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SUPPLEMENTARY MATERIAL

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Colchicine alleviates severe acute pancreatitis in rats by inhibiting acinar cell ferroptosis *via* LCN2/MAPK/ERK signaling axis

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Figure S1.

Colchicine mitigates SAP-associated Acute Lung Injury (ALI) and inflammatory infiltration. (A) Representative H&E staining of the lung from the Sham, SAP, and SAP+COL groups. (B) Representative IHC staining for MPO (brown) in the lung. (C) Representative IHC staining for IL-6 (brown) in the pancreas. Nuclei were counterstained with DAPI (blue). Data are presented as mean \pm SD ($n=6$). Magnification = 400 \times , scale bar = 50 μ m.

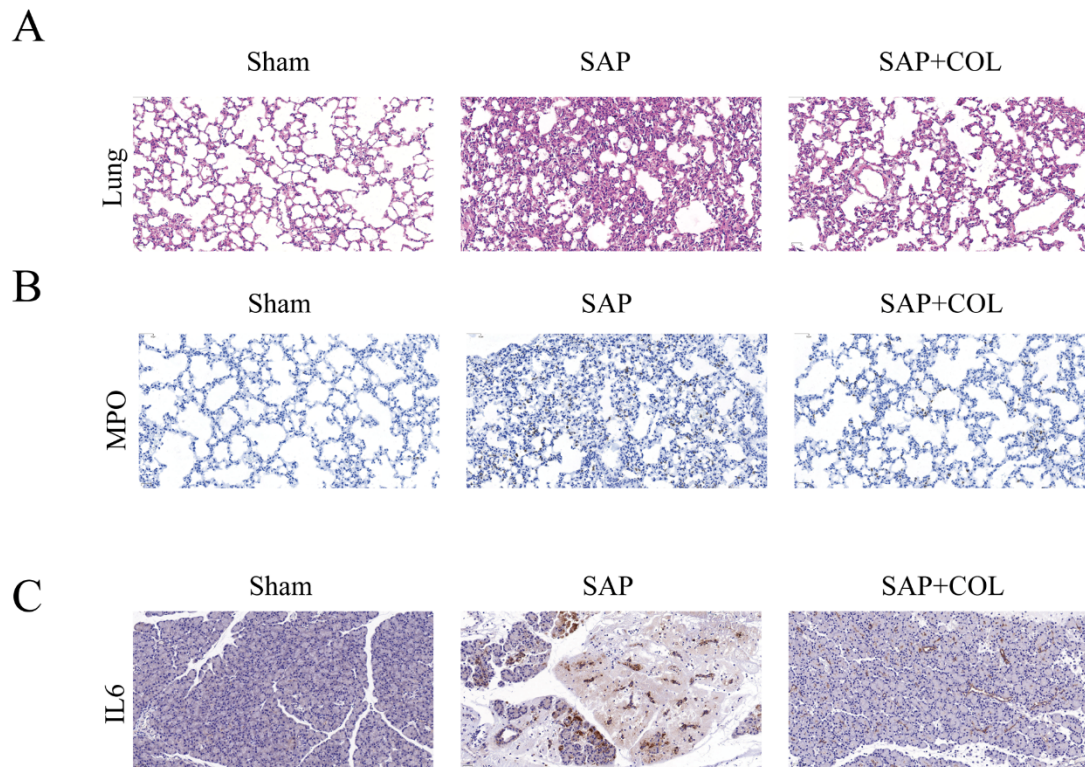
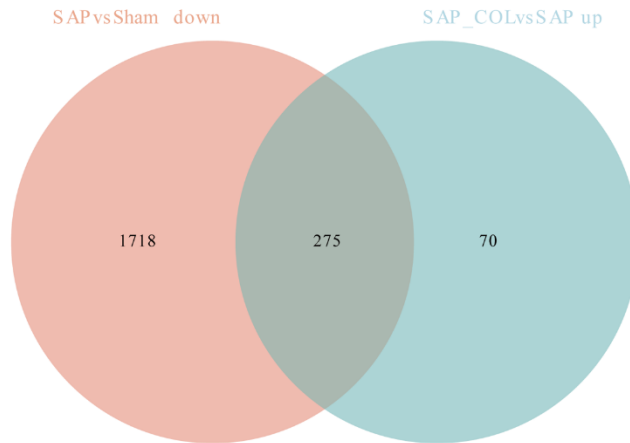


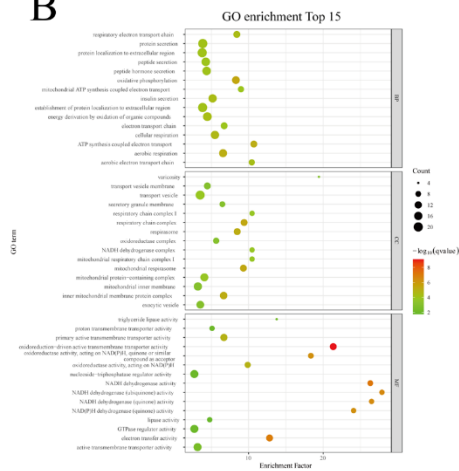
Figure S2.

Functional enrichment analysis of DEGs-2. (A) Venn diagram identifying the intersection of genes downregulated in SAP vs Sham and upregulated in SAP+COL vs. SAP (designated as DEGs-2). (B) Top 15 GO enrichment terms for DEGs-2. (C) Top 15 KEGG pathway enrichment analysis for DEGs-2.

A



B



C

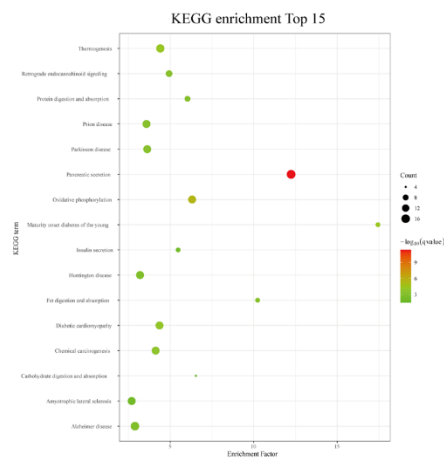
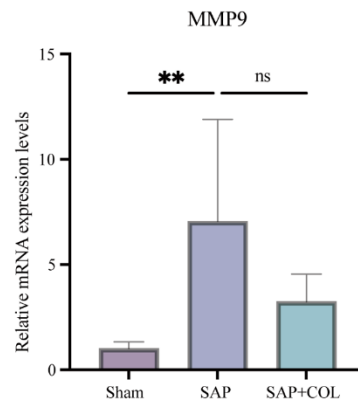


Figure S3.

In vivo validation of MMP9 expression. (A) Relative mRNA levels of *MMP9* in the pancreas from Sham, SAP, and SAP+COL groups. (B) Representative IHC staining for MMP9 (brown) in the pancreas. Nuclei were counterstained with DAPI (blue). Data are presented as mean \pm SD ($n=6$). Magnification = 400 \times , scale bar = 50 μ m.

A



B

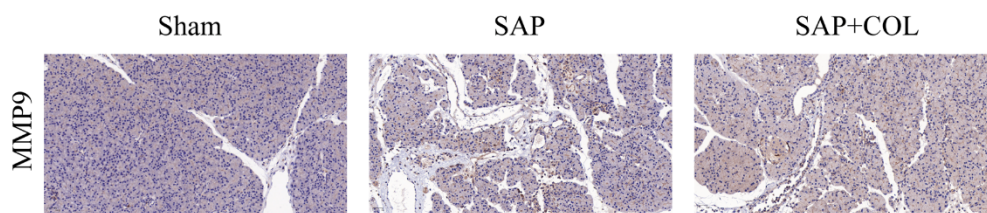


Figure S4.

Validation of AAV-mediated pancreas-specific LCN2 overexpression. (A) Representative *in vivo* bioluminescence imaging of major organs from AAV/PAN-OE-LCN2 rats. (B) Representative fluorescence image of the pancreas showing spontaneous GFP expression (Green). (C-D) Western blot verification and quantification of LCN2 protein overexpression in AAV/PAN-OE-CTR and AAV/PAN-OE-LCN2 groups.

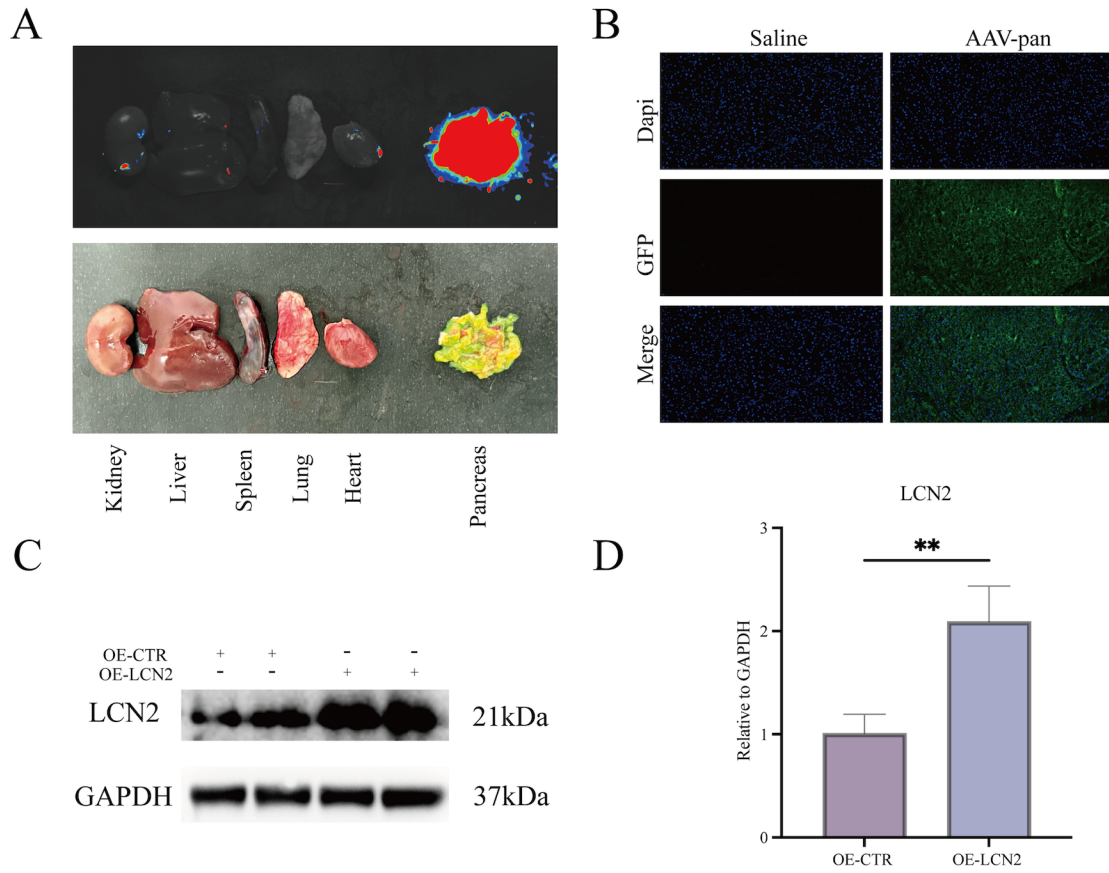


Table S1. The top 10 upregulated DEGs-1 and downregulated DEGs-2 between SAP group and CON group.

Symbol	log2FoldChange	Foldchange	regulated	p value	p adjust
Serpina3n	12.2432333	4848.19926	up	1.6045E-07	2.2635E-06
A2m	11.3243847	2564.36291	up	7.4124E-12	2.2823E-10
Timp1	10.8101217	1795.43993	up	4.9551E-16	2.9093E-14
Osm	10.2512942	1218.84102	up	4.3004E-17	2.9407E-15
Rab44	10.2448089	1213.37424	up	7.4711E-17	4.9498E-15
Ccr1	9.4741651	711.226417	up	4.4876E-15	2.3583E-13
Slc16a3	9.32782532	642.621449	up	1.5279E-18	1.2448E-16
Cxcr2	9.15486354	570.01795	up	3.7951E-13	1.4924E-11
Il1r2	9.12547534	558.523953	up	3.4724E-18	2.6753E-16
Trem3	8.97973805	504.85947	up	2.7853E-10	6.7461E-09
LOC120096962	-9.6831025	0.00121645	down	8.9592E-14	3.9015E-12
LOC102551311	-8.9660351	0.00199965	down	0.000015428	0.00013234
Ucn3	-8.9156664	0.0020707	down	1.85E-08	0.000000315
Lipo1	-8.8839597	0.00211671	down	0.00821824	0.02817801
LOC102551026	-8.4687417	0.00282263	down	1.2804E-08	2.2429E-07
LOC120093143	-8.3335044	0.00310003	down	8.5753E-83	2.4335E-79
Unc5d	-8.0558985	0.00375779	down	2.9338E-17	2.0389E-15
LOC120093125	-7.8710501	0.00427147	down	0.000013733	0.00011954
Irx2	-7.7787333	0.00455374	down	0.00024538	0.00148003
Septin3	-7.7292528	0.00471263	down	0.000002497	0.000026589

Serpin Family A Member 3N(Serpina3n); Alpha-2-Macroglobulin(A2m); TIMP Metallopeptidase Inhibitor 1(Timp1); Oncostatin M(Osm); RAB44, Member RAS Oncogene Family(Rab44); Chemokine Receptor 1(Ccr1); Solute Carrier Family 16 Member 3(Slc16a3); C-X-C Motif Chemokine Receptor 2(Cxcr2); Interleukin-1 Receptor Type 2(Il1r2); Triggering Receptor Expressed on Myeloid Cells 3(Trem3); Urocortin 3(Ucn3); Lipid Droplet Associated Protein 1(Lipo1); Unc-5 Netrin Receptor D(Unc5d); Iroquois Homeobox 2(Irx2).

Table S2. The top 10 upregulated DEGs-2 and downregulated DEGs-1 between SAP+COL group and SAP group.

Symbol	log2FoldChange	Foldchange	regulated	p value	p adjust
Hspb7	-8.8656695	0.00214372	down	0.00037554	0.01318654
Barx1	-8.5994383	0.00257817	down	4.1547E-09	1.5323E-06
LOC120101908	-7.5148156	0.00546783	down	3.3501E-06	0.00036779
Il2rg	-7.3684787	0.00605155	down	6.8733E-09	2.3377E-06
LOC102553902	-7.3479891	0.00613811	down	9.1042E-10	4.1558E-07
Prr33	-7.1420723	0.00707982	down	1.1709E-10	6.7703E-08
LOC120095083	-7.0889746	0.00734524	down	7.4852E-09	2.4969E-06
Oscar	-6.9876927	0.00787943	down	1.3999E-12	1.2141E-09
Lama1	-6.9775276	0.00793515	down	2.634E-08	6.7282E-06
Ffar2	-6.9286896	0.00820836	down	2.1483E-06	0.00026242
LOC102551311	8.55646539	376.489388	up	0.00052554	0.01645483
LOC120093125	8.2488337	304.191008	up	1.7624E-06	0.00022814
LOC102551026	8.02658585	260.761279	up	3.2745E-08	7.5732E-06
Lipo1	7.85242452	231.108181	up	0.00011918	0.00565212
LOC120096962	7.15551242	142.568596	up	0.000014648	0.00116784
Ucn3	7.08055162	135.350051	up	0.00059484	0.01807034
Irx2	6.88460464	118.16055	up	0.00220292	0.04333348
Neurod1	6.50483337	90.8134054	up	5.7159E-06	0.00057138
Cfap44	6.44482259	87.1133906	up	0.000016566	0.00126589
Lilrb3	6.4447269	87.1076124	up	0.00096712	0.02544251

Heat Shock Protein Family B (Small) Member 7(Hspb7); BarH-Like Homeobox 1(Barx1); Interleukin-2 Receptor Subunit Gamma(Il2rg); Proline Rich 33 (Prr33); Osteoclast Associated Receptor(Oscar); Laminin Subunit Alpha 1(Lama1); Free Fatty Acid Receptor 2(Ffar2); Lipid Droplet Associated Protein 1(Lipo1); Urocortin 3(Ucn3); Iroquois Homeobox 2(Irx2); Neuronal Differentiation 1(Neurod1); Cilia And Flagella Associated Protein 44(Cfap44); Leukocyte Immunoglobulin-Like Receptor B3(Lilrb3).

Table S3. Hub genes identified by overlap of top 20 genes from five algorithms and top 30 MCODE modules.

Closeness	Degree	EPC	MNC	Radiality	MCODE	Hub Gene
Il6	Il6	Il6	Il6	Il6	Adipoq	Il6
Mmp9	Mmp9	Mmp9	Mmp9	Mmp9	Csf1	Mmp9
Itgam	Tlr2	Ptprc	Itgam	Hif1a	Ccr1	Hif1a
Hif1a	Itgam	Itgam	Tlr2	Pxdn	Ifnar1	Pxdn
Tlr2	Ptprc	Tlr2	Ptprc	Itgam	Mpo	Itgam
Pxdn	Hif1a	Pxdn	Hif1a	Tlr2	Selp	Tlr2
Ptprc	Pxdn	Hif1a	Pxdn	Ptprc	Il1r1	Ptprc
Nfkbia	Nfkbia	Timp1	Nfkbia	Nfkbia	Nfkbia	Nfkbia
Timp1	Timp1	Cxcl1	Timp1	Itgb1	Mmp9	Cxcl1
Itgb1	Itgb1	Itgax	Cxcl1	Timp1	Hif1a	Timp1
Itgax	Cxcl1	Nfkbia	Itgb1	Adipoq	Cxcl1	Adipoq
Cxcl1	Itgax	Serpine1	Itgax	Itgax	Sell	Itgax
Mpo	Serpine1	Mpo	Serpine1	Thbs1	Itgav	Thbs1
Serpine1	Mpo	Itgb1	Mpo	Mpo	Tlr2	Mpo
Adipoq	Csf1	Csf1	Csf1	Sod2	Cxcl2	Serpine1
Thbs1	Lcn2	Lcn2	Thbs1	Cxcl1	Il6	Csf1
Csf1	Thbs1	Adipoq	Lcn2	B2m	Cd63	Lcn2
Lcn2	Adipoq	Cxcl2	Adipoq	Serpine1	Lcn2	
B2m	Cxcl2	Thbs1	Cxcl2	Csf1	Itgam	
Sod2	Socs3	Cxcr2	Socs3	Lcn2	Thbs1	
					Nt5e	
					Elane	
					Itgax	
					Ptprc	
					Socs3	
					Timp1	
					B2m	
					Pxdn	
					Serpine1	
					Cxcr2	