CONTENTS:

3. 1. Supplemental_Table_S1

Mouse Primers used for QRTPCR:

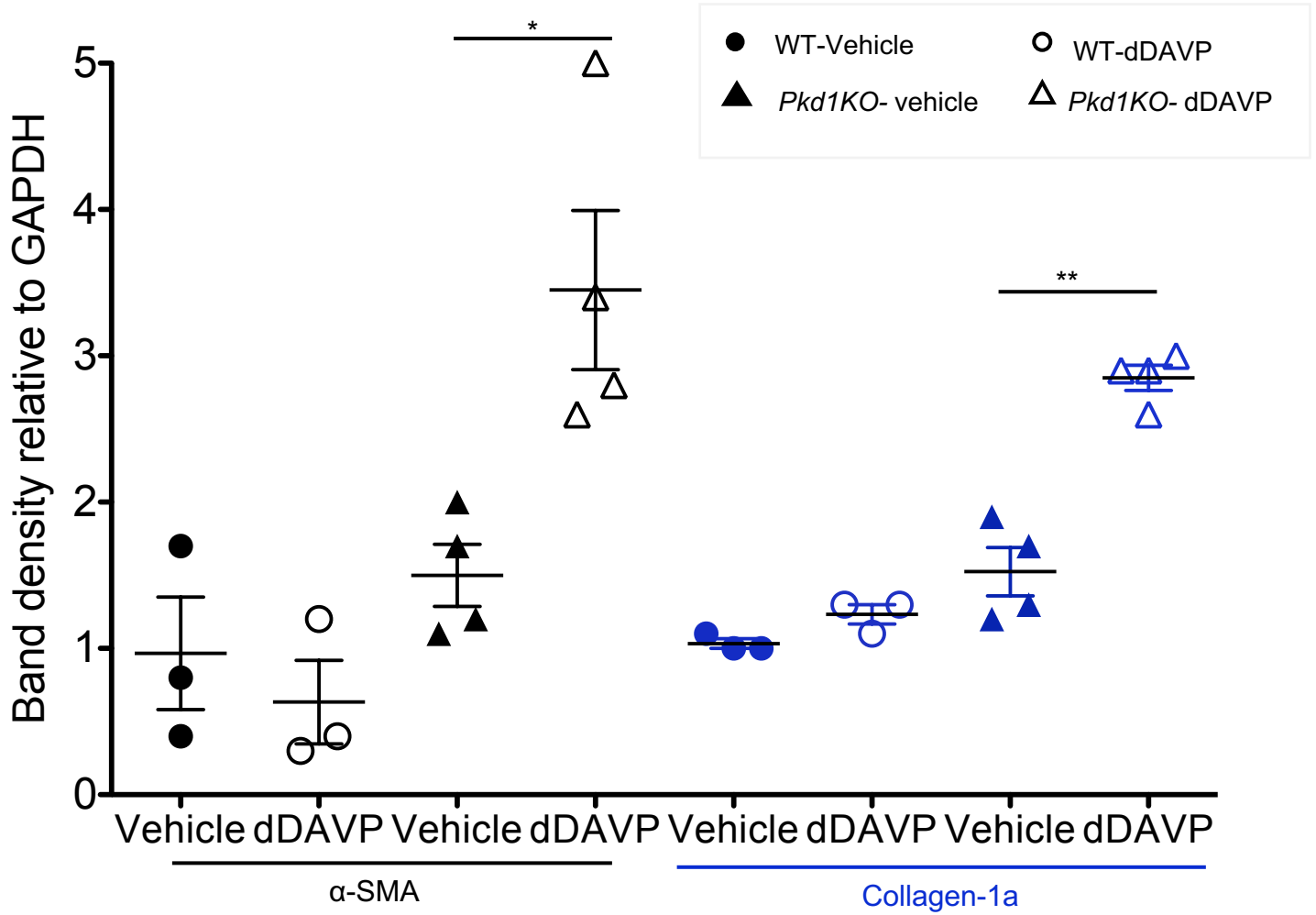
	Gene Name	Primers Forward (F) and Reverse (R)
1	Fibronectin	F ATGTGGACCCCTCCTGATAGT R GCCCAGTGATTTCAGCAAAGG
2	α-SMA	F TCAGGGAGTAATGGTTGGAATG R GGTGATGATGCCGTGTTCTA
3	Collagen-1a1	F AGACATGTTCAGCTTTGTGGAC R GCAGCTGACTTCAGGGATG
4	Collagen-IIIa1	F TCCCCTGGAATCTGTGAATC R TGAGTCGAATTGGGGAGAAT
5	CCN2	F GTGCCAGAACGCACACTG R CCCCGGTTACACTCCAAA
6	TSP1	F CGAGACCAGAGGACGAATTAT R CAGTGACCGGCTCCTTTATAC
7	TNF-α	F ACCCTCACACTCAGATCATCTTC R TGGTGGTTTGCTACGACGT
8	IL-1β	F TTGACGGACCCCAAAAGAT R GAAGCTGGATGCTCTCATCTG
9	IL-6	F CTTCCATCCAGTTGCCTTCT R CTCCGACTTGTGAAGTGGTATAG
10	IL- 10	F TTTGAATTCCCTGGGTGAGAA R ACAGGGGAGAAATCGATGACA
11	ICAM-1	F CTTCCAGCTACCATCCCAAA R CTTCAGAGGCAGGAAACAGG
12	CCL2	F CTCGGACTGTGATGCCTTAAT R TGGATCCACACCTTGCATTTA
13	CCL3	F GAAGATTCCACGCCAATTCATC R GATCTGCCGGTTTCTCTTAGTC
14	CCL11	F ACCCACTCTGCTCCCTATAA R CGTGAGCAGCAGGAATAGAA
15	CCL12	F GTTCCTGACTCCTCTAGCTTT R GCATCTGGTCCAGCCAATA
16	TGF-β1	F TGAGTGGCTGTCTTTTGACG R AGCCCTGTATTCCGTCTCCT
17	PAI-1	F GAGGTGGAAAGAGCCAGATTTA R CCACTGAAGTAGAGGGCATTC
18	AREG	F CAGAAGAATGGAAGAGTCAG R CAGATATGCAGGGAGTCACC
19	Osteopontin	F GACAACAACGGAAAGGGCAG R GATCGGCACTCTCCTGGCT
20	Periostin	F CAAAGCACACAGTTACCTTTCCAGGG R GCAGGAAACCCACATTGCATGAGA
21	FGF-1	F GTAGTTTCCTAGAGGCAGGTTG

		R TGATAAAGTGGAGTGAAGAGAGC
22	FGF-2	F GAAACACTCTTCTGTAACACACTT R GTCAAACTACAACTCCAAGCAG
23	HBEGF	F CGGGGAGTGCAGATACCTG R TTCTCCACTGGTAGAGTCAGC
24	ICAM-1	F CTTCCAGCTACCATCCCAAA R CTTCAGAGGCAGGAAACAGG
25	IFN-G	F GGCCATCAGCAACAACATAAGCGT R TGGGTTGTTGACCTCAAACTTGGC
26	GAPDH	F TGAAGCAGGCATCTGAGG R CGAAGGTGGAAGAGTGGGAG

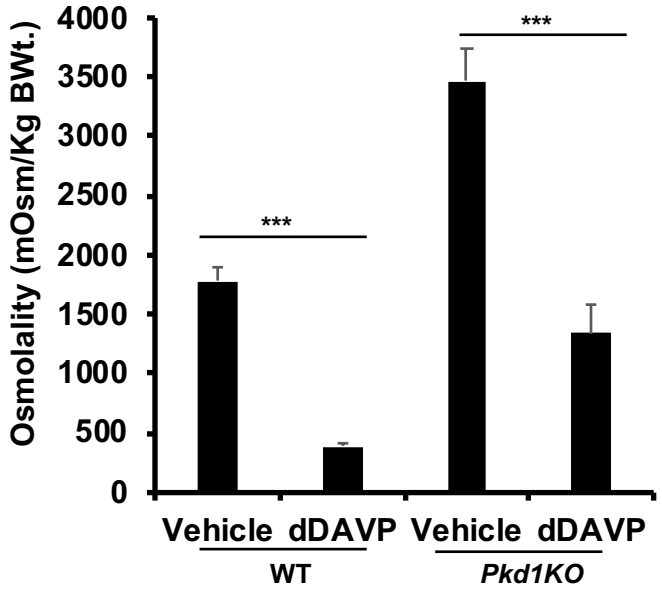
Human Primers used for QRTPCR:

	Gene Name	**Primers Forward (F) and Reverse (R)**
1	CTGF	F CGACTGGAAGACACGT TTGG R AGGCTTGGAGATTTTGGGAG
2	aSMA	F TCAGGGAGTAATGGTTGGAATG R GGTGATGATGCCGTGTTCTA
3	SPARC	F ATCTAAATCCACTCCTTCCACAG R CACCGTTAATGTATTCACTTAAATC
4	OPN	F TGAGAGCAATGAGCATTCCGATG R CAGGGAGTTTCCATGAAGCCAC
5	Fibronectin	F AAACCAATTCTTGGAGCAGG R CCATAAAGGGCAACCAAGAG
6	MMP1	F ACAGCCCAGTACTTATTCCCTTTG R GGGCTTGAAGCTGCTTACGA
7	PAI-1	F GGCCATTACTACGACATCCTG R GGTCATGTTGCCTTTCCAGT
8	AREG	F GTGGTGCTGTCGCTCTTGATA R ACTCACAGGGGAAATCTCACT
9	CYR61	F GAGTGGGTCTGTGACGAGGAT R GGTTGTATAGGATGCGAGGCT
10	Collagen 1A	F TGACGTGATCTGTGACGAGAC R GGTTTCTTGGTCGGTGGGT
11	Collagen 3A	F ATGGTTGCACGAAACACACT R CTTGATCAGGACCACCAATG
12	ICAM1	F CCTTCCTCACCGTGTACTGG R AGCGTAGGGTAAGGTTCTTGC
13	TSP1	F AACAACCCCACACCCCAGTTTG R TTGAAGCAGGCATCAGTCAC
14	TIMP1	F GACGGCCTTCTGCAATTCC R GTATAAGGTGGTCTGGTTGACTTCTG
15	TIMP2	F GAGCCTGAACCACAGGTACCA

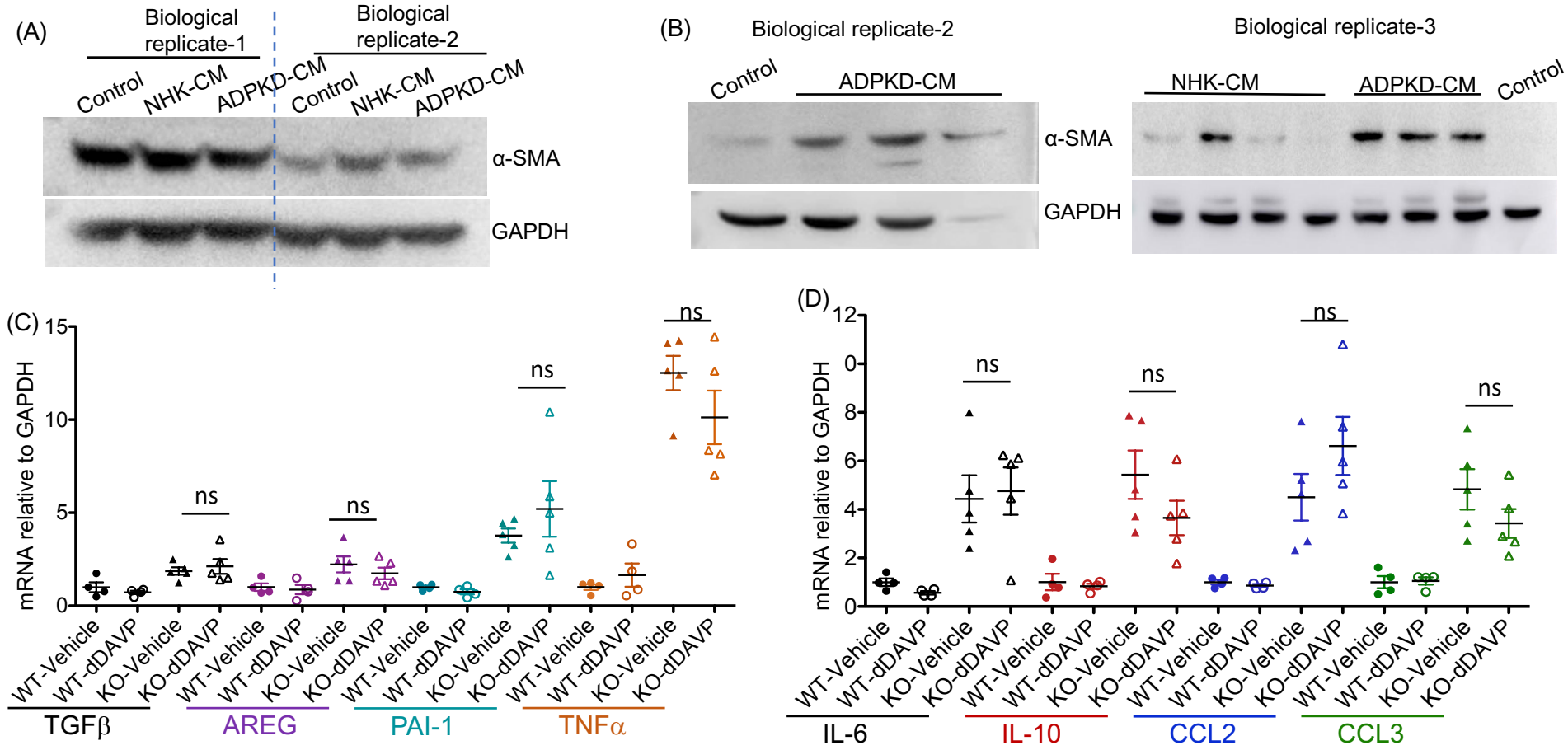
		R TCTGTGACCCAGTCCATCCA
16	TIMP4	F AATCTCCAGTGAGAAGGTAGTTCC R CGATGTCAACAAACTCCTTCCTGA
17	Adamts2	F CTGGCAAGCATTGTTTTAAAGGA R GGAGCCAAACGGACTCCAA
18	TGF-β	F GAGCCTGAGGCCGACTACTA R GGGTTCAGGTACCGCTTCTC
19	CSF-1	F CCAGGAACAGTTGAAAGATCCA R TTATCTCTGAAGCCATGGTGT
20	CSF-2	F CACTGCTGCTGAGATGAATGAAA R GTCTGTAGGCAGGTCGGCTC
21	PDGF-A	F CCCCTGCCCATTCGGAGGAAGAG R TTGGCCACCTTGACGCTGCGGTG
22	Cxcl10	F GTGGCATTCAAGGAGTACCTC R TGATGGCCTTCGATTCTGGATT
23	CCL2	F CCGAGAGGCTGAGACTAAC R CTTGCTGCTGGTGATTCTTC
24	CCL5	F CCTCGCTGTCATCCTCATTG R GGGTTGGCACACACTTGG
25	IL1b	F AAACAGATGAAGTGCTCCTTCCAGG R TGGAGAACACCACTTGTTGCTCCA
26	IL6	F AATTCGGTACATCCTCGACGG R GGTTGTTTTCTGCCAGTGCC
27	IL8	F GACCACACTGCGCCAACAC R CTTCTCCACAACCCTCTGCAC
28	TNFa	F CCGAGGCAGTCAGATCATCTT R AGCTGCCCCTCAGCTTGA
29	SEMA7A	F TGTGTATTCCCTCGGTGACA R GAGTGGAACAATGGCGTCTT
30	TFPI-2	F CCAGATGAAGCTACTTGTATG R GCACATGCACGTTTGCAATC
31	GAPDH	F CCAGGTGGTCTCCTCTGACT R TGCTGTAGCCAAATTCGTTG



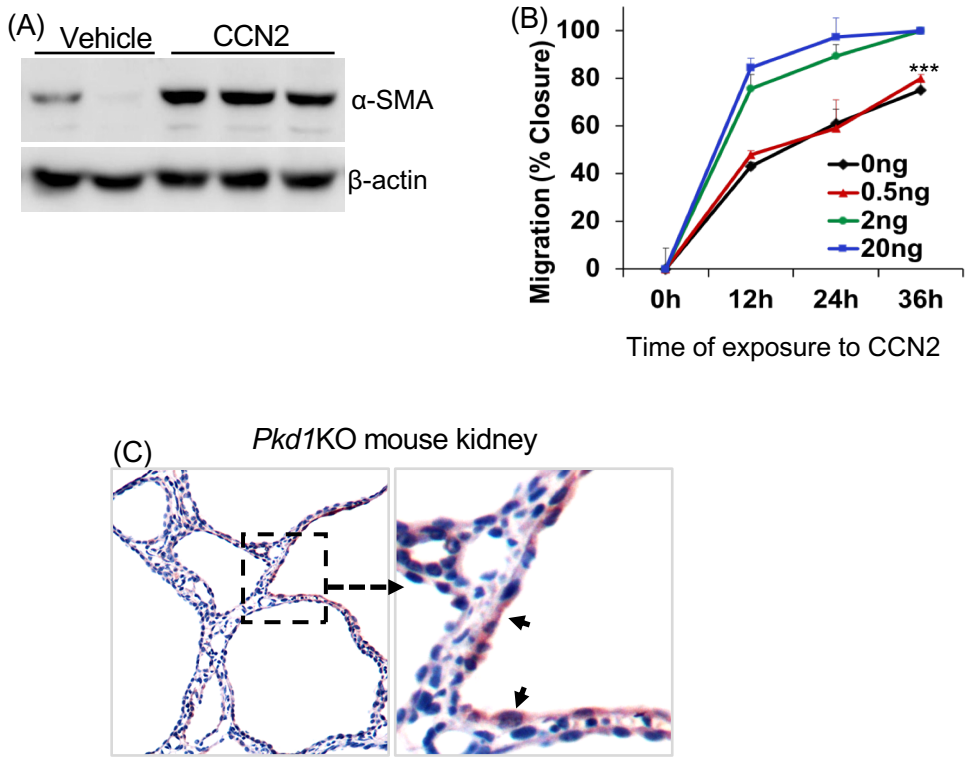
Supplemental-1: Quantitation of band density of α–SMA and Collagen-1a relative to GAPDH for mice treated with dDAVP: Treatment with dDAVP (1µg/Kg BWt /day on P18, P19 and P20 in both WT and *Pkd1KO* mice. Mice sacrificed on P21. n=3 for WT and n=4 for *Pkd1KO* mice. * P<0.05, ** P<0.01, vs vehicle by T-test.



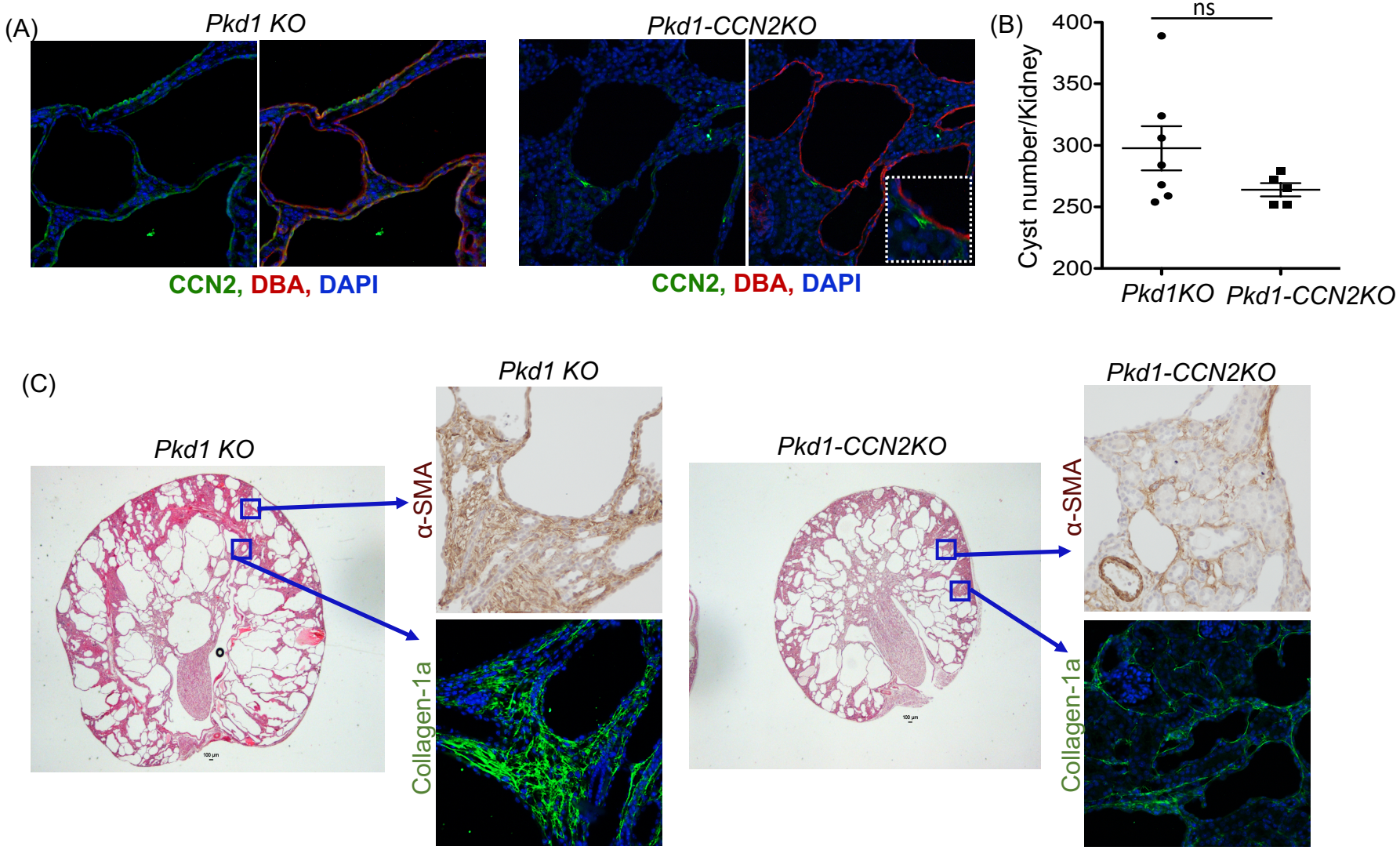
Supplemental-2: Urinary osmolality in mice treated with dDAVP: Treatment with dDAVP (1µg/Kg BWt /day on P18, P19 and P20) decreased urinary osmolality in both WT and *Pkd1KO* mice on P21. n=6 for WT and n=8 for *Pkd1KO* mice. ***P<0.001 vs vehicle by T-test.



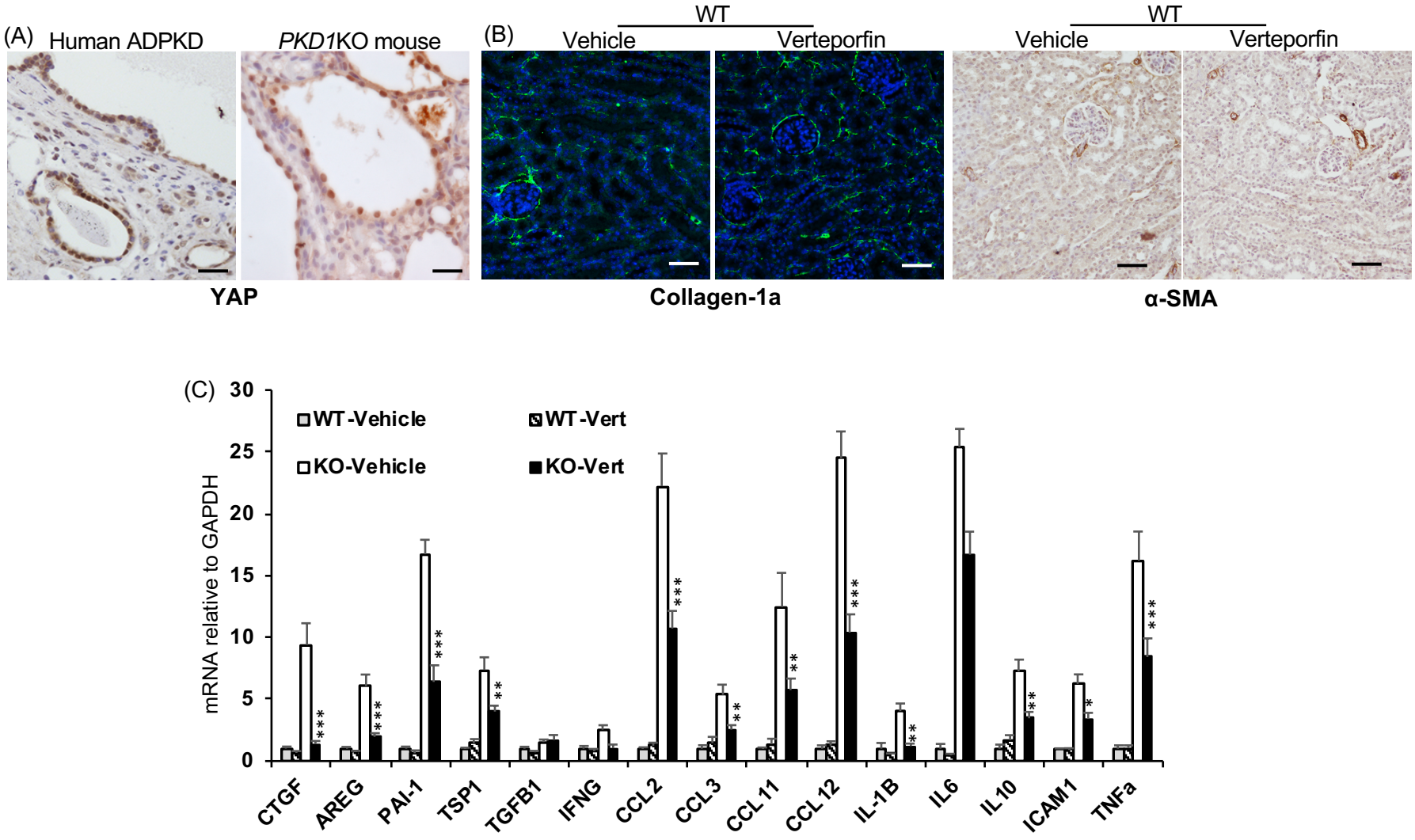
Supplemental-3: Effect of conditioned media from human primary culture NHK or ADPKD renal cystic epithelial cells on human or rodent renal fibroblasts, and mRNA expression of secreted factors from ADPKD mouse kidneys.
(A) Effect of conditioned media from human primary culture NHK or ADPKD renal epithelial cells on primary culture human ADPKD renal myofibroblasts isolated from 2 patients (biological replicates 1 & 2) with n=3 technical replicates each. Immunoblot for α-SMA of the ADPKD myofibroblasts is shown. (B) Immunoblot for α-SMA in NRK-49F rat renal fibroblasts incubated for 48h with CM from primary culture NHK or ADPKD epithelial cells n=3 biological replicates n=1-4 technical replicates each as shown. Biological replicate 1 is shown in Fig 2C. (C) and (D) mRNA levels of secreted factors from vehicle or dDAVP treated Pkd1KO mouse kidneys described in Fig 1C. ns by T-test.



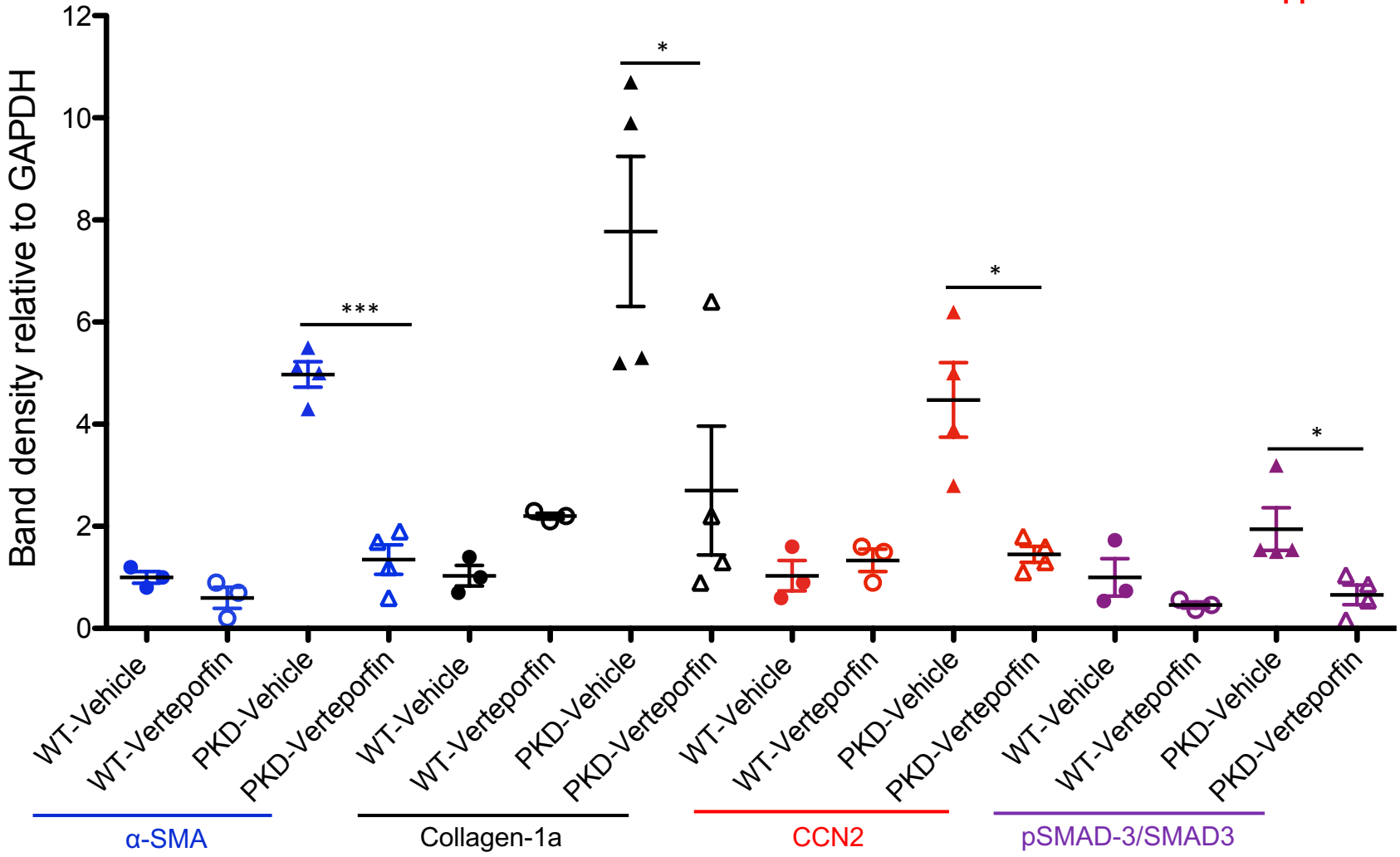
Supplemental 4. CCN2 induces myofibroblast activation and migration *in vitro*, (A) Immunoblot for α-SMA in NRK-49F rat renal fibroblasts incubated for 48h with recombinant CCN2 (2ng/ml). Experiment repeated 2 times. (B) Wound healing (% wound closure in a scratch assay adjusted to cell proliferation) of NRK-49F cells incubated with different doses of recombinant CCN2 (ng/ml). n=4. (C) Immunostaining for CCN2 in *Pkd1*KOmouse kidneys shows localization in cystic epithelium. ***P<0.001 vs 0ng/ml by one-way ANOVA followed by Dunnett's multiple comparison test.



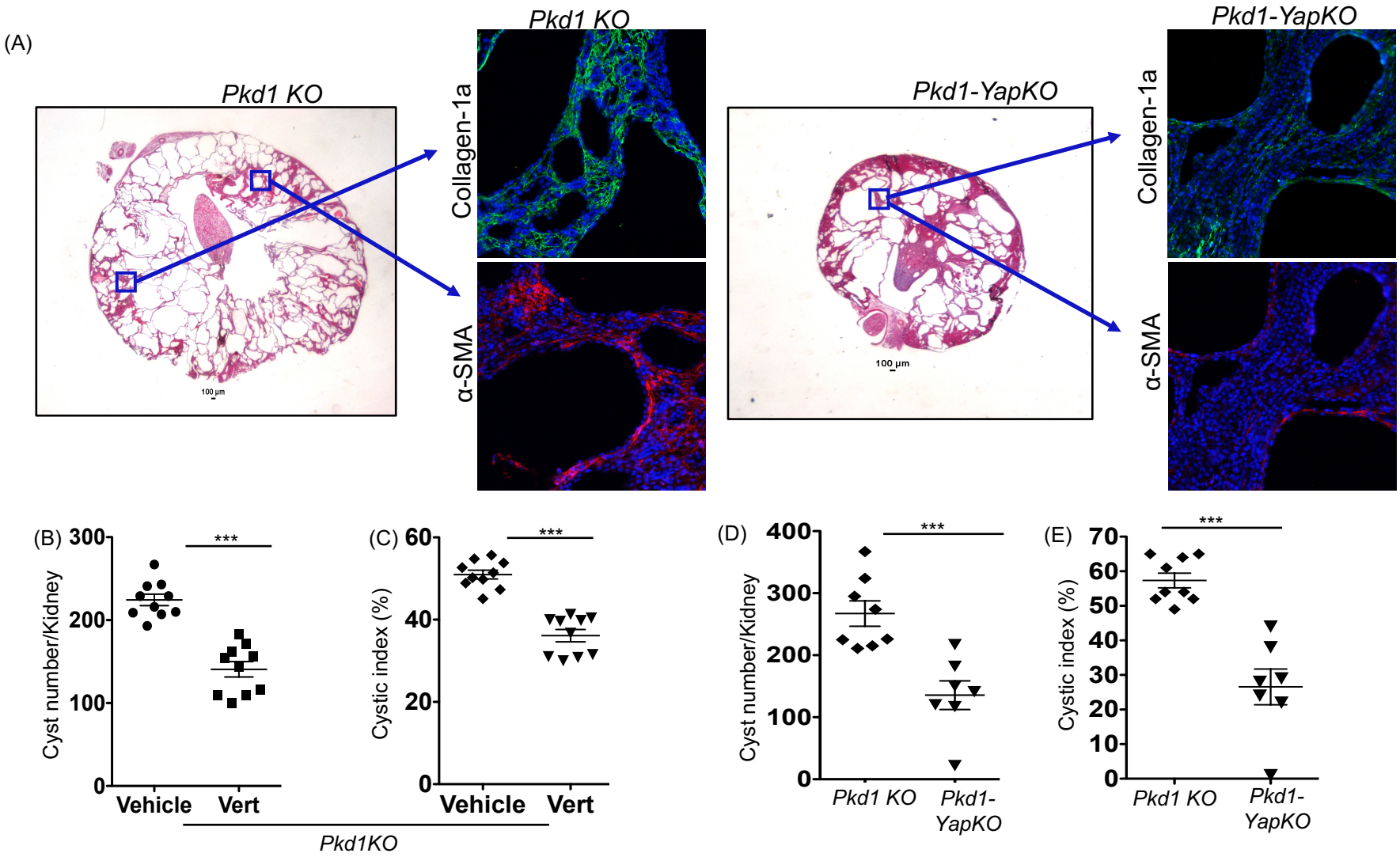
Supplemental 5. Immunostaining and cyst number in Pkd1KO and Pkd1KO-CCN2KO mouse kidneys.
(A) Immunostaining for CCN2 (green) and DBA (red) in *Pkd1*KO and *Pkd1*KO-CCN2KO mouse kidneys. (Inset- CCN2 staining in peri-cystic cells). (B) cystic number. ns by T-test. (C) Images showing the regions of the cystic kidneys from which the higher magnification immunolabeled images originated from.



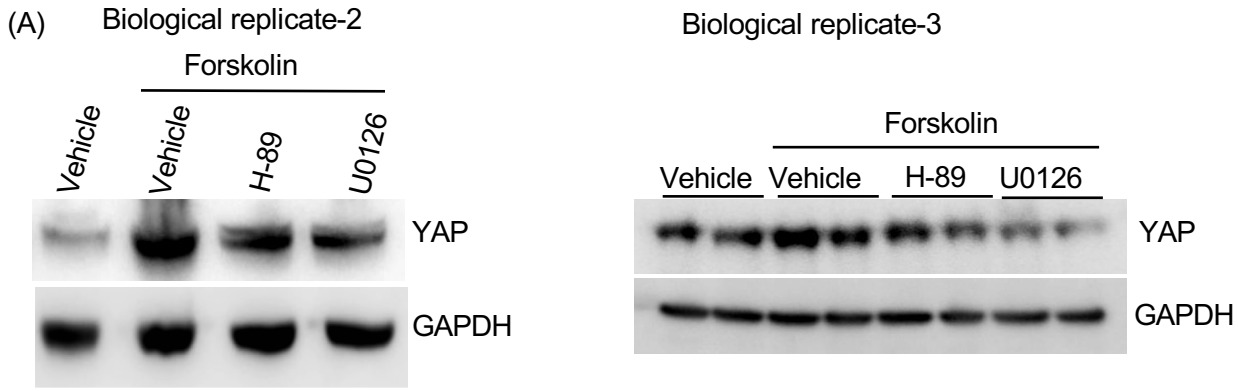
Supplemental-6: Immunostaining for YAP, collagen-1a and α-SMA, and mRNA levels. (A) Immunostaining for YAP (Brown) in human ADPKD tissue and *Pkd1KO* mice (B) Immunostaining for collagen-1a and α-SMA in vehicle or verteporfin treated WT mice and (C) renal mRNA levels of secreted factors from WT or *Pkd1KO* mice treated with vehicle or verteporfin (Vert) (75mg/Kg BWt., IP, on P10, P12, P14, P16) and sacrificed on P18. n=6 * P<0.05, ** P<0.01, ***P<0.001 vs KO vehicle by T-test.



Supplemental-7: Quantitation of band density from immunoblot of kidney lysate from WT or Pkd1KO mice treated with vehicle or verteporfin. WT or *Pkd1KO* mice were treated with vehicle or verteporfin (Vert) (75mg/Kg BWt., IP, on P10, P12, P14, P16) and sacrificed on P18. Quantitation of band density for α–SMA, Collagen-1a, CCN2 and pSMAD-3/SMAD3 levels relative to GAPDH. * P<0.05, ***P<0.001 vs KO vehicle by T-test.



Supplemental-8: Immunostaining, cyst number and cystic index of *Pkd1YAPKO* mice or *Pkd1KO* mice treated with verteporfin (Vert). (A) Images showing the regions of the cystic kidneys from which the higher magnification immunolabeled images originated from. (B) Cyst number and (C) cystic index of *Pkd1KO* mice treated with vehicle or verteporfin (Vert) (75mg/Kg BWt., IP, on P10, P12, P14, P16) and sacrificed on P18. (D) Cyst number and (E) cystic index Pkd1KO and $Yap^{f/f}Pkd1^{f/f}Pkhd1^{cre}$ (Pkd1-YapKO) mice sacrificed on P18. ***P<0.001 vs KO vehicle by T-test.



Supplemental-9: **YAP expression in primary culture human ADPKD cells treated with Forskolin, H-89 or UO126.** (A) Immunoblot for YAP in ADPKD cells treated with Forskolin (5μM) and vehicle, H-89 (5μM) or UO126 (20μM) for 16h. Biological replicates 2 and 3 are shown. Biological replicate 1 is shown in Fig 6D.