Supplemental figures

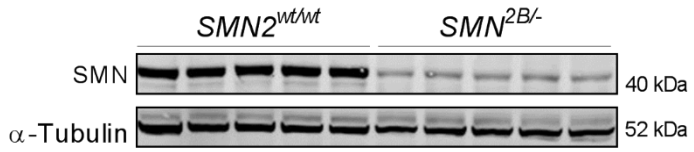


Figure S1. SMN protein content in kidney from *Smn$^{2B/-}$* mice. Representative immunoblot for SMN in kidney samples from *Smn$^{wt/wt}$* and *Smn$^{2B/-}$* mice (n = 5).

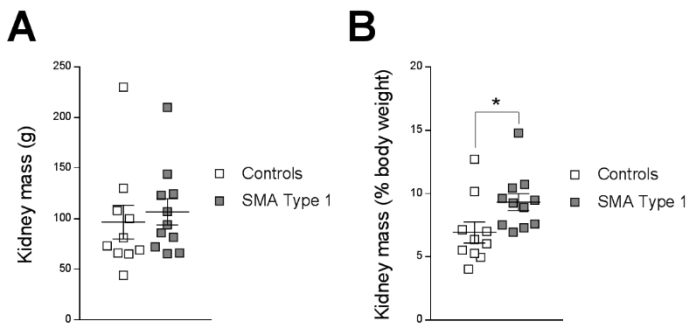


Figure S2. Kidney mass in SMA and control subjects. (**A**) Absolute and (**B**) relative kidney mass (n=10).

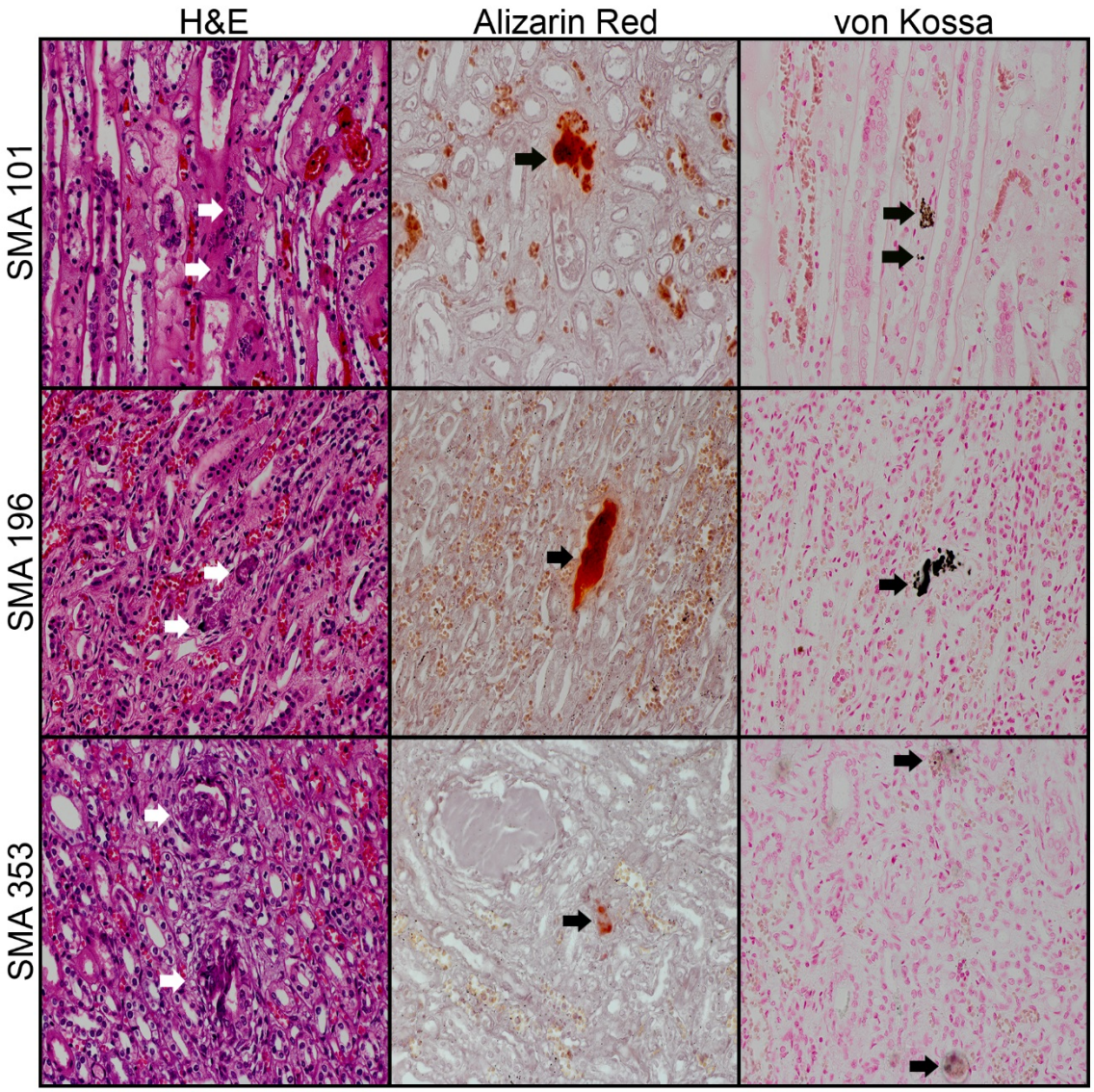


Figure S3. Kidney histopathology in SMA subjects. Additional representative images for Figure 2A and 2B. Images were taken with 400X magnifications.

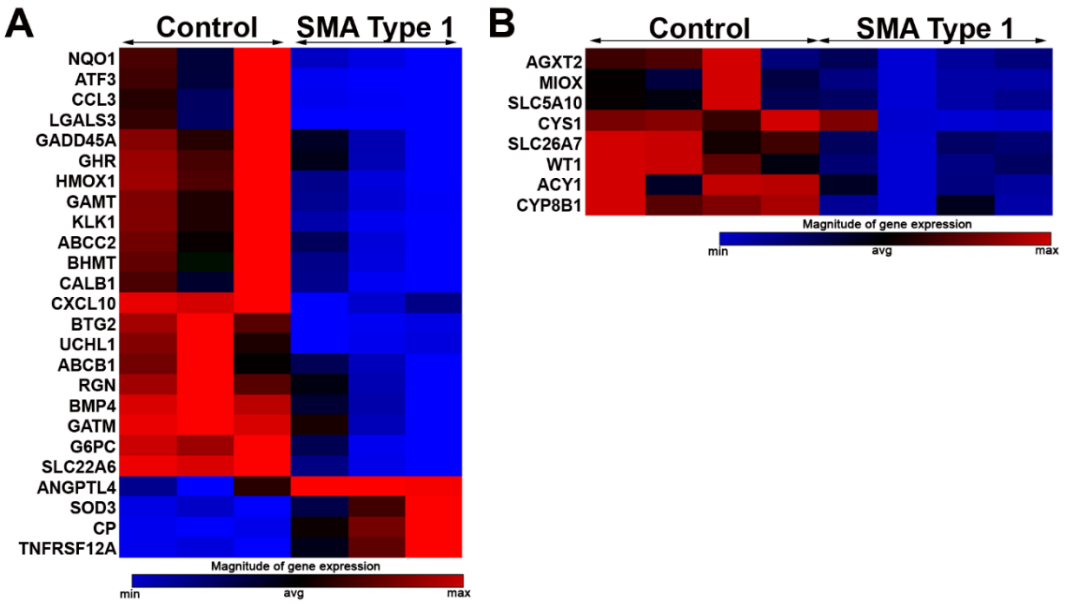


Figure S4. Genes significantly changed in kidney from SMN subjects compared to control subjects. (**A**) Genes significantly changed in the Nephrotoxicity RT^2 Profiler PCR Array (n = 3). (**B**) Genes significantly changed in the Polycystic Kidney Disease RT^2 Profiler PCR Array (n = 4).

Supplemental tables

Table S1. Serum biochemical profile in $SMN2^{wt/wt}$ and $SMN2^{B/-}$ mice.

	Creatinine (mg/dl)	BUN (mg/dl)	Albumin (g/dl)	Calcium (g/dl)	Phosphorus (mg/dl)	Sodium (mEq/L)	Chloride (mEq/L)	Potassium (mEq/L)
WT	0.12 ± 0.01	13.30 ± 0.62	2.6 ± 0.02	10.77 ± 0.10	9.65 ± 0.30	138.25 ± 2.59	103.78 ± 2.00	7.51 ± 0.14
$Smn^{2B/-}$	0.03 ± 0.01	11.5 ± 0.50	2.28 ± 0.04	9.37 ± 0.11	9.71 ± 0.26	137.42 ± 0.62	90.89 ± 1.35	7.27 ± 0.14
p value	**< 0.0001**	**< 0.05**	**< 0.0001**	**< 0.0001**	n.s	n.s	**< 0.0001**	n.s.

Table S2. Demographic, clinical, and autopsy characteristics of SMA subjects.

Pt #	Age of onset (mo)	Age at Death (yr)	Sex	*SMN1*	*SMN 2*	Cause of Death	PMI (h)	Body weight (kg)	Combined Kidney weight (g)	Expected combined Kidney weight (g)	Kidney weight/ body weight ratio	Ethnicity
101	2	10.2	M	0	2	Respiratory failure, pneumonia, shock	3	21.4	198	187	9.25	Caucasian
187	Birth	5.1	F	0	2	Elective withdrawal of ventilation/Acute bronchopneumonia	38	13.8	144	129	10.43	Caucasian
7†	Birth	4	F	0	2	Elective withdrawal of ventilation	18	14	N.i.	N.i.	N.i.	Caucasian
196	1	3.8	F	0	2	Acute respiratory arrest	12	12.5	94	93	7.52	Caucasian
195	1	2.96	M	0	2	Elective withdrawal of ventilation during acute respiratory illness	10	14	124.5	97	8.89	Caucasian
217	0.5	2.75	M	0	2	Pneumonia with respiratory failure	3	14.2	210	93	14.79	Caucasian
206	1	2.34	M	0	2	Elective withdrawal of ventilation during acute respiratory illness	3	12.8	123	93	9.61	Caucasian
403	1	2.3	M	0	1	Cardiorespiratory arrest	20	14.1	107	82	7.59	African American
353	Birth	1.65	F	0	2	Respiratory failure	10	7.6	72	N.i.	9.47	Caucasian
177	1	1.38	M	0	2	Acute respiratory arrest	10	9.4	65.3	N.i.	6.95	Caucasian
251	0.8	1.2	M	0	2	Elective withdrawal of ventilation during acute respiratory illness	7	11.8	86	78	7.29	Caucasian
351	1	0.56	M	0	2	Respiratory arrest during sleep	12	7.6	81.5	51	10.72	Caucasian
272	1	0.34	M	0	2	Elective withdrawal of ventilation	1	4.7	N.i.	N.i.	N.i.	Caucasian

† we did not examine the kidney from this subject. PMI: post-mortem interval. Kg: kilograms. M: male. F: female. N.i.: not informed.

Table S3. Demographic, clinical, and autopsy characteristics of the age- and sex-matched control subjects.

Pt #	Age at Death (yr)	Sex	*SMN1*	*SMN2*	Cause of Death	PMI (h)	Body weight (kg)	Combined Kidney weight (g)	Kidney weight/ body weight ratio	Ethnicity
5334	12	M	2	1	Drowning	16	61.3	270	4.40	Caucasian
1499	4	F	2	2	Lymphocytic Myocarditis	21	18.1	230	12.71	Asian
4379	3	M	3	2	Drowning	15	N.i.	N.i.	N.i.	Caucasian
4394	3.22	M	2	1	Fever, Undetermined	12	16.3	81	4.97	Caucasian
5564	2	M	3	0	Airway obstruction of food bolus	13	20.4	130	6.37	African American
5871	2	M	2	2	Drowning	9	18.1	100	5.52	Caucasian
5282	1.83	M	2	2	Asphyxia, chocking on food bolus (hot dog)	16	18.1	73	4.03	Hispanic
1798	1.75	F	2	1	Intussusception of the small bowel	24	12.3	108	8.78	African American
1453	1.17	F	2	2	Choking/Asthma	19	N.i.	N.i.	N.i.	African American
5891	1.08	M	2	1	Sudden Unexplained Death in Infancy	24	13.1	69	5.27	Caucasian
4360	0.56	M	1	2	Asphyxiation	33	7.3	44	6.03	African American
4376	0.5	M	2	2	Probable asphyxiation	25	9.1	65	7.14	Caucasian
5883	0.31	M	4	0	Sudden Unexplained Death in Infancy	34	6.5	66	10.15	African American

PMI: post-mortem interval. Kg: kilograms. M: male. F: female. N.i., not informed.

Table S4. Estimated glomerular filtration rate for SMA type I patients.

Patient ID	Age (yr)	Sex	$eGFR_{Cre}$	$eGFR_{CysC}$	$eGFR_{Cre/CysC}$
			Normal range: 80-120		
351	0.2	M	65	73.3	60
251	0.38	M	117.08	84.08	94.27
195	0.76	M	254.68	153.76	182.85
217	0.82	M	188.28	112.69	136.06
187	0.92	F	175.53	105.57	119.31
196	1.7	F	198.47	103.93	127.38
187	1.74	F	225	126	149
195	2.09	M	303.4	174.1	207.92
196	2.35	F	213	119.1	138
Mean	1.22		193.38	116.95	134.98

$eGFR_{Cre}$, Creatinine (Cre)-based estimated glomerular function (eGFR); $eGFR_{CysC}$, Cystatin (CysC)–based eGFR; $eGFR_{Cre/CysC}$, CysC with Cre-based eGFR; M, male; F, female

Table S5. Pathologic findings in age- and sex-matched controls.

				Interstitium			Interstitium					
Pt #	**Autopsy report**	**Glomerular changes**	**Tubular changes**	**Calci.**	**Infl.**	**Fibr.**	**Calci.**	**Fibr.**	**AR**	**VK**	**PB**	**CD3/CD68**
5387	No reported abnormalities	None	Mild	None	None	None	None	None	Neg	Neg	Neg	Neg
1499	The kidneys may be somewhat congested, but otherwise appear normal	<1% global sclerosis	None	None	None	None	None	None	Neg	Neg	Neg	N.t.
4379	No reported abnormalities	None	Mild	None	None	None	None	None	Neg	Neg	N.t.	Neg
4394	No reported abnormalities	None	None	None	None	None	Intratubular, rare <1%	None	Neg	Neg	Neg	Neg
5564	The cortices were slightly congested, but otherwise appear normal	None	None	None	None	None	None	None	Neg	Neg	Neg	Neg
5871	The kidneys may be somewhat congested, but otherwise appear normal	None	None	None	None	None	None	None	Neg	Neg	N.t.	N.t.
5282	No reported abnormalities	None	None	None	None	None	Intratubular, rare <1%	None	Pos (intratubular)	Pos (intratubular)	Neg	na
1798	The cortices were slightly congested, but otherwise appear normal	None	None	None	None	None	None	None	Neg	Neg	N.t.	N.t.
1453	No reported abnormalities	<5% global sclerosis	None	None	None	<5%	None	None	Neg	Neg	Neg	Neg
5891	No reported abnormalities	None	None	None	None	None	None	None	Neg	Neg	N.t.	N.t.
4360	No reported abnormalities	None	None	None	None	None	None	None	Neg	Neg	N.t.	N.t.
4376	The medulla was congested, but otherwise appear normal	None	None	None	None	None	None	None	Neg	Neg	Neg	Neg
5883	Rare sclerotic glomeruli with foci of interstitial inflammation	Mild	None	None	None	None	None	None	Neg	Neg	Neg	N.t.

Calci., calcification; Infl., inflammation; Fibr., fibrosis; AR, Alizarin red; VK, von Kossa; PB, Prussian blue; Pos, positive; Neg, negative; N.t., not tested.

Table S6. Genes from Nephrotoxicity PCR Array.

Symbol	Function	log2(FC)	p-value
G6PD	Oxidative Stress, Cytoskeleton Regulators	-0.89	0.00015
CXCL10	Cell Proliferation	-1.84	0.00030
SLC22A6	Transporters	-4.32	0.00034
BTG2	Apoptosis, Cell Proliferation	-2.64	0.00114
SLC22A5	Transporters	-0.86	0.00179
CST3	Tissue Remodeling, Extracellular Matrix (ECM) Molecules	-0.71	0.00200
G6PC	Glucose Metabolism	-5.06	0.00307
CCS	Metal Ion Binding	-0.94	0.00321
BMP4	Apoptosis, Cell Cycle, Cell Proliferation, Extracellular Matrix (ECM) Molecules	-1.32	0.00371
HMOX1	Apoptosis, Metal Ion Binding, Oxidative Stress, Cell Proliferation	-2.74	0.00392
UCHL1	Cell Proliferation	-1.00	0.00473
CP	Metal Ion Binding	2.73	0.00610
KLK1	Cell Adhesion/ECM Remodeling, Fibrin Clotting Cascade	-4.64	0.00649
IDH1	Metal Ion Binding, Oxidative Stress	-0.60	0.00692
GAMT	Metabolism, Arginine and Proline Metabolism	-2.18	0.00921
GATM	Oxidative Stress	-2.32	0.01123
ANGPTL4	Apoptosis, Extracellular Matrix (ECM) Molecules	1.27	0.01272
TNFRSF12A	Apoptosis	2.20	0.01293
GHR	Apoptosis	-1.60	0.02015
RGN	Metal Ion Binding	-1.84	0.02073
BHMT	Metal Ion Binding	-2.94	0.02076
ATF3	Cell Proliferation	-3.84	0.02122
ABCC2	Transporters	-2.94	0.02302
NQO1	Apoptosis, Oxidative Stress	-1.64	0.02603
CCND1	Cell Cycle, Cell Proliferation	-0.86	0.02657
ABCB1	Transporters	-1.32	0.02722
MCM6	Cell Cycle	-0.51	0.02753
GADD45A	Apoptosis, Cell Cycle	-1.36	0.02948
CALB1	Calcium-binding Protein Superfamily	-5.06	0.03014

FN1	Tissue Remodeling	0.89	0.03168
SOD3	Metal Ion Binding, Oxidative Stress, Extracellular Matrix (ECM) Molecules	1.46	0.03191
GSTK1	Xenobiotic Metabolism	-0.71	0.03229
LGALS3	Extracellular Matrix (ECM) Molecules	-1.22	0.03521
CCL3	Extracellular Matrix (ECM) Molecules, Cytoskeleton Regulators	-2.56	0.03714
VIM	Cytoskeleton Regulators	-0.67	0.04854
ALDH1A1	Drug Metabolism	-0.94	0.05440
CYP2D6	Xenobiotic Metabolism	-1.94	0.05999
RTN4	Apoptosis	-0.54	0.06444
OAT	Arginine and Proline Metabolism	-0.67	0.06471
HSP90AA1	Cell Proliferation	-2.06	0.06738
VCAM1	Cell Proliferation	-1.47	0.08603
SCD	Metal Ion Binding	-0.74	0.08881
NPHS2	Primary Focal Segmental Glomerulosclerosis	-5.06	0.08920
SOD2	Oxidative Stress, Apoptosis, Metal Ion Binding, Cell Proliferation	0.73	0.09226
GSTP1	Apoptosis, Xenobiotic Metabolism	1.34	0.09496
ANXA5	Apoptosis	0.44	0.09614
NOX4	Cell Proliferation	-1.29	0.09658
CYP2C19	Xenobiotic Metabolism	-0.64	0.10119
CTSS	Metal Ion Binding	0.99	0.13467
FMO2	Xenobiotic Metabolism	-0.71	0.15875
CXCL1	Cell Proliferation	0.26	0.18447
IPMK	Metabolism	-0.56	0.21316
TIMP1	Cell Proliferation, Tissue Remodeling, Extracellular Matrix (ECM) Molecules	2.17	0.21952
GPX2	Oxidative Stress	-0.36	0.22739
HAVCR1	Tissue Remodeling	-0.84	0.23408
FGB	Extracellular Matrix (ECM) Molecules	-0.81	0.24768
CAT	Apoptosis, Oxidative Stress	-0.15	0.25446
SPP1	Tissue Remodeling	1.20	0.25856
HMOX2	Metal Ion Binding, Oxidative Stress	-0.67	0.26093
CD44	Apoptosis, Extracellular Matrix (ECM) Molecules	-0.67	0.26329
CLU	Apoptosis, Oxidative Stress, Cell Proliferation	1.10	0.27944
LCN2	Glucose Transport	6.25	0.28989

IGFBP1	IGF Pathway	-1.69	0.30959
SLC22A1	Transporters	-0.84	0.31900
MGP	Extracellular Matrix (ECM) Molecules	0.96	0.33490
A2M	IL6-mediated Signaling	0.33	0.33917
GPX8	Oxidative Stress	0.59	0.34058
SPRR1A	Cytoskeleton Regulators	0.90	0.34464
MT1A	Metal Ion Binding	0.73	0.35883
IGFBP3	Apoptosis, Cell Proliferation	0.37	0.37300
SOCS3	Apoptosis	0.42	0.41691
EGF	Cell Cycle, Cell Proliferation	-1.47	0.44085
TMSB10	Cytoskeleton Regulators	0.21	0.46055
GLUL	Cell Proliferation	-0.18	0.52170
BMP1	Metal Ion Binding	-0.42	0.54168
CD24	Apoptosis, Cell Proliferation	0.32	0.59384
GC	Metabolism	-2.06	0.60641
GPNMB	Cell Proliferation	-0.81	0.62816
AASS	Metabolism	-0.97	0.64162
CYR61	Extracellular Matrix (ECM) Molecules	-0.42	0.66145
CCNG1	Cell Cycle	-0.09	0.92242
ODC1	Cell Proliferation	-0.20	0.94706
UGT1A1	Drug Metabolism	-0.10	0.95288
CDKN1A	Apoptosis, Cell Cycle, Cell Proliferation	0.11	0.97125

Table S7. Genes from Polycystic Kidney Disease PCR Array.

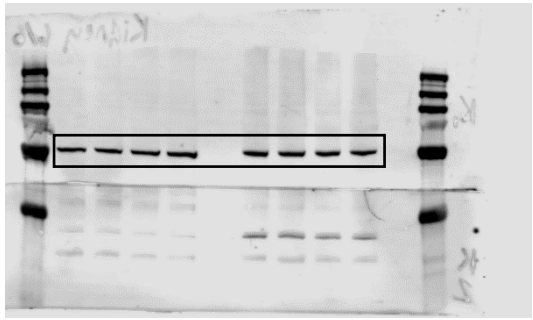
Symbol	Function	log2(FC)	p-value
CYP8B1	Angiogenic Growth Factors, Immune and Inflammatory Responses	-1.64	0.00136
WT1	Transcription Factors	-2.47	0.00496
SLC26A7	Calcium Signaling	-1.89	0.00616
ACY1	cAMP Signaling	-2.47	0.00755
MIOX	Inositol Phosphate Pathway, Iron Ion Binding, Oxidoreductase Activity Calcium Signaling	-3.47	0.02226
SLC5A10	Calcium Signaling	-2.56	0.02979
CYS1	Immune and Inflammatory Responses	-1.09	0.03244
AGXT2	Metabolism	-3.18	0.03962
FGF1	Intergrin Signaling	-3.64	0.05368
HSD11B2	Metabolism, Steroid Hormone Biosynthesis	-2.00	0.05913
VEGFA	Angiogenic Growth Factors	-1.22	0.06004
DPEP1	Primary Cilia	-3.32	0.06750
FGFR3	Growth Factors and Receptors	-2.40	0.07428
PRLR	Immune and Inflammatory Responses	-1.79	0.07839
PIK3R1	mTOR Signaling	-1.09	0.10269
PKHD1	Primary Cilia	-1.40	0.11351
KNG1	Immune and Inflammatory Responses	-1.56	0.11559
JUN	Transcription Factors	-1.56	0.11632
BMP4	BMP / TGFβ / Activin Signaling	-1.60	0.11798
IGF1R	Primary Cilia	-1.18	0.12443
P2RX7	cAMP Signaling	-2.32	0.13653
FOSB	Intergrin Signaling	-3.06	0.13656
BMP7	BMP / TGFβ / Activin Signaling	-2.84	0.13706
APOM	Nephron Segment Differentiation	-1.84	0.16365
ITGA8	Intergrin Signaling	-0.92	0.16451
CLCNKA	Ion Channel Activity	-1.43	0.17178
ALDH8A1	Oxidoreductase Activity	-1.60	0.17243
LGALS3	Primary Cilia	-0.71	0.17383
PKD1	Calcium Signaling	-2.56	0.17787
NAPSA	Protein Metabolism	-1.60	0.17910

BMP2	BMP / TGFβ / Activin Signaling	-2.32	0.18716
CREBBP	cAMP Signaling	-1.15	0.19305
HRG	Response to Elevated Platelet Ca2+	-1.60	0.20442
PTGER2	cAMP Signaling	0.44	0.21002
BCL2L1	Apoptosis	-1.36	0.21939
GREM1	Primary Cilia, Transcription Factors	2.07	0.23150
NOG	BMP / TGFβ / Activin Signaling	-1.74	0.23752
PTGER3	cAMP Signaling	-1.74	0.23775
NRG1	Immune and Inflammatory Responses	-1.15	0.24669
ADCY7	cAMP Signaling	-1.79	0.24688
APOE	Nephron Segment Differentiation	-1.69	0.24868
NRP2	Angiogenic Growth Factors	-2.12	0.24920
IL17D	Growth Factors and Receptors	-1.36	0.26304
FBLN1	Growth Factors and Receptors	1.80	0.31507
EDN1	IL-1 Family Signaling	-0.84	0.31579
IL6	Immune and Inflammatory Responses	1.99	0.32653
EGR3	Angiogenic Growth Factors	-1.51	0.33153
CFD	Immune and Inflammatory Responses	-1.51	0.33259
NTRK3	Growth Factors and Receptors	-1.60	0.33406
ADCY3	cAMP Signaling	-0.97	0.33573
OSR2	Nucleic Acid Binding	1.39	0.33701
DAPL1	Primary Cilia	-1.12	0.34108
PRKCB	Immune Response	-1.06	0.34677
TPM1	Angiogenic Growth Factors	-1.06	0.35455
WNT11	BMP / TGFβ / Activin Signaling	-0.94	0.35734
SPRY1	Intergrin Signaling	-1.18	0.37066
PCDH7	Intergrin Signaling	-0.76	0.37995
PTGS2	cAMP Signaling	0.33	0.38252
GLI2	Transcription Factors	-0.89	0.38851
CLU	Intergrin Signaling	0.51	0.40166
CXCL1	Immune and Inflammatory Responses	0.44	0.40403
ANGPT2	Nephron Segment Differentiation	-0.58	0.42711
RET	Calcium Ion Binding	-0.71	0.42920

PTPRZ1	Immune and Inflammatory Responses	-0.94	0.45537
SLC2A9	Calcium Signaling	-0.58	0.45808
ADCY2	cAMP Signaling	-0.58	0.46357
PCK1	Immune and Inflammatory Responses	-1.56	0.50267
PKD2	Calcium Signaling	-0.38	0.50818
VGLL3	Transcription Coactivator Activity	0.60	0.52351
IFT88	Organelle Biogenesis and Maintenance	0.23	0.54091
SCN5A	Development	0.79	0.61078
TMEM27	Primary Cilia	-0.30	0.64034
CLDN10	Intergrin Signaling	-0.12	0.68591
HGD	BMP / TGFβ / Activin Signaling	-0.56	0.70645
COL12A1	Intergrin Signaling	-0.34	0.71875
CXCL8	Immune and Inflammatory Responses	0.14	0.73701
UMOD	Primary Cilia	-1.15	0.75870
FN1	Growth Factors and Receptors	0.00	0.77004
COL3A1	Intergrin Signaling	0.70	0.81508
RHOA	Intergrin Signaling	-0.03	0.84946
TGFB3	Growth Factors and Receptors	0.43	0.87275
PIK3CA	mTOR Signaling	0.01	0.89624
DNAH5	Apoptosis	0.11	0.91727
PDGFRA	Primary Cilia	0.32	0.96799

Uncropped Blots

α-tubulin



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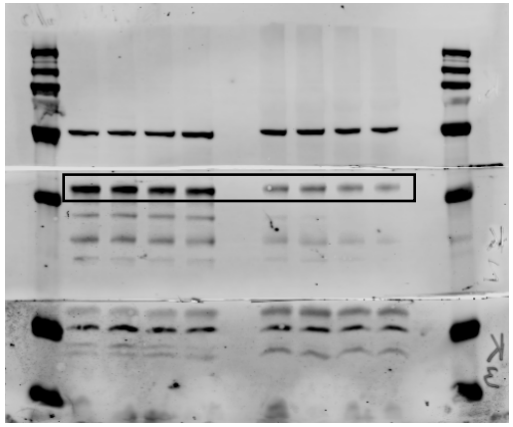
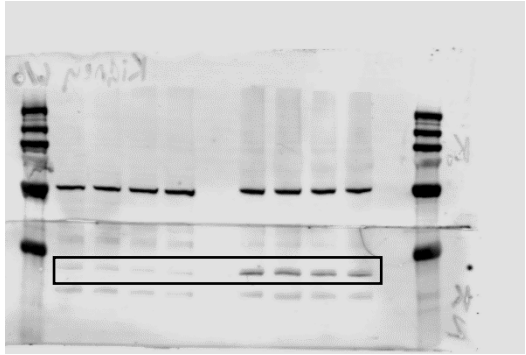
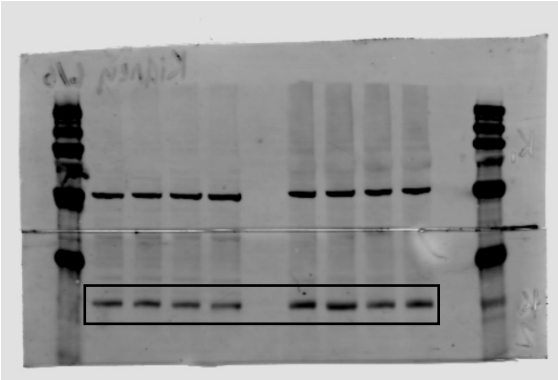


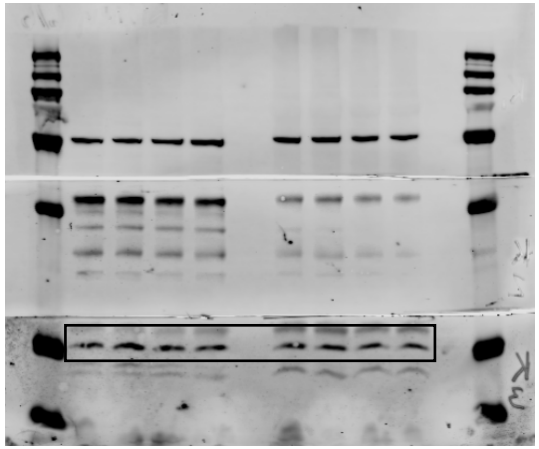
IGFBP1



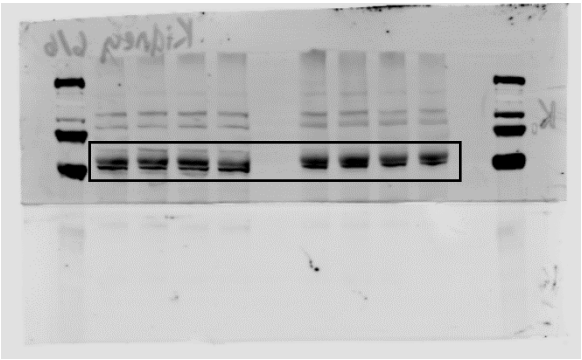
IGFBP3



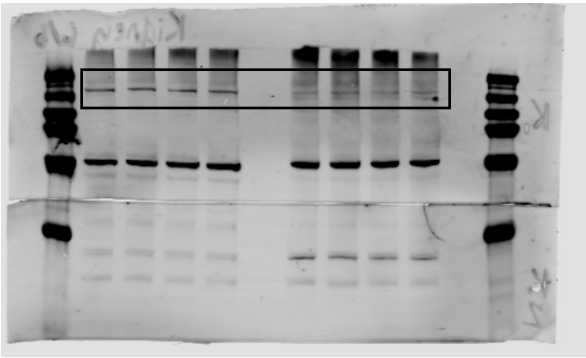
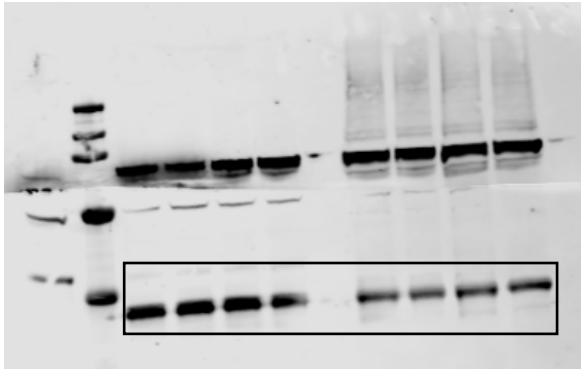
IGF1



IGFALS



CaSR



CALB1 – different membrane