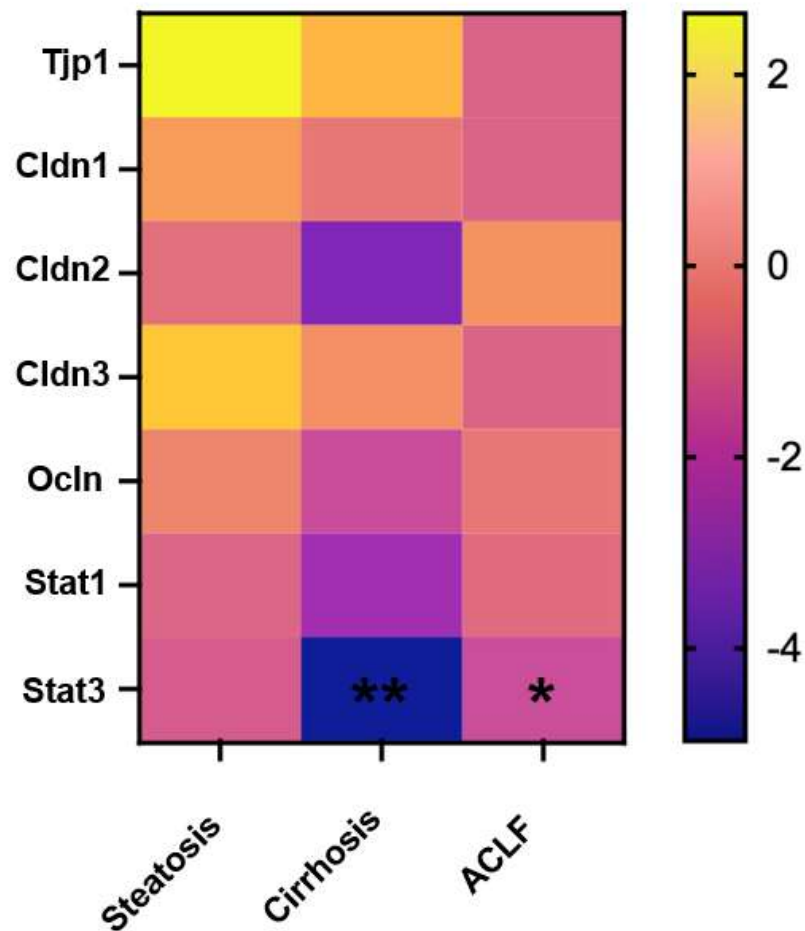


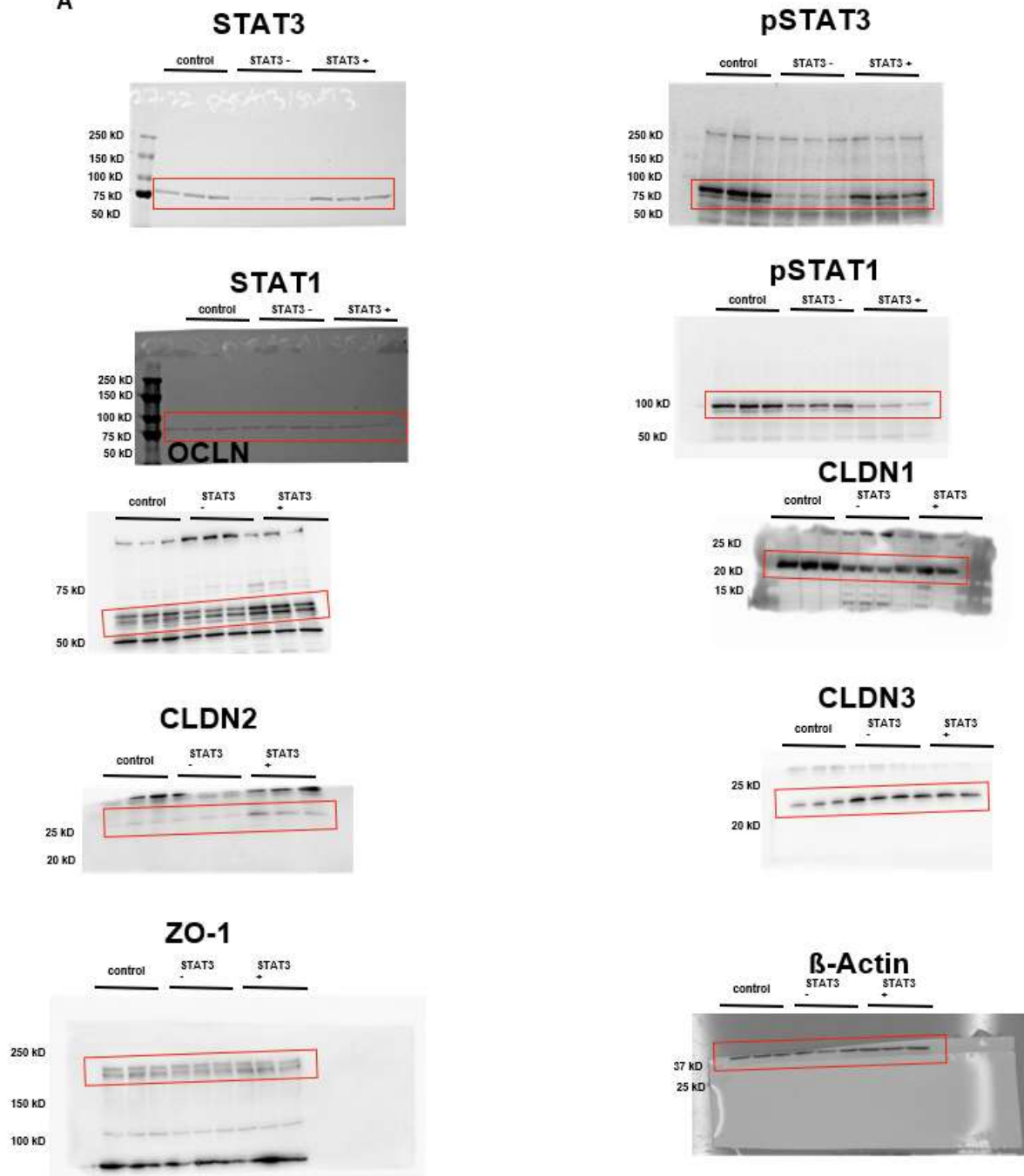


Supplementary Figure 1 Progressive changes in tight-junction mRNA levels from steatosis to ACLF, with *Stat3* upregulation occurring only in cirrhotic mice. RNA was isolated from intestinal tissue of mouse models generating steatosis, cirrhosis, and ACLF and mRNA expression levels of *Tjp1*, *Cldn1*, *Cldn2*, *Cldn3*, *Ocln*, *Stat1*, and *Stat3* were determined by RT-qPCR and compared to healthy controls. Results are shown as heatmap depicting log₂ fold changes normalized to healthy controls. While most transcripts displayed consistent trends across disease stages, STAT3 expression was significantly increased in cirrhosis ($P < 0.05$) and further elevated in ACLF ($P < 0.01$). Statistical analysis was assessed by one-way ANOVA with Dunnett's multiple comparisons test. * $P < 0.05$ and ** $P < 0.01$



Supplementary Figure 2 Original uncropped Western blot images corresponding to Figure 2A. STAT3 protein levels were assessed in Caco-2 and T84 cells with reduced or enhanced STAT3 expression compared to endogenous STAT3-expressing controls. Representative full-length blots from four independent experiments are shown.

A



B



Supplementary Figure 3 Original uncropped Western blot images corresponding to Figures 3 and 4. (A) Full-length blots from Caco-2 cells showing STAT3, phosphorylated STAT3 (pSTAT3), STAT1, phosphorylated STAT1 (pSTAT1), occludin (OCN), claudin-1 (CLDN1), claudin-2 (CLDN2), claudin-3 (CLDN3), zonula occludens-1 (ZO-1), and β -actin under conditions of reduced or enhanced STAT3 expression compared to endogenous controls. (B) Full-length blots from T84 cells showing the same protein panel under identical experimental conditions.

Representative uncropped blots from independent experiments, including loading controls, are presented.

Supplementary Table 1 Cross-validated lipid species significantly altered in STAT3-overexpressing (STAT3 +) Caco-2 and T84 cells, shown as normalized signal intensities (a.u.) across biological replicates (n = 5)

ACell line	Lipid	PC 18:1_18:1	O- PC O-34:1	SM 36:0;O2
Caco-2	control	0,79700	4,46333	0,03337
		1,68333	6,83667	0,08293
		1,58333	5,97333	0,05037
		1,34667	5,30667	0,04920
		0,73833	2,65333	0,02453
	STAT3 +	1,19067	5,06333	0,05190
		3,07667	18,06667	0,40333
		2,64667	13,16667	0,24400
		3,23667	13,50000	0,42633
		3,15000	13,16667	0,43200
T84	control	16,53333	117,33333	0,13900
		12,53333	92,70000	0,05819
		12,80000	99,13333	0,04887
		14,70000	110,66667	0,08547
		8,31667	71,93333	0,01446
	STAT3 +	19,76667	128,66667	0,11570
		21,26667	118,33333	0,14133
		24,36667	130,33333	0,17700
		20,56667	114,00000	0,15567
		27,20000	139,33333	0,23733

Supplementary Table 2 Cross-validated lipid species significantly altered in STAT3-knock down (STAT3 -) Caco-2 and T84 cells, shown as normalized signal intensities (a.u.) across biological replicates (n = 5)

Cell line		PG 40:8	LPC 18:2	LPC 20:3	PC 39:4	PC O- 36:1	TG 52:1	TG O- 50:1	TG O- 50:2	TG O- 50:3	TG O- 52:3
Caco-2	contr	0,18	0,03	0,02	0,00	1,2233	4,79	0,10	0,10	0,01	0,01
	ol	733	787	260	770	3	333	967	250	133	243
		0,20	0,04	0,01	0,00	1,7066	4,24	0,11	0,06	0,00	0,01
		167	997	900	604	7	000	213	853	999	140
		0,22	0,06	0,02	0,00	1,5200	4,81	0,09	0,06	0,01	0,01
		100	403	537	625	0	667	787	783	093	233
		0,21	0,05	0,02	0,00	1,3300	4,60	0,11	0,08	0,01	0,01
		233	583	407	676	0	000	667	963	100	450
		0,15	0,03	0,01	0,00	0,8330	4,02	0,07	0,05	0,00	0,00
		600	920	853	494	0	000	363	873	719	998
	STA	0,09	0,03	0,01	0,00	5,0233	7,44	0,56	0,25	0,02	0,03
	T3 -	787	283	840	338	3	333	167	367	750	490
		0,11	0,03	0,01	0,00	2,9633	4,28	0,26	0,11	0,01	0,01
		037	087	142	111	3	000	167	503	012	540
		0,11	0,02	0,01	0,00	7,5866	6,40	0,75	0,33	0,02	0,03
		500	693	613	175	7	667	033	067	617	737
T84		0,09	0,02	0,01	0,00	9,0933	8,69	0,84	0,38	0,03	0,05
		093	903	897	624	3	000	433	967	693	587
		0,09	0,02	0,01	0,00	8,5233	7,66	0,73	0,29	0,02	0,03
		147	933	700	363	3	667	700	967	280	557
	contr	0,30	0,08	0,05	0,00	43,333	0,80	0,20	0,11	0,01	0,01
	ol	133	363	260	135	33	167	700	050	280	500
		0,24	0,06	0,04	0,00	29,166	0,55	0,12	0,05	0,00	0,00
		767	590	693	136	67	033	733	810	825	921
		0,16	0,05	0,03	0,00	32,100	0,50	0,13	0,05	0,00	0,00
		167	483	700	062	00	567	600	317	711	773
		0,24	0,07	0,04	0,00	34,766	0,67	0,20	0,09	0,01	0,01
		100	613	483	176	67	567	733	493	100	207

	0,09	0,04	0,02	0,00	20,200	0,26	0,08	0,03	0,00	0,00
	330	937	820	020	00	700	280	797	394	449
STA	0,01	0,03	0,01	0,00	38,166	1,03	0,26	0,16	0,01	0,01
T3 -	623	497	877	000	67	233	033	067	430	707
	0,02	0,03	0,02	0,00	50,433	0,86	0,31	0,17	0,01	0,01
	510	570	203	009	33	367	100	900	450	880
	0,02	0,05	0,02	0,00	75,733	1,71	0,51	0,28	0,01	0,02
	613	263	933	009	33	000	300	133	920	763
	0,03	0,04	0,03	0,00	87,066	2,08	0,71	0,42	0,03	0,04
	267	917	077	044	67	667	067	333	513	510
	0,04	0,05	0,04	0,00	117,66	3,41	0,95	0,54	0,03	0,05
	413	967	033	072	667	000	500	633	560	377