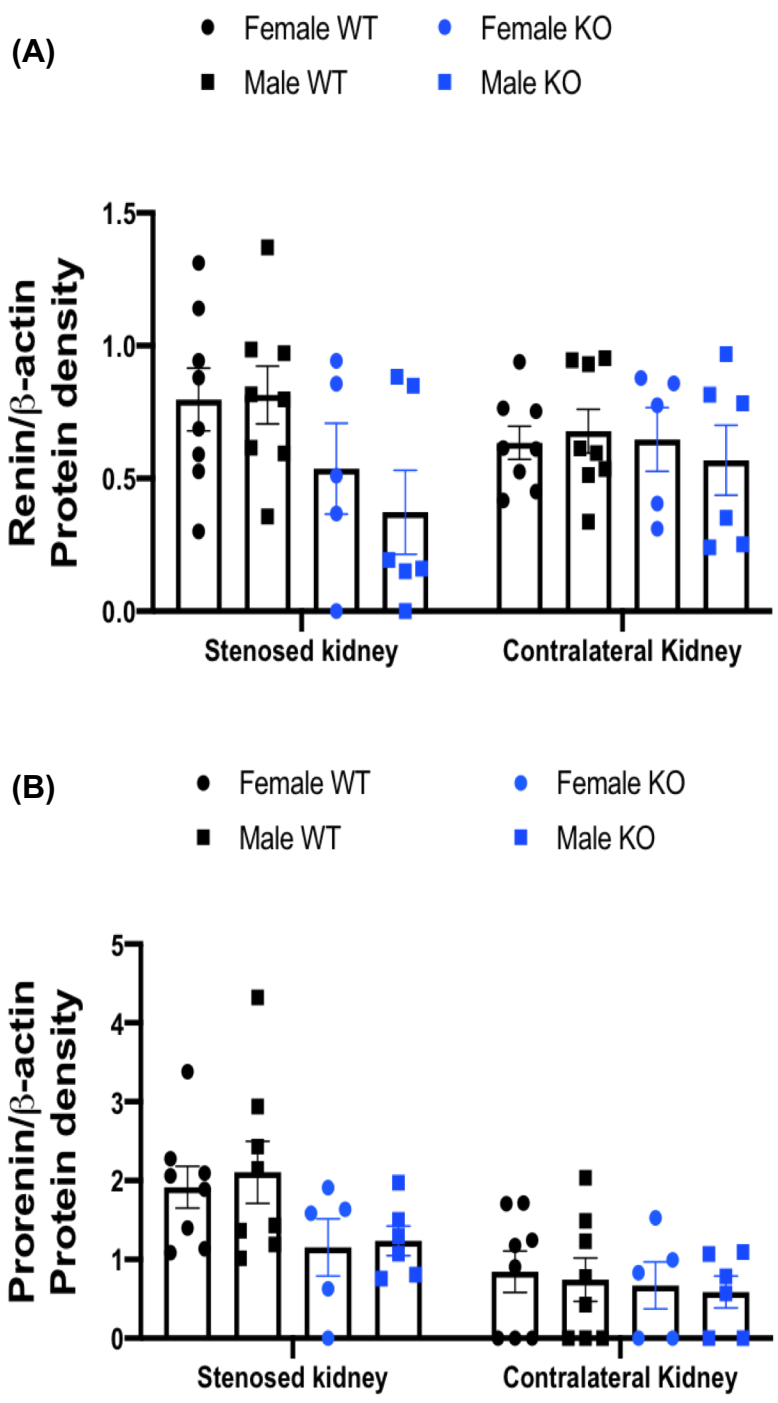


Figure S3. There are no significant differences in renin and prorenin expressions between males and females within each group in stenosed mice in acute settings. Three days after the surgery, kidneys were harvested, and Western blot was performed. (**A**) Densitometric analysis of renin protein bands. (**B**) Densitometric analysis of prorenin protein bands. N= Female: Sox6 WT 8, Sox6 KO 5; Male: Sox6 WT 8, Sox6 KO 6. Data are presented as the mean ± SEM. P calculated with two-way ANOVA followed by Tukey post-hoc test. A p-value equal or less than 0.05 was considered significant.

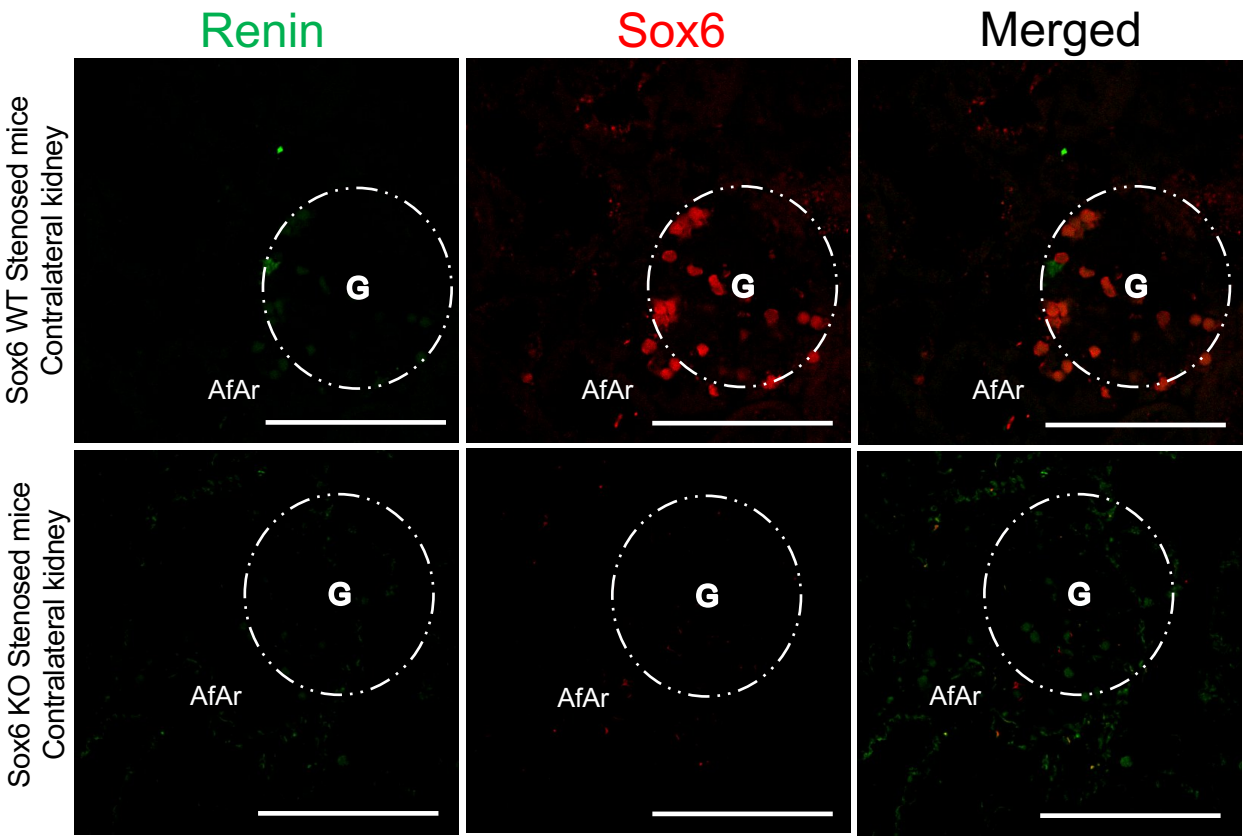
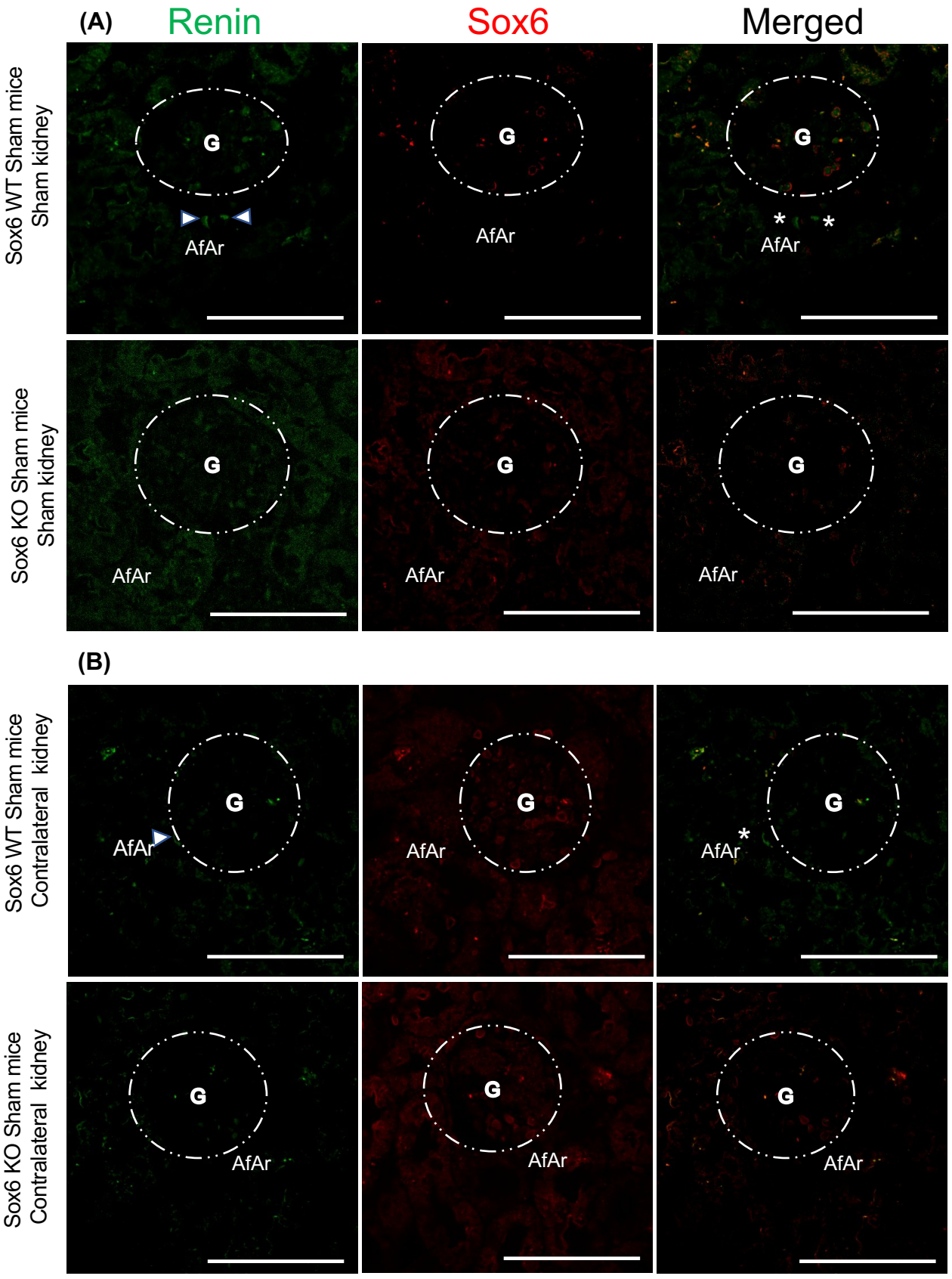


Figure S4. Knock out of Sox6 in renin expressing cells does not affect renin expression in the contralateral kidneys during renal artery stenosis. Three days after the surgery, kidneys were harvested, and immunohistochemistry was performed. Upper panel is showing renin (green), and Sox6 (red) expression in contralateral kidney from stenosed, Sox6 WT mice. Similarly, lower panel is showing the expression of renin (green), and Sox6 (red) in contralateral kidney from stenosed, Sox6 KO mice. Scale bar 30 µm, magnification 60X. G= glomerulus, AfAr= Afferent arteriole. Circle is depicting glomerulus location, N= 5.


(A)
Renin
Sox6
Merged
Sox6 WT Sham mice
Sham kidney
Sox6 KO Sham mice
Sham kidney
G
AfAr
(B)
Sox6 WT Sham mice
Contralateral kidney
Sox6 KO Sham mice
Contralateral kidney

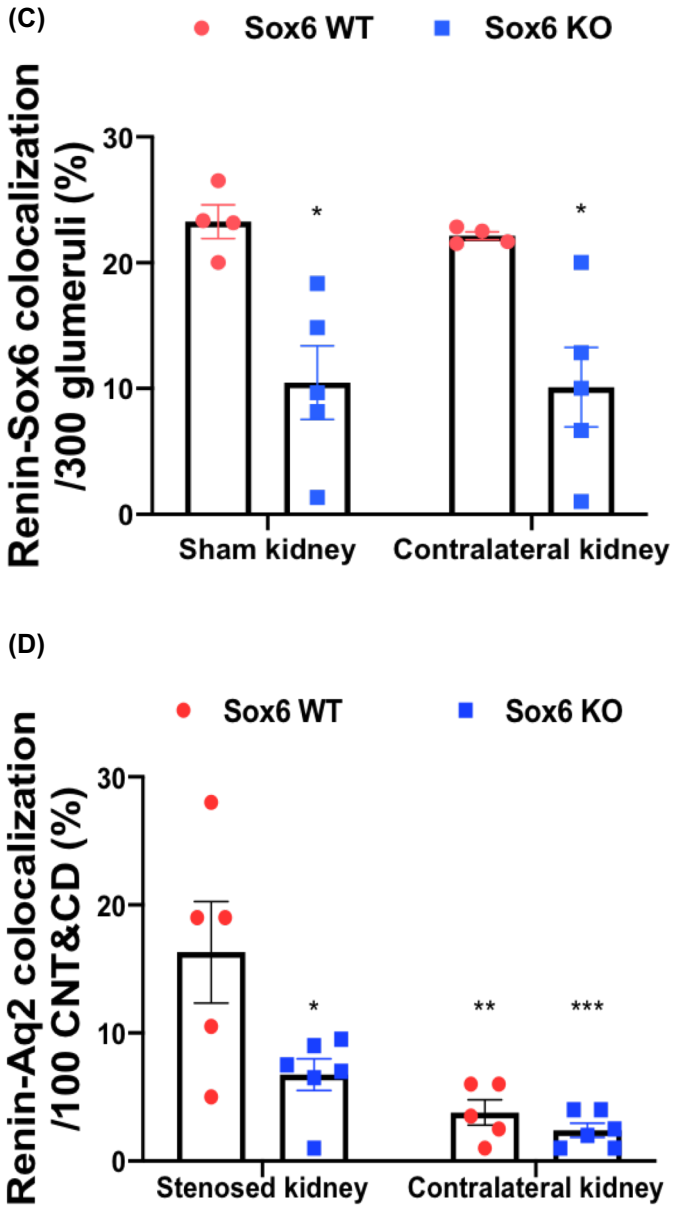


Figure S5. Knock out of Sox6 in renin expressing cells inhibits renin expression. Three days after the surgery, kidneys were harvested, and immunohistochemistry was performed. (**A**) Upper panel is showing renin (green), and Sox6 (red) expression in sham kidney from Ren1d^{Cre}Sox6$^{wt/wt}$ (Sox6 WT) sham mice. Lower panel is showing renin (green), and Sox6 (red) expression in sham kidney from Ren1d^{Cre}Sox6$^{fl/fl}$ (Sox6 KO) sham mice. (**B**) Upper panel is showing renin (green), and Sox6 (red) expression in contralateral kidney from Sox6 WT sham mice. Lower panel is showing renin (green), and Sox6 (red) expression in contralateral kidney from Sox6 KO sham mice. (**C**) Quantification of three hundred glomeruli per kidney to see co-expression of renin and Sox6 in sham mice. G= glomerulus, AfAr= Afferent arteriole. Scale bar 30 µm, magnification 60X. N=4-5. Knock out of Sox6 in renin expressing cells inhibits renin expression in CNTs and CDs. (**D**) Quantification of one hundred connecting tubules (CNTs) and collecting ducts (CDs) per kidney to see co-expression of renin and aquaporin-2 (Aq2) in stenosed mice. N=5-6.

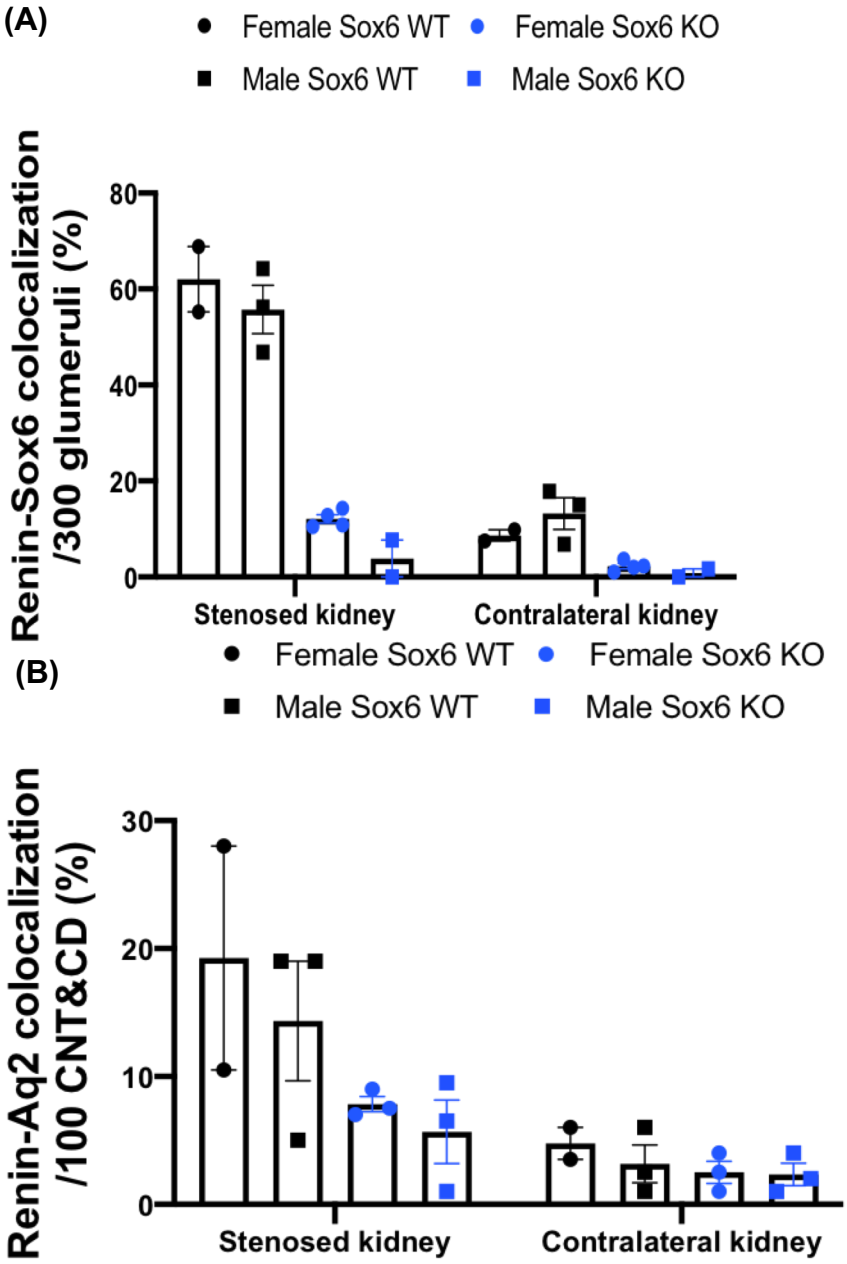


Figure S6. There are no significant differences in co-localization of renin and Sox6 expression between males and females within each group in stenosed mice. Three days after the surgery, kidneys were harvested, fixed and IHC was performed. **(A)** Quantification of three hundred glomeruli per sample expressing renin protein along the afferent arteriole from IHC experiment is shown in the bar graph. N= Female: Sox6 WT 2, Sox6 KO 4; Male: Sox6 WT 3, Sox6 KO 2. There are no significant differences in renin expression in CNTs and CDs between males and females within each group in stenosed mice. **(B)** Quantification of one hundred CNTs and CDs per kidney co-expressing renin and Aq2 from IHC experiment is shown in the bar graph. N= Female: Sox6 WT 2, Sox6 KO 3; Male: Sox6 WT 3, Sox6 KO 3. Data are presented as the mean ± SEM. P calculated with two-way ANOVA followed by Tukey post-hoc test. A p-value equal or less than 0.05 was considered significant.

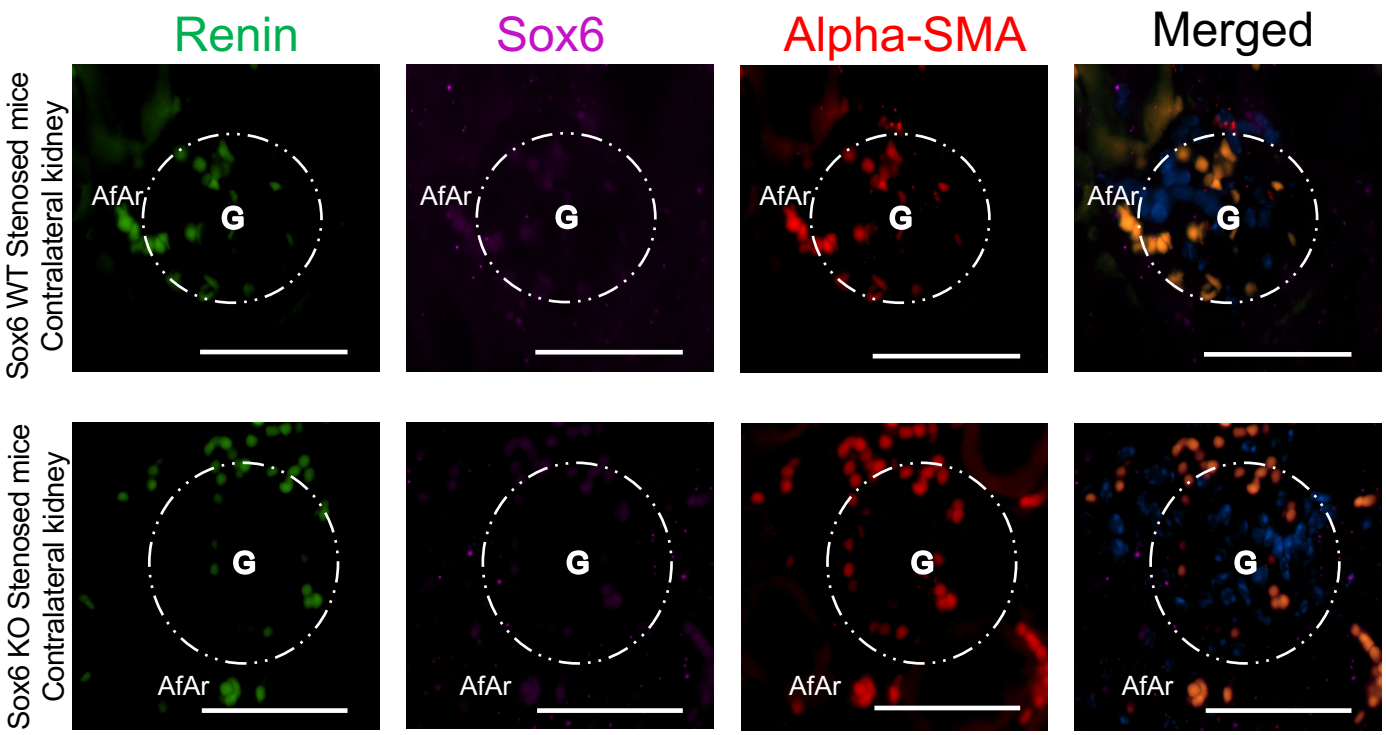
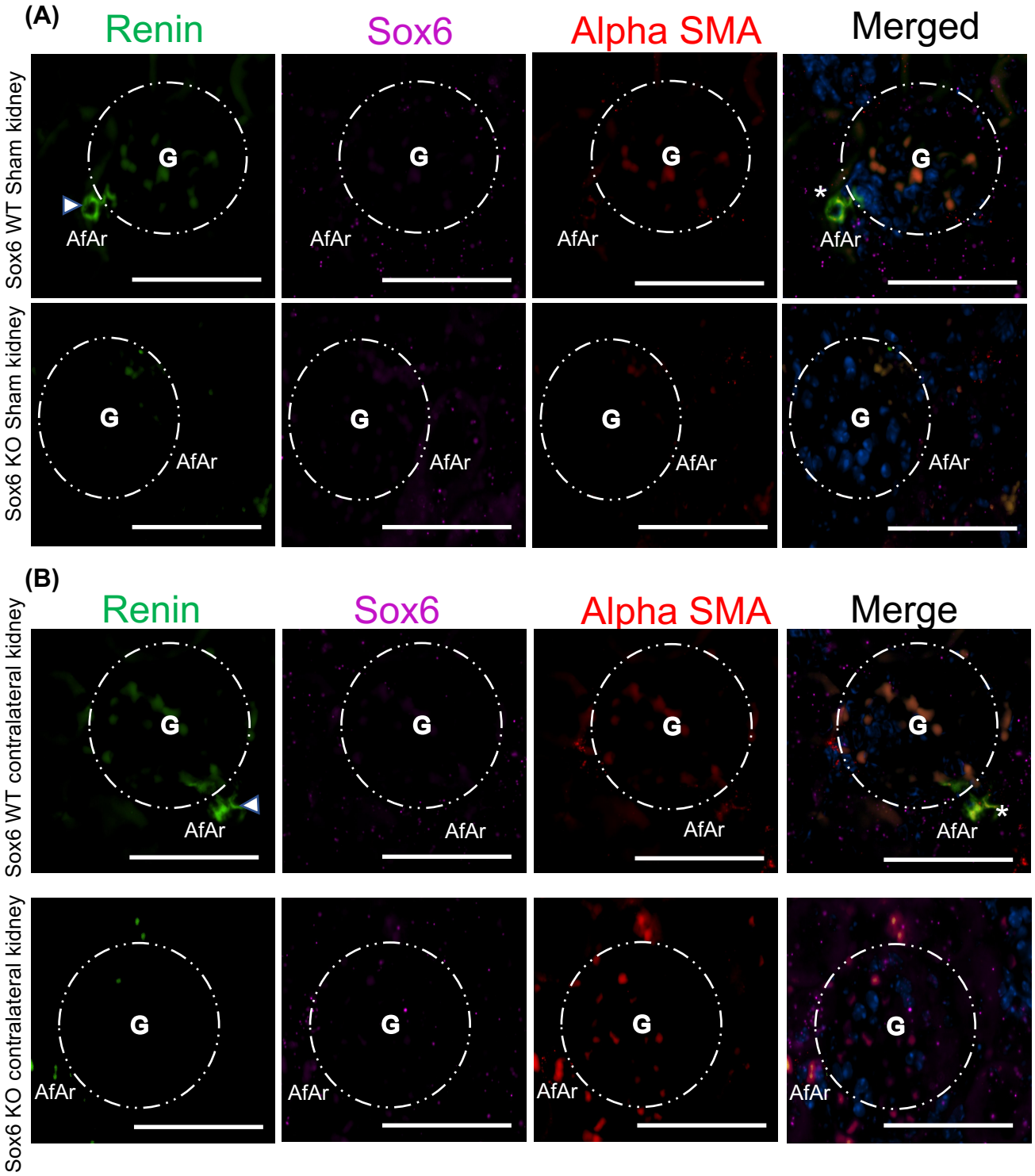


Figure S7. Knock out of Sox6 in renin expressing cells does not affect mRNA levels of renin expression in the contralateral kidneys during renal artery stenosis. Three days after the surgery, kidneys were harvested, and *in situ* hybridization was performed. Upper panel is showing mRNA expression of renin (green), Sox6 (magenta), and alpha smooth muscle actin (a-SMA, red) in contralateral kidneys from stenosed, Sox6 WT mice. Similarly, lower panel is showing the expression of renin (green), Sox6 (magenta), and a-SMA (red) in contralateral kidneys from stenosed, Sox6 KO mice. Scale bar 10 μm, magnification 90X. G= glomerulus, AfAr= Afferent arteriole N=5-6.


(A)
Renin
Sox6
Alpha SMA
Merged
Sox6 WT Sham kidney
Sox6 KO Sham kidney
G
AfAr
*
(B)
Renin
Sox6
Alpha SMA
Merge
Sox6 WT contralateral kidney
Sox6 KO contralateral kidney
G
AfAr
*

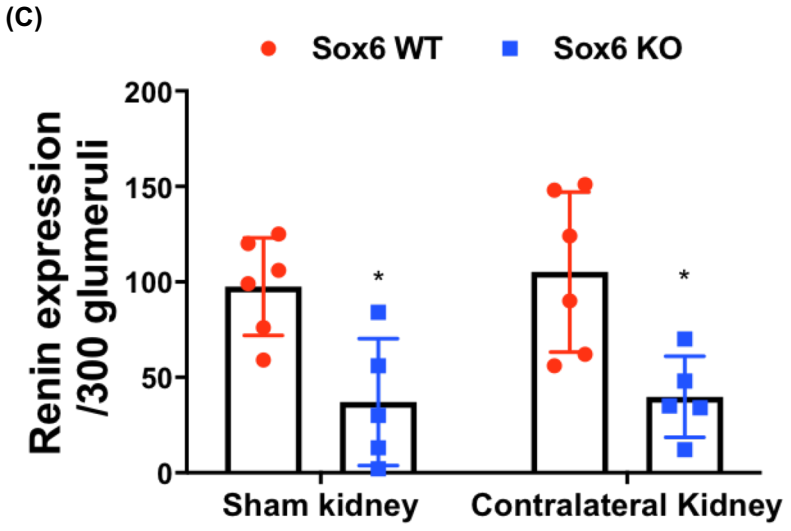


Figure S8. Knock out of Sox6 in renin expressing cells inhibits renin mRNA expression. Three days after surgery, kidneys were harvested, and in situ hybridization was performed. (**A**) Upper panel is showing mRNA expression of renin (green), Sox6 (magenta), and a-SMA (red) in sham kidney from Sox6 WT sham mice. Similarly, lower panel is showing the expression of renin (green), Sox6 (magenta), and a-SMA, (red) in sham kidneys from Sox6 KO sham mice. (**B**) Upper panel is showing mRNA expressions of renin (green), Sox6 (magenta), and a-SMA (red) in contralateral kidney from Sox6 WT sham mice. Likewise, lower panel is showing the expression of renin (green), Sox6 (magenta), and a-SMA (red) in contralateral kidneys from Sox6 KO sham mice. (**C**) Quantification of three hundred glomeruli per kidney expressing renin mRNA. Scale bar 10 μm, magnification 90X. G= glomerulus, AfAr= Afferent arteriole. Circle is depicting glomerulus location. Data are presented as the mean ± SD. P calculated with two-way ANOVA followed by Tukey post-hoc test. *P< 0.05. N=5-6.

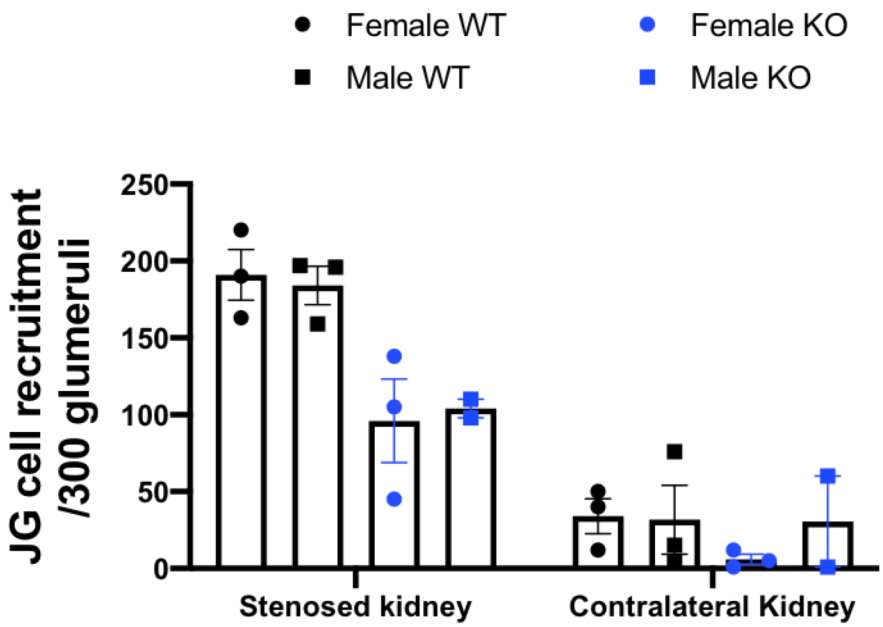


Figure S9. There are no significant differences in JG cell recruitment/expansion between males and females within each group in stenosed mice. Three days after the surgery, kidneys were harvested, fixed and *in situ* hybridization was performed. Quantification of three hundred glomeruli per sample expressing renin mRNA along the afferent arteriole from in situ hybridization experiment is shown in the bar graph. N= Female: Sox6 WT 3, Sox6 KO 3; Male: Sox6 WT 3, Sox6 KO 2. Data are presented as the mean ± SEM. P calculated with two-way ANOVA followed by Tukey post-hoc test. A p-value equal or less than 0.05 was considered significant.

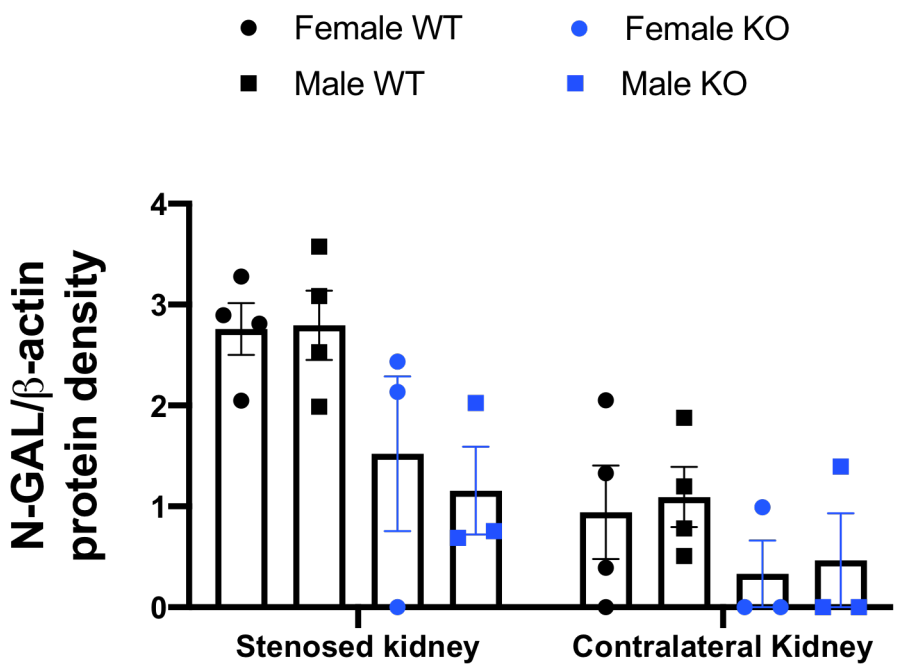


Figure S10. There are no significant differences in N-GAL expression between males and females within each group in stenosed mice. Three days after the surgery, kidneys were harvested, and Western blot was performed. Densitometric analysis of N-GAL protein bands are shown in the bar graph. N= Female: Sox6 WT 4, Sox6 KO 3; Male: Sox6 WT 3, Sox6 KO 3. Data are presented as the mean ± SEM. P calculated with two-way ANOVA followed by Tukey post-hoc test. A p-value equal or less than 0.05 was considered significant.

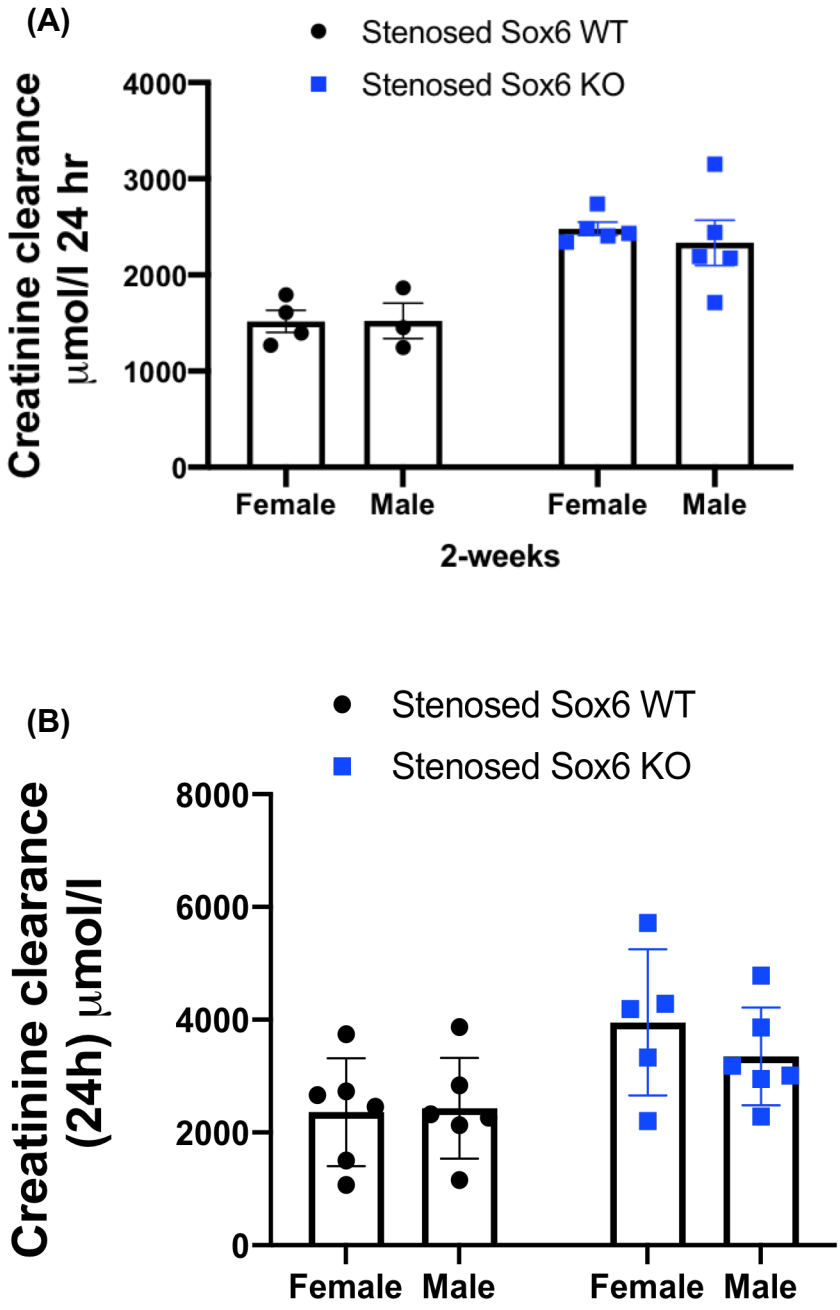


Figure S11. There are no significant differences in creatinine clearance between males and females within each group in stenosed mice. Creatinine was measured with a colorimetric kit following manufactures' instructions (**A**) Creatinine analysis from two-week study. N= Female: Sox6 WT 4, Sox6 KO 5; Male: Sox6 WT 3, Sox6 KO 5. (**B**) Creatinine analysis from three days study. N= Female: Sox6 WT 6, Sox6 KO 5; Male: Sox6 WT 6, Sox6 KO 6. Data are presented as the mean ± SEM. P calculated with two-way ANOVA followed by Tukey post-hoc test. A p-value equal or less than 0.05 was considered significant.

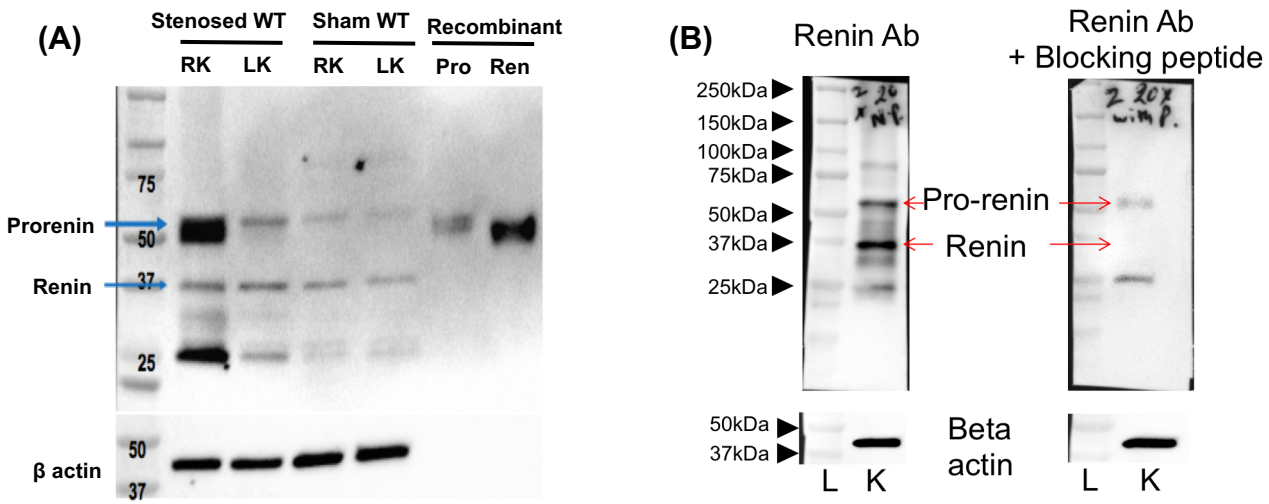


Figure S12. (A). Prorenin and renin Western blot analysis and molecular weight determination. Sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) was performed with protein samples from kidney tissue cortex from Sox6 WT mice (Stenosed mice, Lane 1 & 2; Sham mice, Lane 3 & 4), and commercially available recombinant prorenin (Anaspec Cat # AS-72174; Lane 5) and recombinant renin (R&D Systems Cat # 4277-AS; Lane 6). Following gel was transferred on to nitrocellulose membrane and incubated with renin antibody (Santa Cruz Biotechnology Cat # sc-137252). A protein molecular weight ladder (L) is provided. (**B). Prorenin and renin expression in kidneys.** Protein samples isolated from kidney tissue (K) were subjected to SDS-PAGE. Immunoblots were then incubated with the renin antibody (left panel) or renin antibody with renin blocking peptide in 5x excess (right panel). Bands were visualized with an HRP-conjugated secondary antibody. Molecular weight was determined by the indicated protein ladder (L).