

Supplementary Information

Supplementary Table 1. Patient demographics

Characteristic s	T1a RCC non-tumoral adjacent tissues (n=6)	Nephrocalcinosis-related CKD (n=6)
Age, year	64.17±7.27	59.00±11.87
Man/Woman	4/2	2/4
Affected side left/right	3/3	4/2
Cr, mol/L	63.17±6.28	81.83±19.33
GFR, ml/min (Affected side)	50.38±8.78	5.82±3.17

RCC, Renal Cell Carcinoma; CKD, chronic kidney diseases; Cr, serum creation; GFR, agglomerate filtration rate.

Supplementary Table 2. Macrophage-to-myofibroblast transition regulators

Name	Gene ID	Description	Location (GRCm39)	Aliases
				0610041G09R
<i>Acta2</i>	11475	actin alpha 2, smooth muscle, aorta	Chromosome 19, NC_000085.7 (34217736..34232985, complement)	ik, Actvs, SMAalpha, SMalphaA, a-SMA, alphaSMA
<i>Col1a1</i>	12842	collagen, type I, alpha 1	Chromosome 11, NC_000077.7 (94827050..94843868)	Col1a-1, Cola-1, Cola1, Mov-13, Mov13
<i>Col1a2</i>	12843	collagen, type I, alpha 2	Chromosome 6, NC_000072.7 (4505618..4541543)	Col1a-2, Cola-2, Cola2, oim
<i>Egfr</i>	13649	epidermal growth factor receptor	Chromosome 11, NC_000077.7 (16700153..16868158)	9030024J15Ri k, Erbb, Errb1, Errp, Wa5, wa-2, wa2
<i>Fn1</i>	14268	fibronectin 1	Chromosome 1, NC_000067.7 (71624632..71692439, complement)	E330027I09, Fn, Fn-1
<i>IL13</i>	16163	interleukin 13	Chromosome 11, NC_000077.7 (53522150..53525529, complement)	Il-13
<i>IL13RA1</i>	16164	interleukin 13 receptor, alpha 1	Chromosome X,	CD213a1, IL-13R-alpha-

			NC_000086.8 (35375761..35434915) Chromosome X,	1, IL-13r[a], Il13ra, NR4
<i>IL13RA2</i>	16165	interleukin 13 receptor, alpha 2	NC_000086.8 (146166474..146214982, complement) Chromosome 11,	CD213a2, IL-13R-alpha-2
<i>IL4</i>	16189	interleukin 4	NC_000077.7 (53503287..53509492, complement) Chromosome 7,	BSF-1, Il-4
<i>Il4ra</i>	16190	interleukin 4 receptor, alpha	NC_000073.7 (125151443..125178646) Chromosome 4,	CD124, Il4r
<i>Jak1</i>	16451	Janus kinase 1	NC_000070.7 (101009171..101122493, complement) Chromosome 19,	BAP004, C130039L05R ik
<i>Jak2</i>	16452	Janus kinase 2	NC_000085.7 (29229006..29290495) Chromosome 8,	Fd17
<i>Jak3</i>	16453	Janus kinase 3	NC_000074.7 (72129027..72143221) Chromosome 18,	fae, wil
<i>Smad2</i>	17126	SMAD family member 2	NC_000018.10 (47808957..47930872, complement) Chromosome 9,	CHTD8, JV18, JV18-1, LDS6, MADH2, MADR2, hMAD-2, hSMAD2
<i>Smad3</i>	17127	SMAD family member 3		Madh3

			NC_000075.7 (63554048..63665276, complement) Chromosome 18,	
<i>Smad4</i>	17128	SMAD family member 4	NC_000084.7 (73767861..73836862, complement) Chromosome 2,	D18Wsu70e, DPC4, Madh4
<i>Src</i>	20779	Rous sarcoma oncogene	NC_000068.8 (157265790..157313758) Chromosome 10,	pp60c-src
<i>Stat6</i>	20852	signal transducer and activator of transcription 6	NC_000076.7 (127478855..127496856) Chromosome 7,	
<i>Tgfb1</i>	21803	transforming growth factor, beta 1	NC_000073.7 (25386406..25404503) Chromosome 4,	TGF-beta1, TGFbeta1, Tgfb, Tgfb-1
<i>Tgfb1</i>	21812	transforming growth factor, beta receptor I	NC_000070.7 (47353222..47414926) Chromosome 9,	ALK5, Alk-5, ESK2, TGFR-1, TbetaR-I, TbetaRI
<i>Tgfb2</i>	21813	transforming growth factor, beta receptor II	NC_000075.7 (115916763..116004431, complement)	1110020H15R ik, DNIIR, RIIDN, TBR-II, TbetaR-II, TbetaRII

Gene ID is from NCBI (<https://www.ncbi.nlm.nih.gov/gene>).

Supplementary Table 3. Histone Methyltransferase genes

Name	Gene ID	Description	Location (GRCm39)	Aliases
<i>Ash1L</i>	192195	ASH1 like histone lysine methyltransferase	Chromosome 3, NC_000069.7 (88857721..88986682)	8030453L17Rik, Ash1, E430018P19Rik, Kmt2h
<i>Ehmt1</i>	77683	euchromatic histone methyltransferase 1	Chromosome 2, NC_000068.8 (24680781..24809658, complement)	9230102N17Rik, D330003E03, Eu-HMTase1, GLP, GLP1, KMT1D, mKIAA1876
<i>Ehmt2</i>	110147	euchromatic histone lysine N-methyltransferase 2	Chromosome 17, NC_000083.7 (35117426..35133049)	Bat8, D17Ert710e, G9a, KMT1C, NG36
<i>Ezh2</i>	14056	enhancer of zeste 2 polycomb repressive complex 2 subunit	Chromosome 6, NC_000072.7 (47507208..47572309, complement)	Enx-1, Enx1h, KMT6, mKIAA4065
<i>Jmjd1C</i>	108829	jumonji domain containing 1C	Chromosome 10, NC_000076.7 (66932189..67092105)	5430433L24Rik, D630035I23Rik, Jmjd1c, TRIP8
<i>Kdm1A</i>	99982	lysine (K)-specific demethylase 1A	Chromosome 4, NC_000070.7 (136277844..136330127, complement)	1810043O07Rik, Aof2, D4Ert478e, Kdm1, Lsd1, mKIAA0601
<i>Kdm1B</i>	218214	lysine (K)-specific demethylase 1B	Chromosome 13, NC_000079.7 (47196849..47238755)	4632428N09Rik, Aof1
<i>Kdm2A</i>	225876	lysine (K)-specific demethylase 2A	Chromosome 19, NC_000085.7 (4366172..4448749, complement)	100043628, 5530401A10Rik, Cxxc8, Fbl11, Fbl7, Fbxl11, Gm4560, Jhdm1, Jhdm1a, lalina
<i>Kdm2B</i>	30841	lysine (K)-specific	Chromosome 5,	Cxxc2, Fbl10,

		demethylase 2B	NC_000071.7 (123008727..123 127333, complement)	Fbxl10, Jhdm1b, PCCX2
<i>Kdm3A</i>	104263	lysine (K)-specific demethylase 3A	Chromosome 6, NC_000072.7 (71565954..7160 9963, complement)	1700105C21Rik, C230043E16Rik , JHDM2a, Jmjd1, Jmjd1a, KDM2A, TGSA, Tsga
<i>Kdm3B</i>	277250	KDM3B lysine (K)-specific demethylase 3B	Chromosome 18, NC_000084.7 (34910061..3497 2423)	5830462I21Rik, JHDM2B, Jmjd1b, mKIAA1082
<i>Kdm4A</i>	230674	lysine (K)-specific demethylase 4A	Chromosome 4, NC_000070.7 (117994154..118 037242, complement)	D4Ert222e, JHDM3A, Jmjd2, Jmjd2a, mKIAA0677
<i>Kdm4B</i>	193796	lysine (K)-specific demethylase 4B	Chromosome 17, NC_000083.7 (56632975..5671 0774)	4732474L06Rik, Jmjd2b
<i>Kdm4C</i>	76804	lysine (K)-specific demethylase 4C	Chromosome 4, NC_000070.7 (74160734..7432 4101)	2410141F18Rik, Gasc1, Jmjd2c
<i>Kdm4D</i>	244694	lysine (K)-specific demethylase 4D	Chromosome 9, NC_000075.7 (14373844..1441 1818, complement)	4932416A15, Jmjd2d
<i>Kdm4DI</i>	547035	lysine (K)-specific demethylase 4D-like	Chromosome 9, NC_000075.7 (14362311..1436 3318, complement)	EG547035, Gm27205, Gm6017
<i>Kdm5A</i>	214899	lysine (K)-specific demethylase 5A	Chromosome 6, NC_000072.7 (120341060..120 421535)	Jarid1a, RBP2, Rbbp2
<i>Kdm5B</i>	75605	lysine (K)-specific demethylase 5B	Chromosome 1, NC_000067.7 (134487916..134	2010009J12Rik, 2210016I17Rik, D1Ert202e,

			560621)	Jarid1b, PLU-1, PUT1, Plu1, RBBP2H1A, Rb-Bp2, mKIAA4034
<i>Kdm5C</i>	20591	lysine (K)-specific demethylase 5C	Chromosome X, NC_000086.8 (151015698..151062098)	D930009K15Rik, Jarid1c, Smcx, mKIAA0234
<i>Kdm5D</i>	20592	lysine (K)-specific demethylase 5D	Chromosome Y, NC_000087.8 (897566..943813)	HY, Jarid1d, Smcy
<i>Kdm6A</i>	22289	lysine (K)-specific demethylase 6A	Chromosome X, NC_000086.8 (18027101..18146175)	Utx
<i>Kdm6B</i>	216850	KDM1 lysine (K)-specific demethylase 6B	Chromosome 11, NC_000077.7 (69289334..69311188, complement)	1700064E03Rik, Jmjd3
<i>Kdm7A</i>	338523	lysine (K)-specific demethylase 7A	Chromosome 6, NC_000072.7 (39113554..39183707, complement)	A630082K20Rik, Jhdm1d, mKIAA1718
<i>Kmt2A</i>	214162	lysine (K)-specific methyltransferase 2A	Chromosome 9, NC_000075.7 (44714652..44793492, complement)	6430520K01, ALL-1, All1, Cxxc7, HRX, HTRX1, MII, MII1, mKIAA4050
<i>Kmt2B</i>	75410	lysine (K)-specific methyltransferase 2B	Chromosome 7, NC_000073.7 (30268280..30288371, complement)	2610014H22Rik, MII2, Wbp7, mKIAA0304
<i>Kmt2C</i>	231051	lysine (K)-specific methyltransferase 2C	Chromosome 5, NC_000071.7 (25476793..25703853, complement)	E330008K23Rik, HALR, MII3
<i>Kmt2D</i>	381022	lysine (K)-specific	Chromosome 15,	ALR,

		methyltransferase 2D	NC_000081.7 (98729550..98771958, complement) Chromosome 19, NC_000085.7 (3816436..3868303) Chromosome 7, NC_000073.7 (4743091..4750513)	C430014K11Rik , KMT2B, MII2, MII4 C630029K18Rik , Suv4-20h1, Suv420h1 Suv4-20h2, Suv420h2 D630039M04Rik , Evi-1, Evi1, Jbo, Mds, Mds1, Mds1-Evi1, Prdm3, Znfpr1b1 KMT3B 5830445G22Rik , 9430010A17Rik, C130020C13Rik , D030027O06Rik , D930023B08Rik , MMSET, Whsc1, Whsc1l, mKIAA1090 6720429E03, A530023P05, WHISTLE, Whsc1l1 9830141C09Rik, mKIAA1111 5730557K01Rik, csp1, mel1
<i>Kmt5B</i>	225888	lysine methyltransferase 5B		
<i>Kmt5C</i>	232811	lysine methyltransferase 5C		
<i>Mecom</i>	14013	MDS1 and EVI1 complex locus	Chromosome 3, NC_000069.7 (30005445..30563937, complement)	
<i>Nsd1</i>	18193	nuclear receptor-binding SET-domain protein 1	Chromosome 13, NC_000079.7 (55357595..55466138)	
<i>Nsd2</i>	107823	nuclear receptor binding SET domain protein 2	Chromosome 5, NC_000071.7 (33974286..34055310)	
<i>Nsd3</i>	234135	nuclear receptor binding SET domain protein 3	Chromosome 8, NC_000074.7 (26091617..26209694) Chromosome X, NC_000086.8 (150303621..150416855)	
<i>Phf8</i>	320595	PHD finger protein 8		
<i>Prdm16</i>	70673	PR domain containing 16	Chromosome 4, NC_000070.7 (154400579..154	

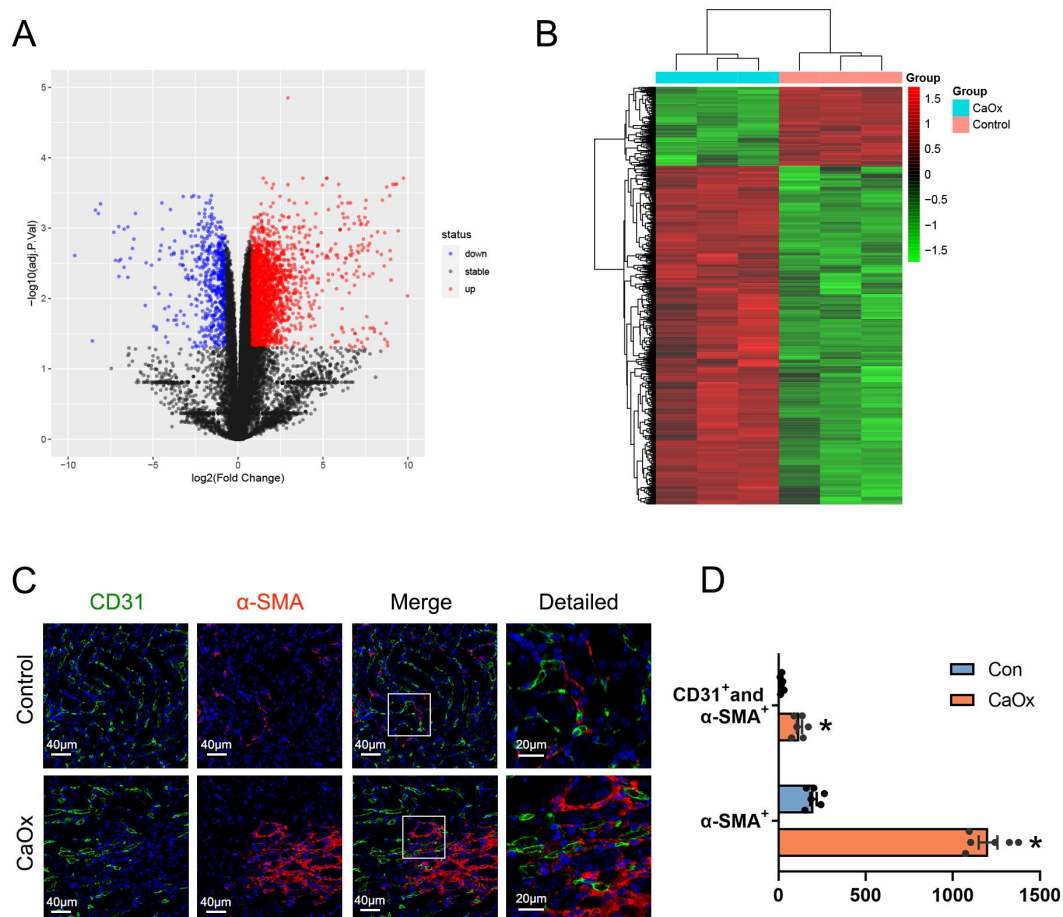
			721851, complement)	
<i>Prdm2</i>	110593	PR domain containing 2, with ZNF domain	Chromosome 4, NC_000070.7 (142833961..142 939560, complement)	4833427P12Rik, E330024L24Rik, Gm1033, Gm19732, KMT8, Riz, Riz1, Znfpr1c1
<i>Prdm8</i>	77630	PR domain containing 8	Chromosome 5, NC_000071.7 (98315070..9833 5313)	4930565F05Rik, PFM5
<i>Prdm9</i>	56979	PR/SET domain 9	Chromosome 5, NC_000005.10 (23507155..2352 8093)	KMT8B, MEISETZ, MSBP3, PFM6, ZNF899
<i>Setd2</i>	235626	SET domain containing 2	Chromosome 9, NC_000075.7 (110361368..110 447701)	4921524K10Rik, KMT3A
<i>Setd1A</i>	233904	SET domain containing 1A	Chromosome 7, NC_000073.7 (127376561..127 399294)	KMT2F, Nscn1, mKIAA0339, mNSC1
<i>Setd1B</i>	208043	SET domain containing 1B	Chromosome 5, NC_000071.7 (123280109..123 306693)	KMT2G, mKIAA1076
<i>Setd7</i>	73251	SET domain containing (lysine methyltransferase) 7	Chromosome 3, NC_000069.7 (51422739..5146 8519, complement)	1600028F23Rik, H3K4MT, KMT7, Set7, Set7/9, mKIAA1717
<i>Setdb1</i>	84505	SET domain, bifurcated 1	Chromosome 3, NC_000069.7 (95230836..9526 4513, complement)	ESET, KMT1E, mKIAA0067
<i>Setdb2</i>	239122	SET domain, bifurcated 2	Chromosome 14, NC_000080.7 (59639458..5967 8329, complement)	Cllid8, Gm293, KMT1F
<i>Smyd2</i>	226830	SET and MYND	Chromosome 1,	1110020E07Rik,

		domain containing 2	NC_000067.7 (189612689..189 654758, complement) Chromosome 1, NC_000067.7 (178779525..179 345618, complement) Chromosome X, NC_000086.8 (7927410..79409 99, complement) Chromosome 2, NC_000068.8 (3456852..34760 85, complement)	4930402C15, KMT3C, Zmynd14 2410008A19Rik, Zmynd1 DXHXS7466e, H3-K9-HMTase 1, KMT1A, mIS6 4930507K23Rik, D030054H19Rik , D2Ert544e, KMT1B
<i>Smyd3</i>	69726	SET and MYND domain containing 3		
<i>Suv39H</i> 1	20937	suppressor of variegation 3-9 1		
<i>Suv39H</i> 2	64707	suppressor of variegation 3-9 2		

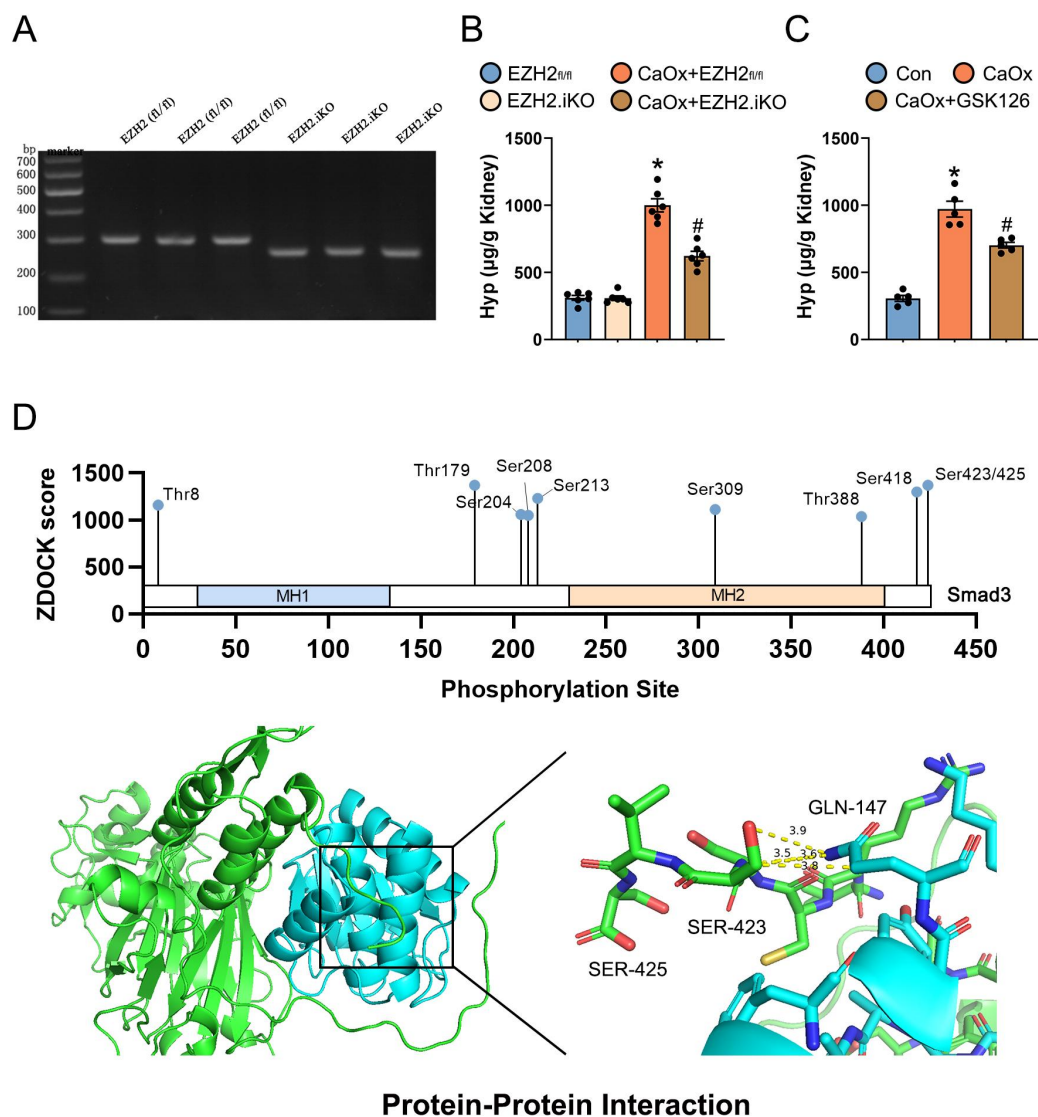
Gene ID is from NCBI (<https://www.ncbi.nlm.nih.gov/gene>).

Supplementary Table 4. Antibodies

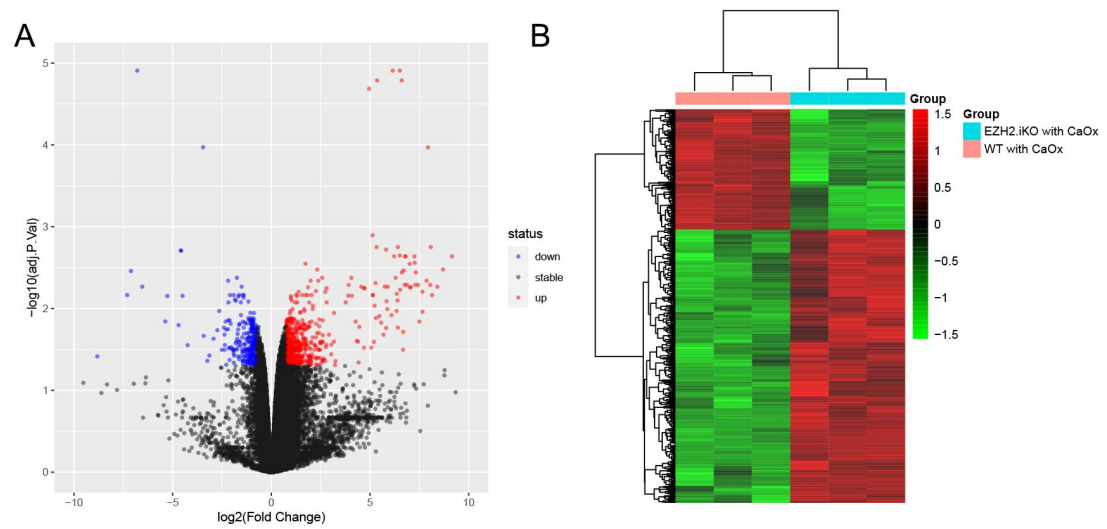
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EZH2	CST	#5246	1:1000
α -SMA	CST	#19245	1:2000
Collagen I	Affinity	AF7001	1:1000
Fibronectin	CST	#26836	1:1000
GAPDH	GAPDH	GB15004-100	1:2000
DUSP23	Genetex	108245	1:1000
H3K27me3	ABclonal	A2363	1:1000
H3	ABclonal	A17562	1:2000
SMAD3	CST	#9523	1:1000
pSMAD3-Ser423/ 425	CST	#9520	1:1000
pSMAD3-T179	Abcam	74062	1:1000



Supplementary Fig. 1 Volcano plots (**A**) and heatmaps (**B**) of differentially expressed genes between CaOx nephrocalcinosis mice and normal mice. **C** Two-color immunofluorescence identifies EndMT cells that coexpress endothelial (CD31, green) and myofibroblast (α -SMA, red) markers in nephrocalcinosis mice. **D** Quantification of the number of α -SMA⁺ cells, and CD31⁺ α -SMA⁺ cells (n=6). Data are presented as the mean $\pm$ SEM. * $P < 0.05$ versus control group. P values were determined by the two-tailed Student's t -test.



Supplementary Fig. 2 **A** PCR-based genotyping was performed to identify the gene knockout mice. **B** Hydroxyproline content were measured on day 12 of modelling in EZH2^{fl/fl} and EZH2.iKO mice (n=6). **C** Hydroxyproline content were measured on day 12 of modelling (n=5). **D** The molecular docking analysis in mouse was conducted to predict the potential amino acid binding sites between DUSP23 and SMAD3. Data are presented as the mean $\pm$ SEM. * $P < 0.05$ versus control group. P values were determined by the two-tailed Student's t -test.



Supplementary Fig. 3 Volcano plots (**A**) and heatmaps (**B**) of differentially expressed genes between wild-type (WT) mice and EZH2.iKO mice with CaOx nephrocalcinosis.

Original Blots (Chosen)

Figure 4

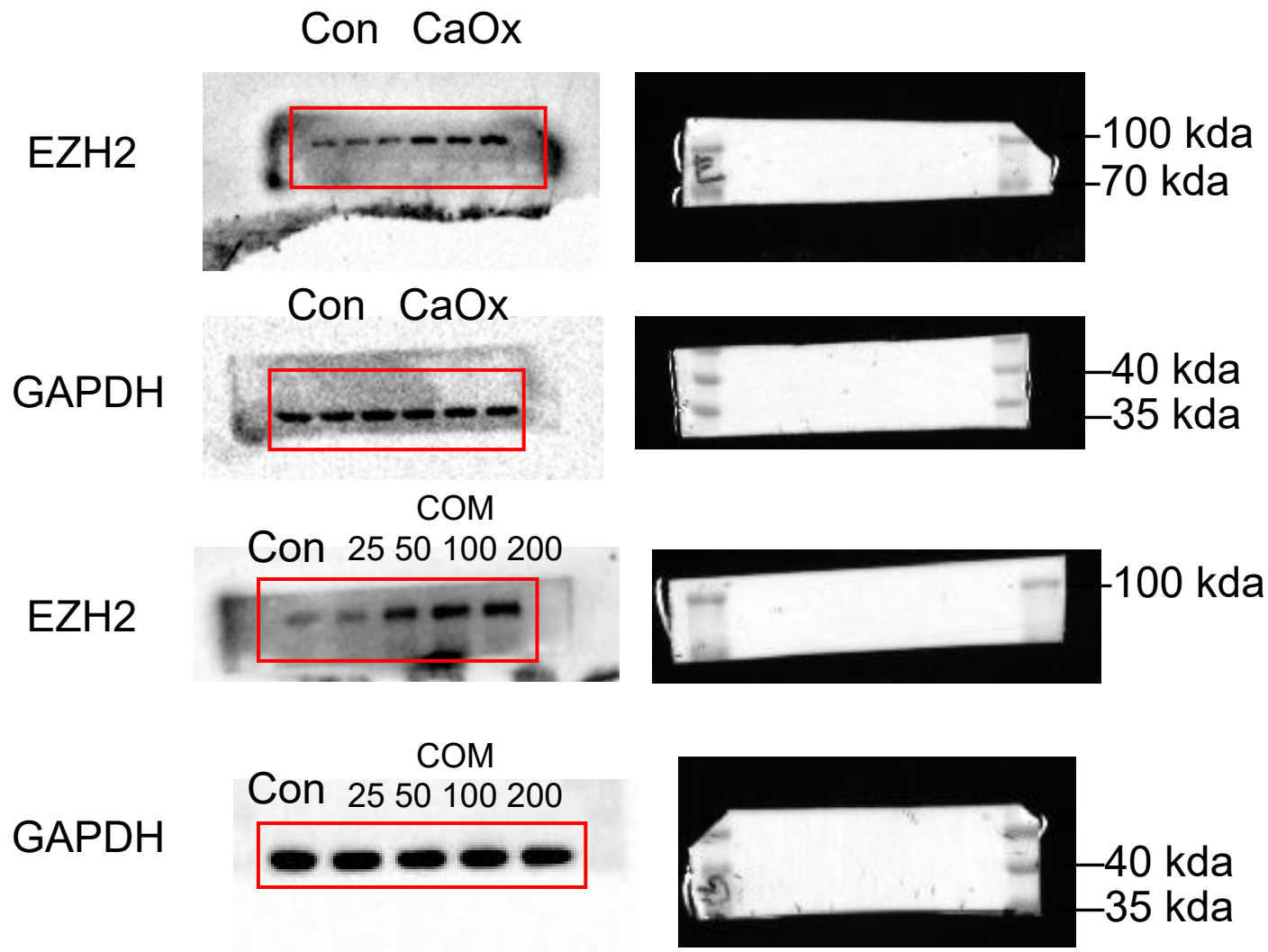


Figure 5F

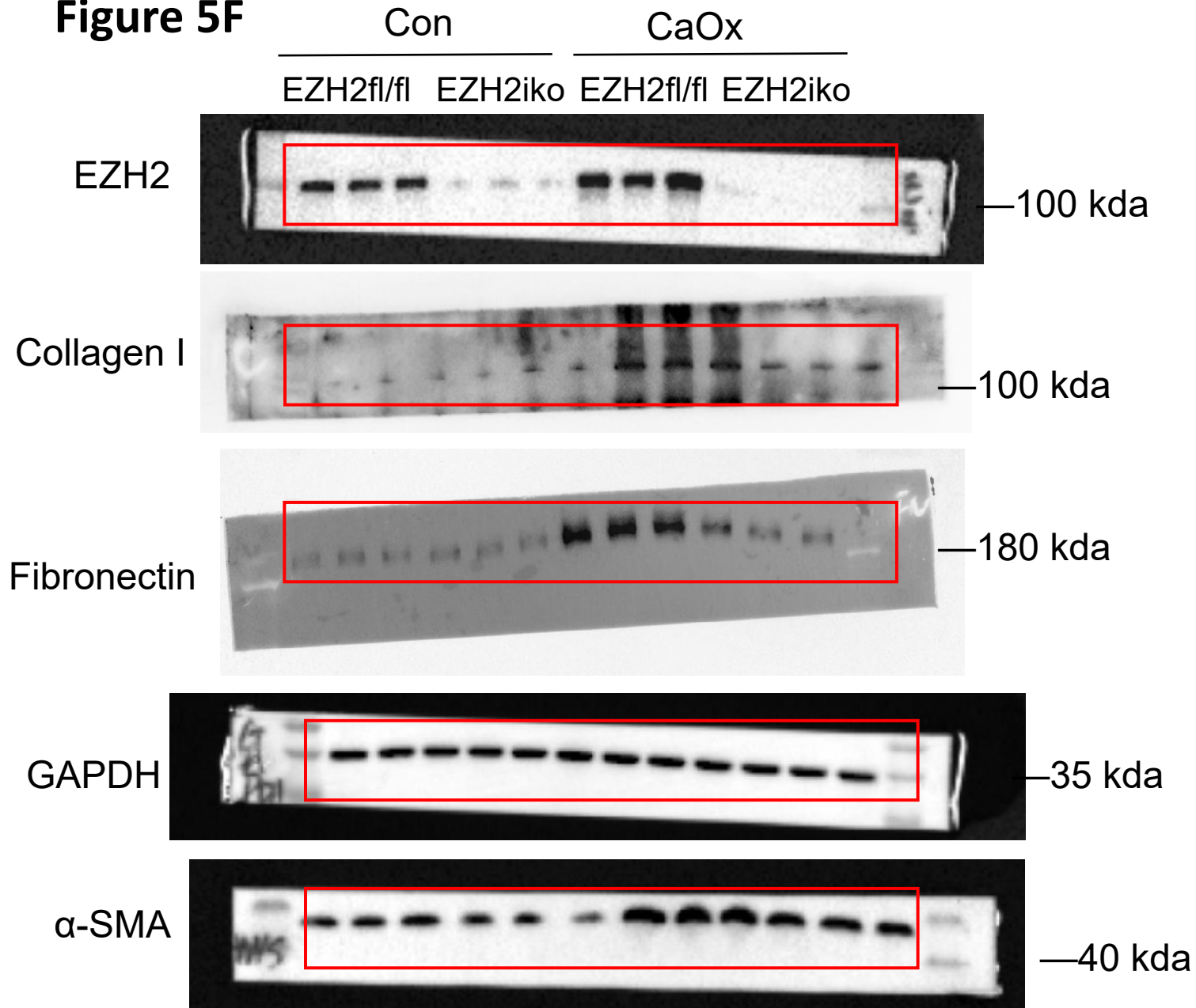


Figure 6

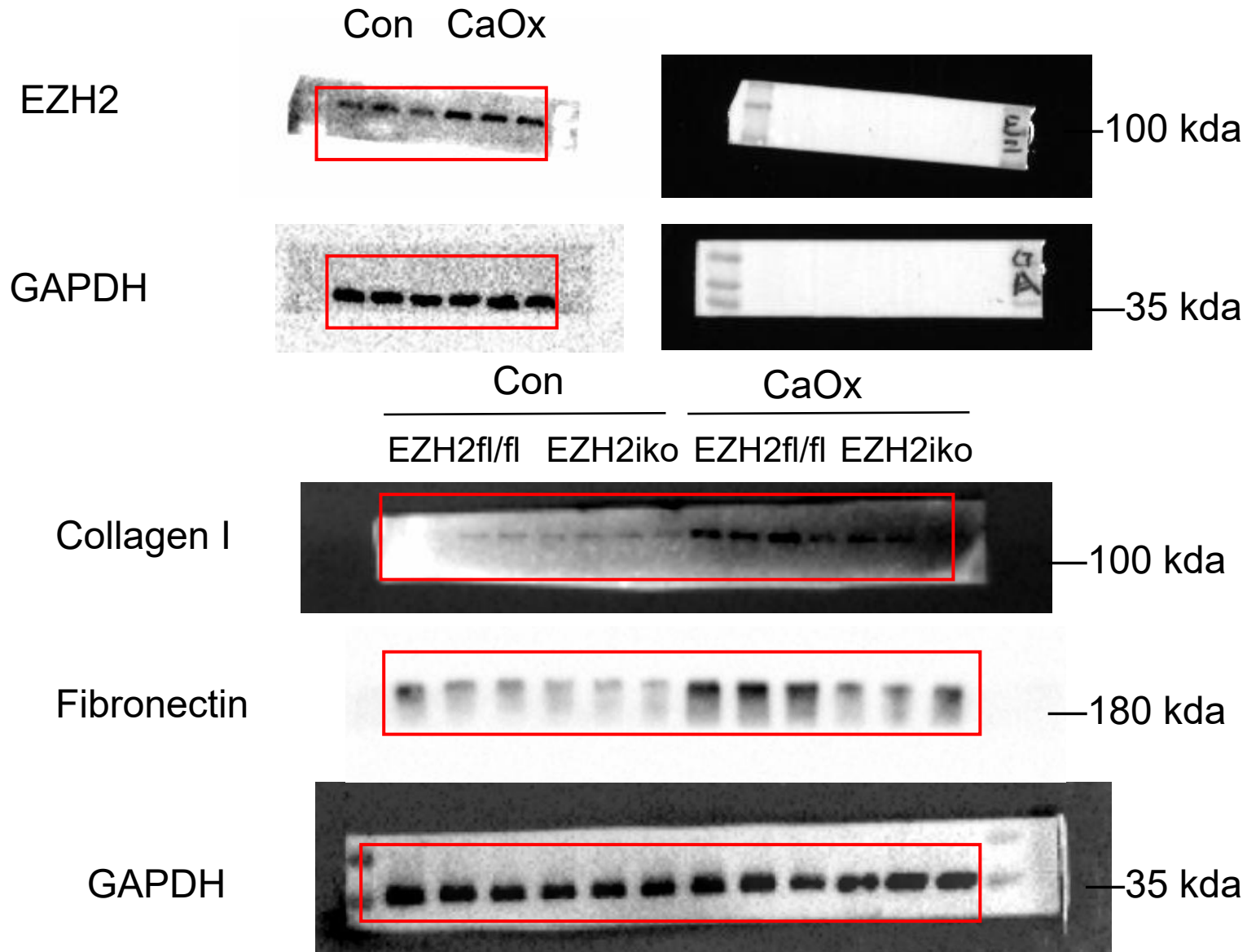


Figure 7D

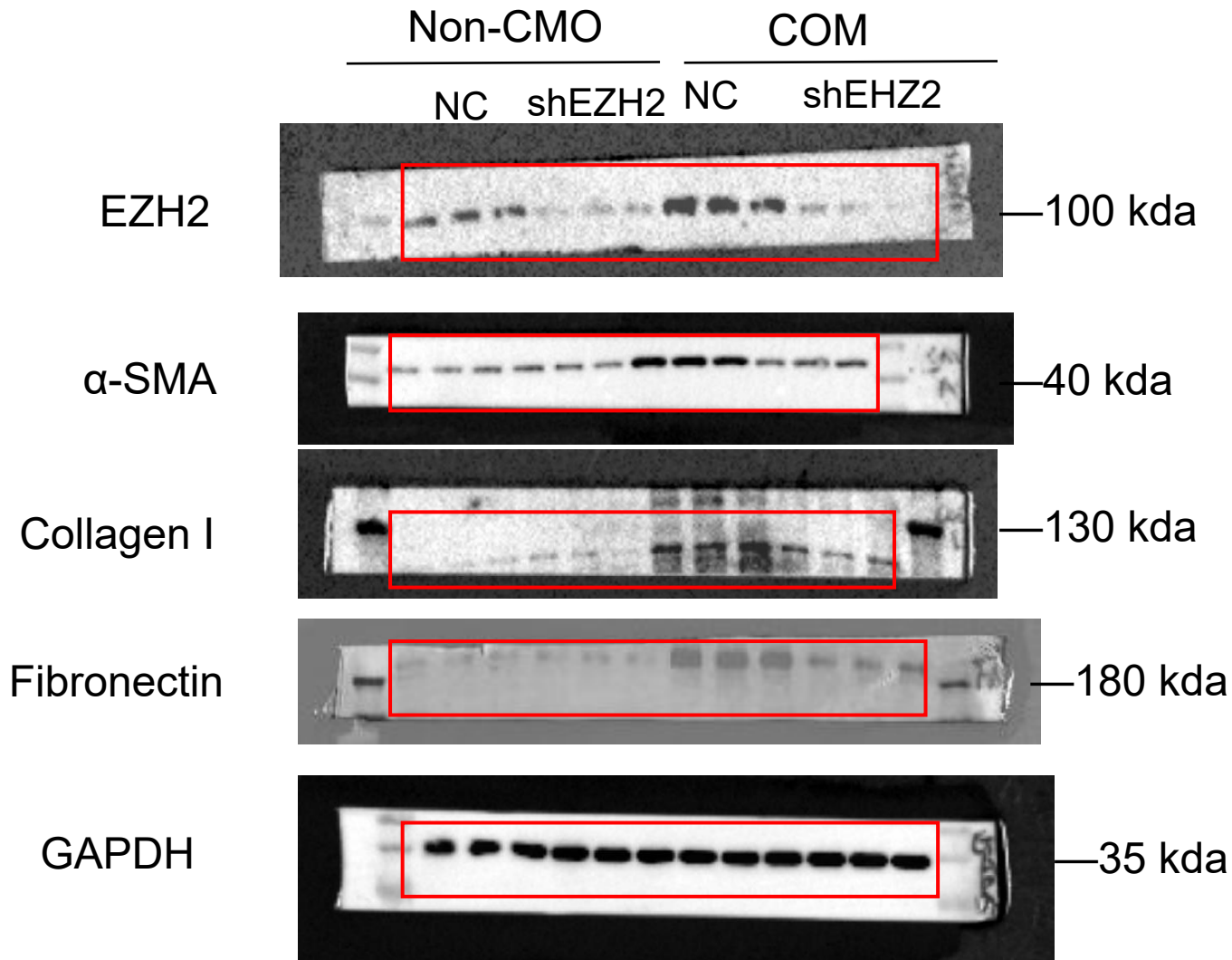


Figure 8D

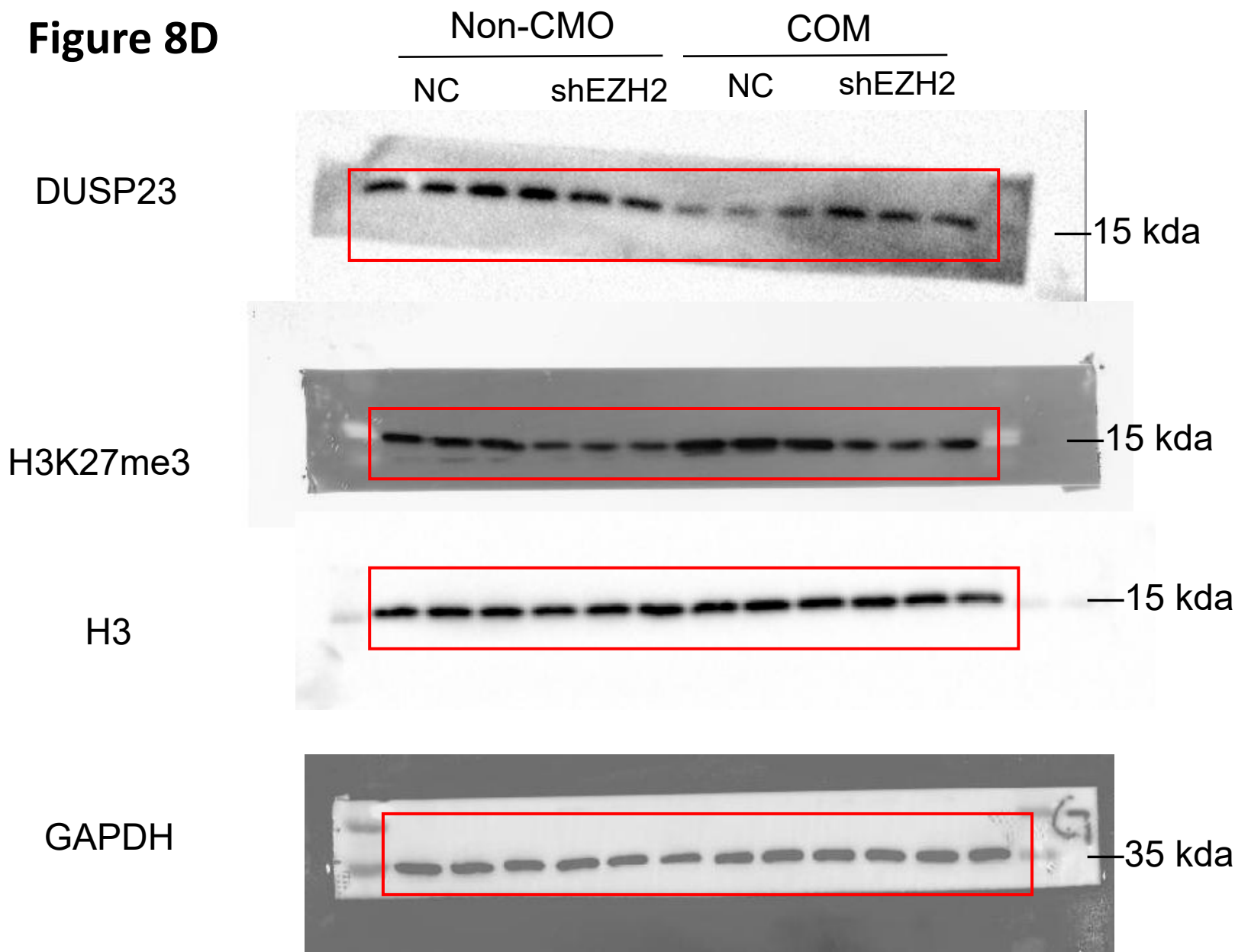


Figure 8H

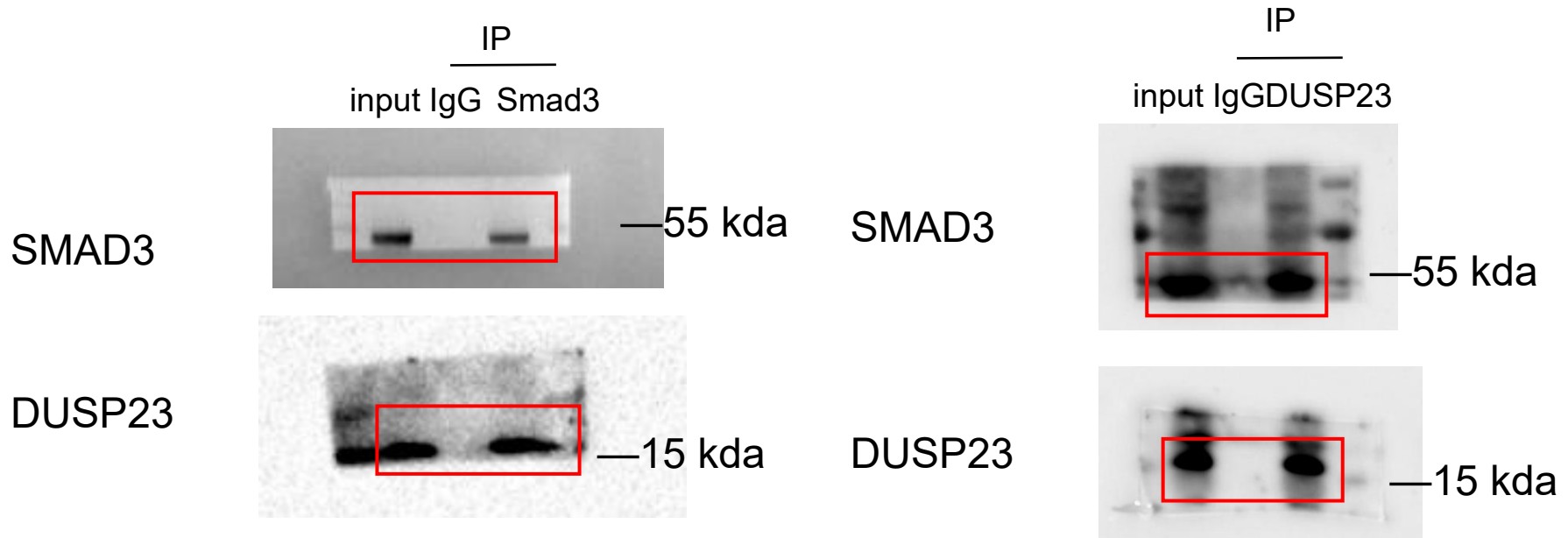


Figure 8l

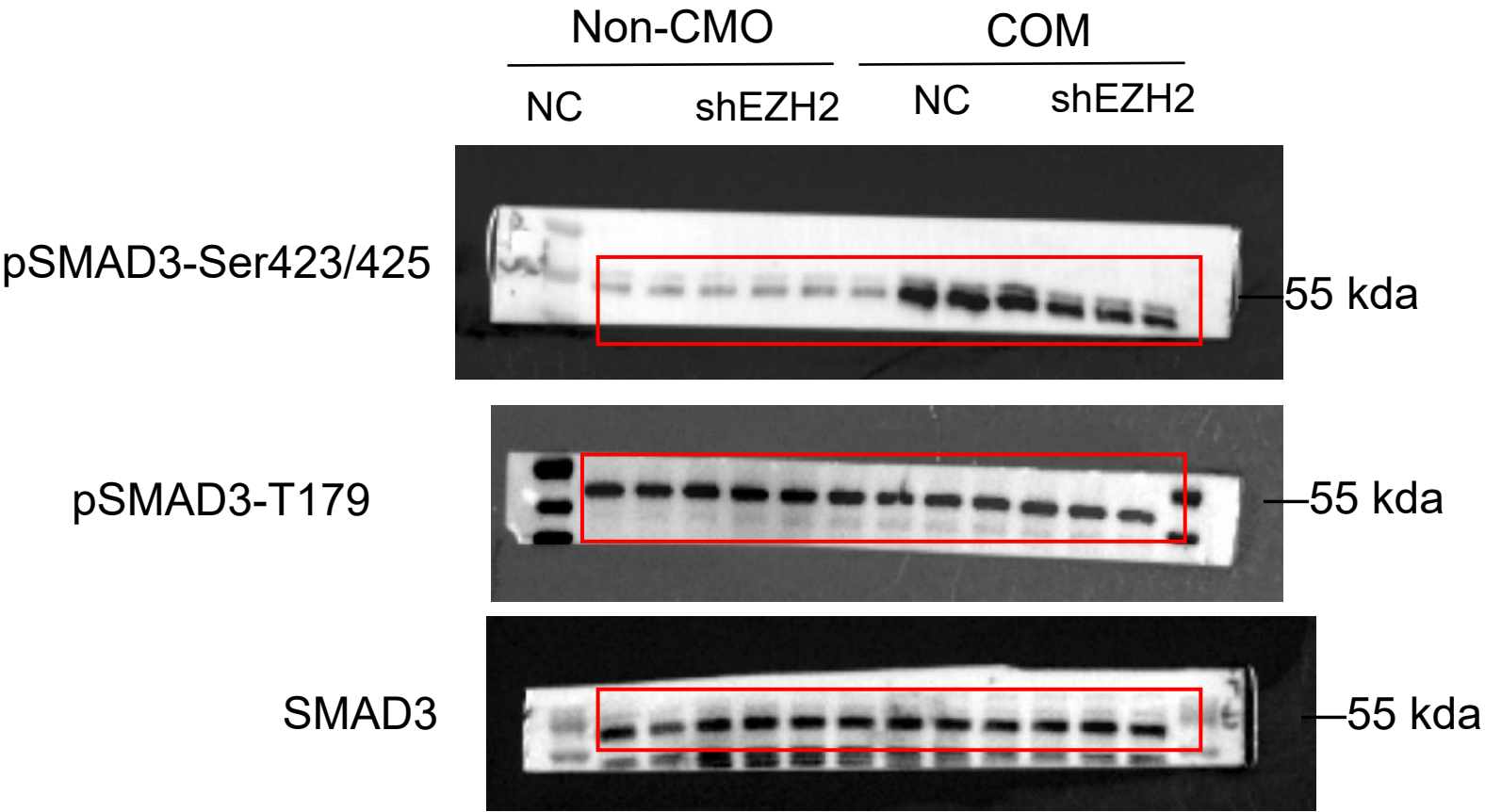


Figure 8J

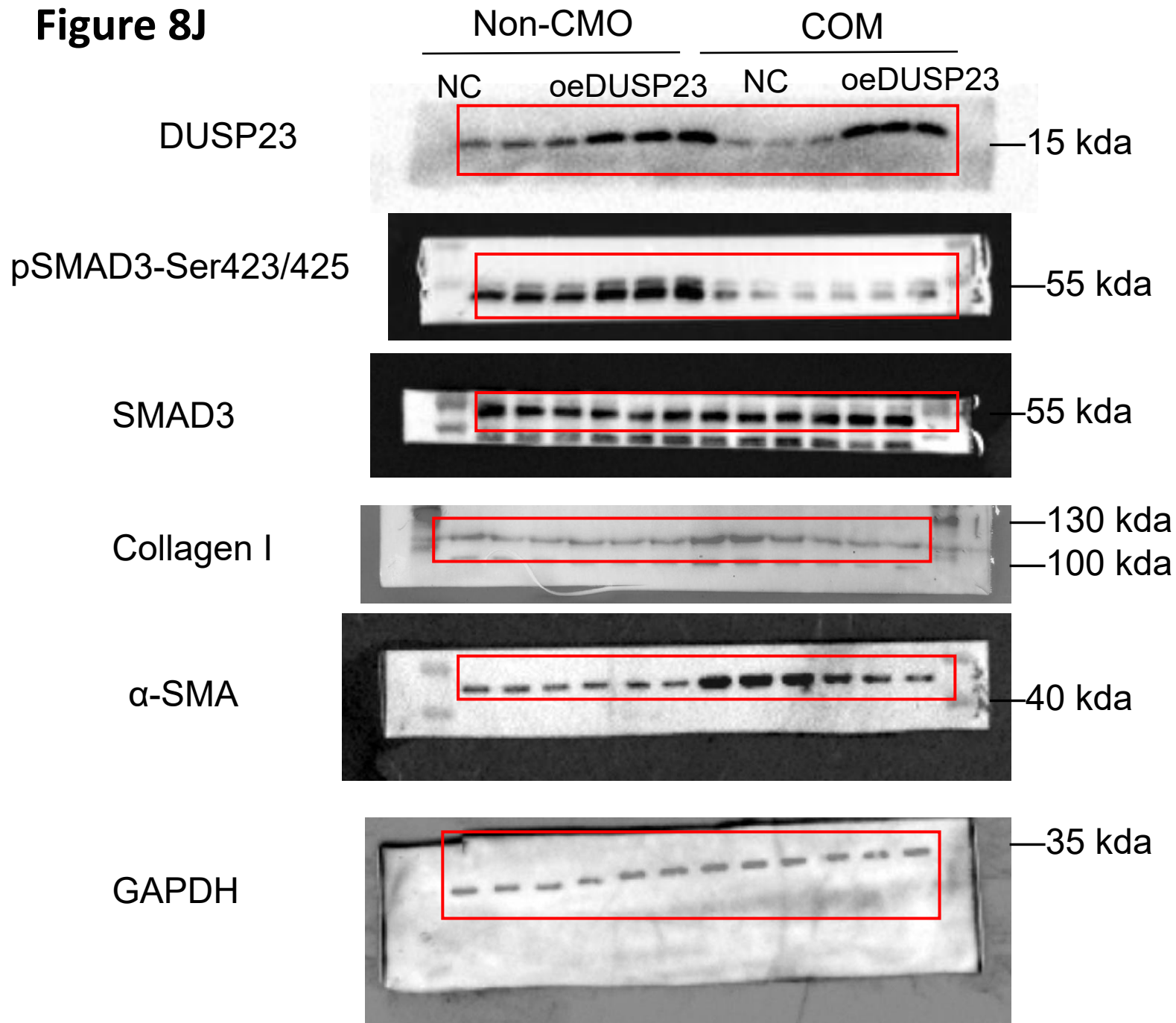
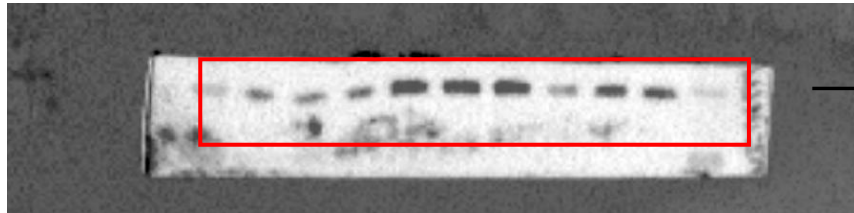


Figure 9E

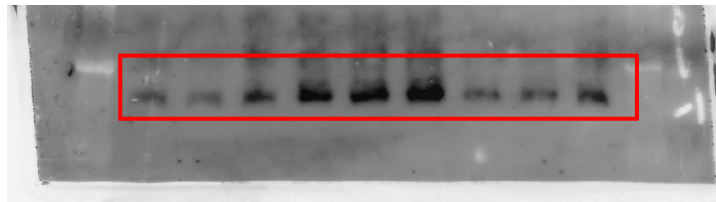
Con CaOx CaOx+
GSK126

EZH2



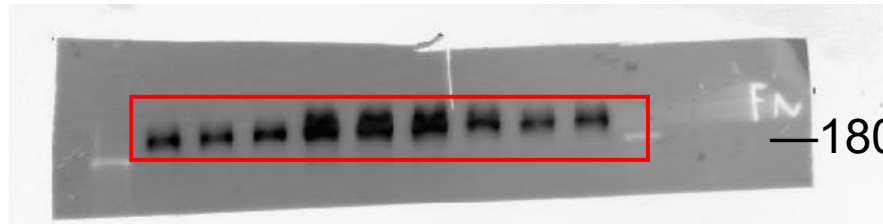
—100 kda

Collagen I



—130 kda

Fibronectin



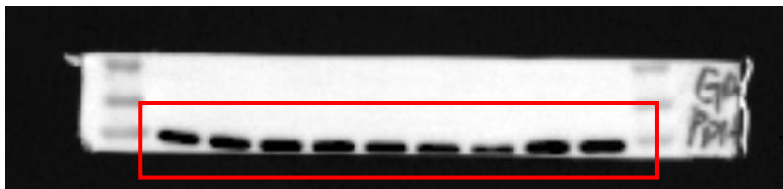
—180 kda

α -SMA



—40 kda

GAPDH



—35 kda

Figure 9G

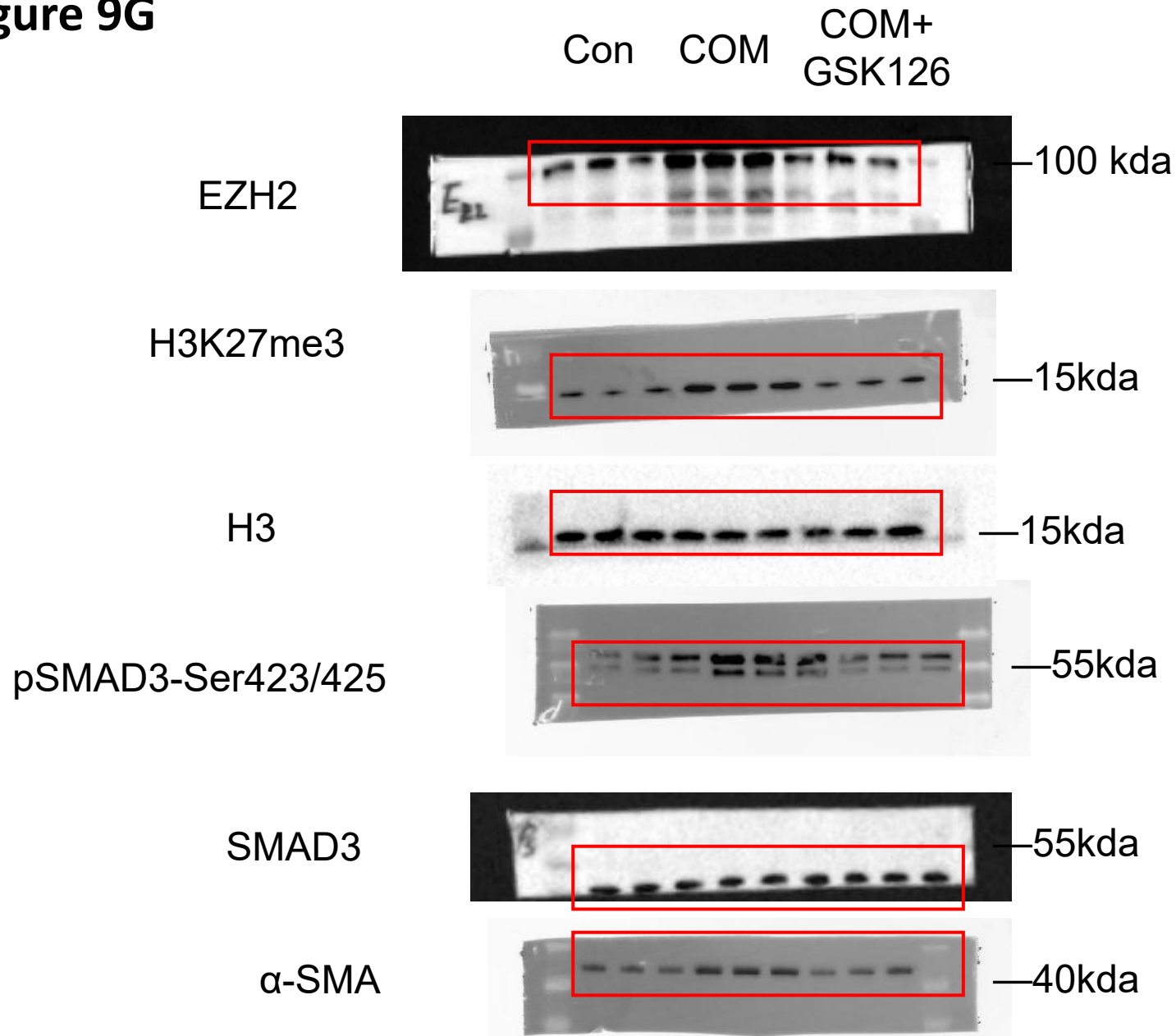


Figure 9G

