Additional file

Lrp6 Genotype Affects Individual Susceptibility to Nonalcoholic Fatty Liver Disease and Silibinin Therapeutic Response via Wnt/β-catenin-Cyp2e1 Signaling

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Additional file 1.

Table S1. Comparison of odd ratios for NAFLD between different SNP genotypes and their possible influences

Gene name	**SNP**	**Nucleotide change**	**Protein change**	**Compared genotype groups**	**Odd ratios for NAFLD (95% CI)**	**P value**	**Possible influence**
PEMT	rs7946	g.17409560C>T	p.Val212Met	CT+TT vs CC	0.899(0.549-1.472)	0.672	Lipid import/synthesis
				TT vs CT+CC	0.733(0.143-3.757)	0.710	
PGC1β	rs7732671	g.149212243G>C	p.Ala203Pro	CG+CC vs GG	1.699(0.768-3.758)	0.191	
				GC vs GG	1.551(0.892-2.696)	0.120	
SLC27A5	rs35350976	g.59023174A>G	p.Met50Thr	AG+GG vs AA	0.894(0.399-2.006)	0.787	
				GG vs AG+AA	1.429(0.062-32.823)	0.823	
PNPLA3	rs738409	g.44324727C>G	p.Ile148Met	CG+GG vs CC	1.080(0.681-1.713)	0.744	Lipid export/oxidation
				GG vs CG+CC	1.155(0.621-2.148)	0.648	
MTTP	rs2306985	g.100516022C>G	p.His297Gln	CG+GG vs CC	0.930(0.468-1.848)	0.836	
				GG vs CG+CC	1.070(0.680-1.682)	0.770	
CYP2E1	rs6413419	g.135345675G>T	p.Val179Phe	Only GG genotype	-	-	Lipid peroxidation
L-FABP	rs2241883	g.88424066T>C	p.Thr94Ala	**CT+CC vs TT**	**0.606(0.380-0.968)**	**0.036**	**Cholesterol absorption/synthesis**
				CC vs CT+TT	0.955(0.304-3.000)	0.937	
FASN	rs2228305	g.80042792C>T	p.Val1483Ile	CT+TT *vs* CC	1.470(0.125-17.291)	0.760	Fatty acid/triglyceride synthesis
				CT vs CC	0.150(0.012-1.834)	0.138	
ApoE	rs440446	g.45409167C>G	p.Asn14Lys	CG+GG vs CC	0.925(0.574-1.490)	0.749	VLDL synthesis/export
				GG vs CG+CC	1.067(0.570-1.996)	0.839	
mTOR	rs28990992	g.11249789G>C	p.Glu51Asp	CG+CC vs GG	0.878(0.377-2.043)	0.762	
				CC vs CG+GG	0.550(0.040-7.529)	0.654	
TCF7L2	rs77961654	g.114925369C>A	p.Pro200Thr	CA+AA vs CC	0.948(0.603-1.493)	0.819	Glucose metabolism/insulin resistance
				AA vs CA+CC	0.895(0.421-1.904)	0.773	
PPARG	rs1801282	g.12393125C>G	p.Pro12Ala	GG vs GC	1.271(0.687-2.351)	0.445	
IL6	rs2069849	g.22771156C>T	p.Phe201Leu	CT vs CC	2.724(0.197-37.696)	0.455	Cytokines
Fas	rs3218619	g.90762801G>A	p.Ala16Thr	Only GG genotype	-	-	Metabolic Stress

TLR4	rs4986790	g.120475302A>G	p.Asp299Gly	Only AA genotype	-	-	Steatohepatitis-endotoxin response
LRP6	rs2302685	g.12301898C>T	p.Val1062Ile	CT+TT vs CC	0.367(0.035-3.831)	0.402	**Wnt/β-catenin signaling pathway**
				TT vs CT+CC	**2.853(1.378-5.910)**	**0.005**	
APC1	rs459552	g.112176756T>A	p.Val1822Asp	AT+AA vs TT	1.931(0.235-15.894)	0.541	
				AA vs AT+TT	0.692(0.392-1.219)	0.202	
DVL1	rs61735963	g.1277183C>T	p.Ala157Thr	Only CC genotype	-	-	
SIRT3	rs28365927	g.236091G>A	p.Arg80Trp	GA+AA vs GG	1.557(0.927-2.616)	0.094	Apoptosis signaling pathway
				AA vs GA+GG	0.972(0.150-6.310)	0.976	
HIF3A	rs3764609	g.46823702A>G	p.Gln274Arg	AG+GG vs AA	1.186(0.742-1.895)	0.476	HIF signaling pathway
				GG vs AG+AA	1.173(0.639-2.155)	0.607	
NFKBID	rs8113704	g.36387881A>G	p.Val181Ala	GA+GG vs AA	1.062(0.618-1.826)	0.828	NFKB signaling pathway
				GG vs GA+AA	2.903(0.399-21.121)	0.292	
STAT2	rs2066811	g.56742997T>C	p.Ile464Val	only TT genotype	-	-	JAK-STAT signaling pathway

Note: "-" indicates that statistic analysis cannot be performed due to only one genotype group.

Abbreviations: *PEMT*, phosphatidylethanolamine N-methyltransferase; *PGC 1β*, peroxisome proliferator-activated receptor gamma coactivator 1β; *SLC27A5*, solute carrier family 27 member 5; *PNPLA3*, patatin-like phospholipase domain-containing protein 3; *MTTP*, microsomal triglyceride transfer protein; *CYP2E1*, cytochrome P450, family 2, subfamily E, polypeptide 1; *FABP1*, fatty acid binding protein 1; *FASN*, fatty acid synthase; *ApoE*, apolipoprotein E; *mTOR*, mechanistic target of rapamycin; *TCF7L2*, transcription factor 7 like 2; *PPARG*, peroxisome proliferator activated receptor gamma; *IL6*, interleukin 6; *Fas*, Fas cell surface death receptor; *TLR4*, toll-like receptor 4; *LRP6*, low density lipoprotein receptor-related protein 6; *APC1*, adenomatous polyposis coli; *DVL1*, dishevelled segment polarity protein 1; *SIRT3*, sirtuin3; *HIF3A*, hypoxia-inducible factor 3-alpha; *NFKBID*, NF-Kappa-B Inhibitor Delta; *STAT2*, signal transducers and activators of transcription 2.

Additional file 2.

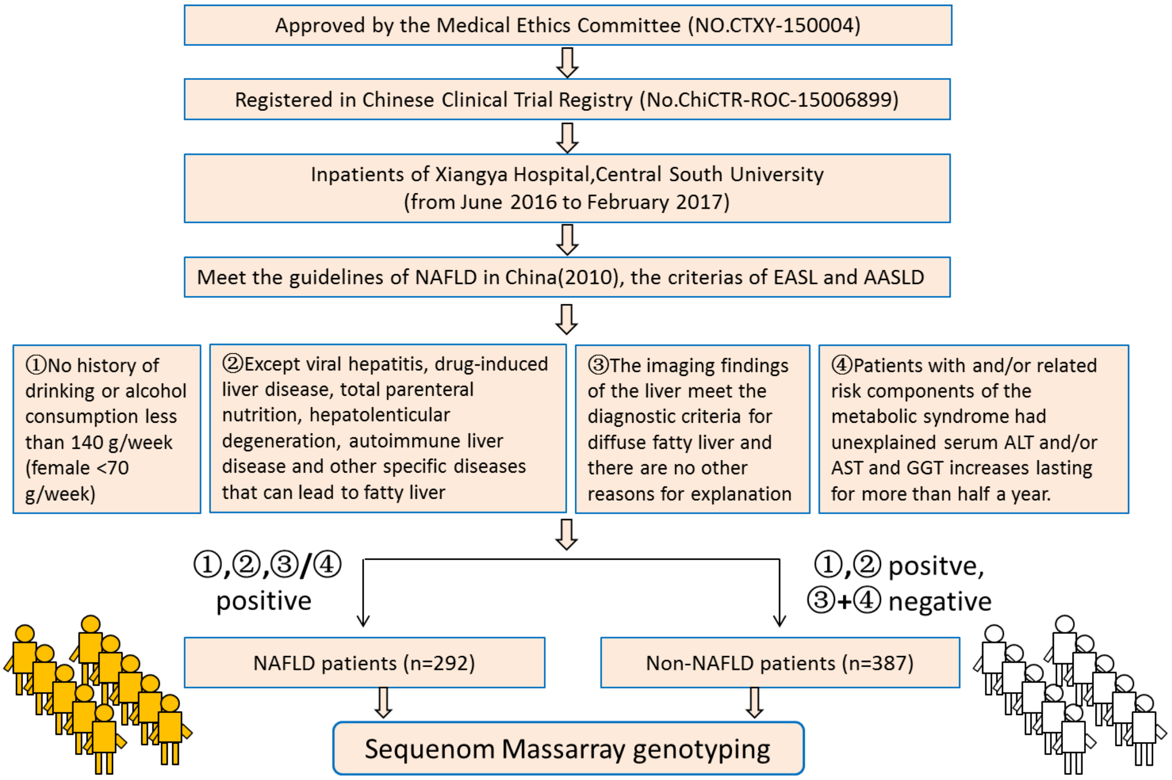

Figure S1. Schematic diagram of screening procedures for NAFLD and non-NAFLD subjects in clinical patient blood sample and data collection.

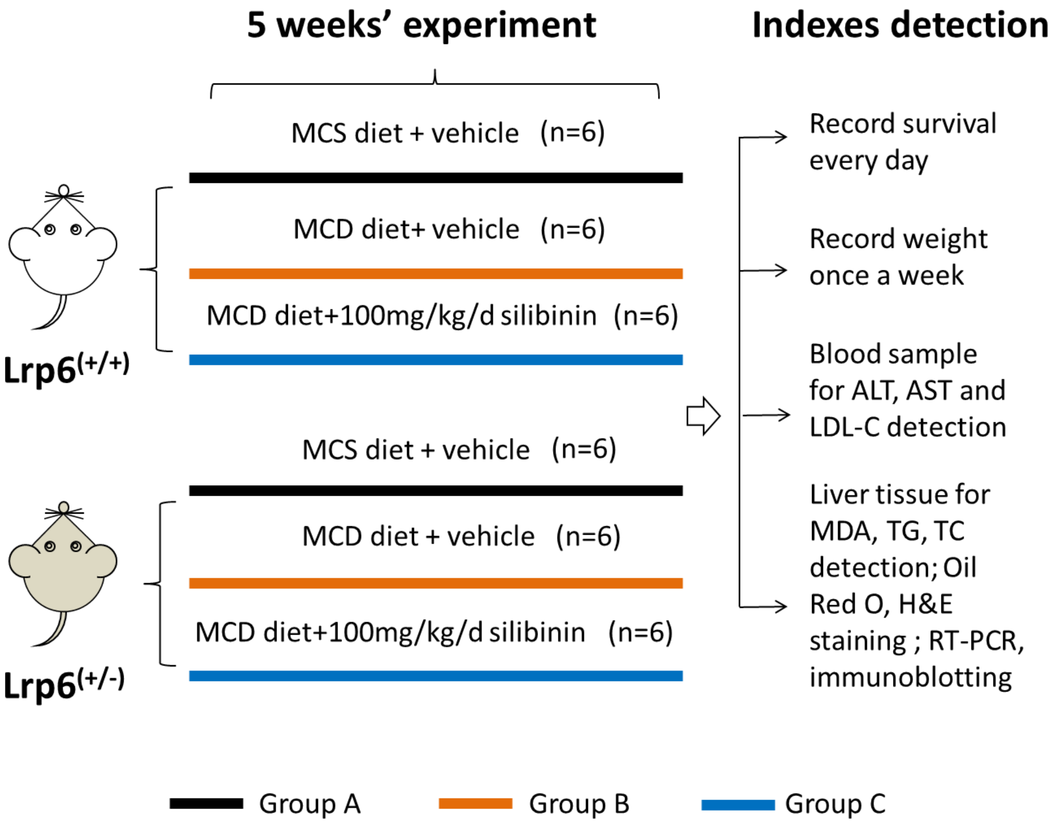

Figure S2. The experiment procedure and index detection during MCD diet-induced NAFLD and silibinin treatment between *Lrp6*$^{(+/+)}$ and *Lrp6*$^{(+/-)}$ mice, with a MCS diet as the control.

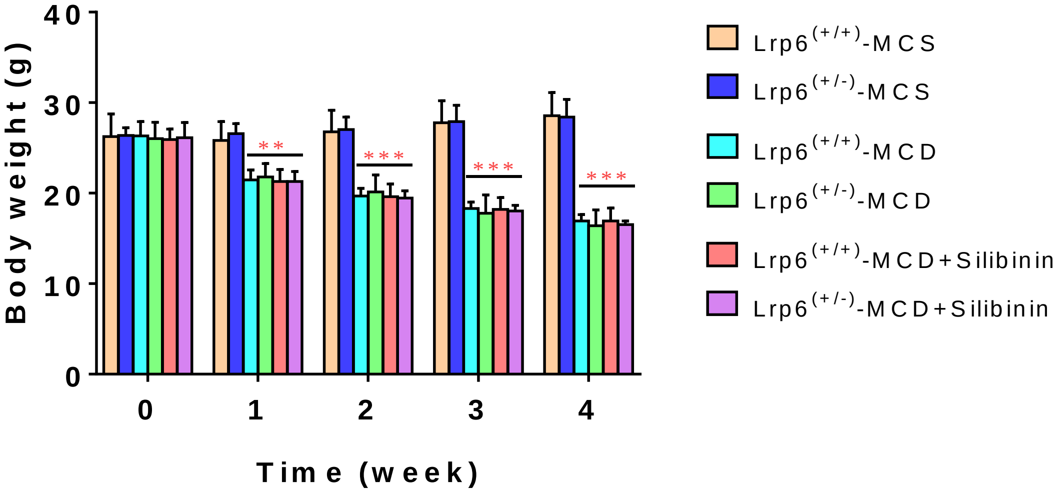

Figure S3. The changes in the mice’s body weight during NAFLD moulding with and without the treatment of silibinin between the *Lrp6*$^{(+/+)}$ and the *Lrp6*$^{(+/-)}$ mice groups.

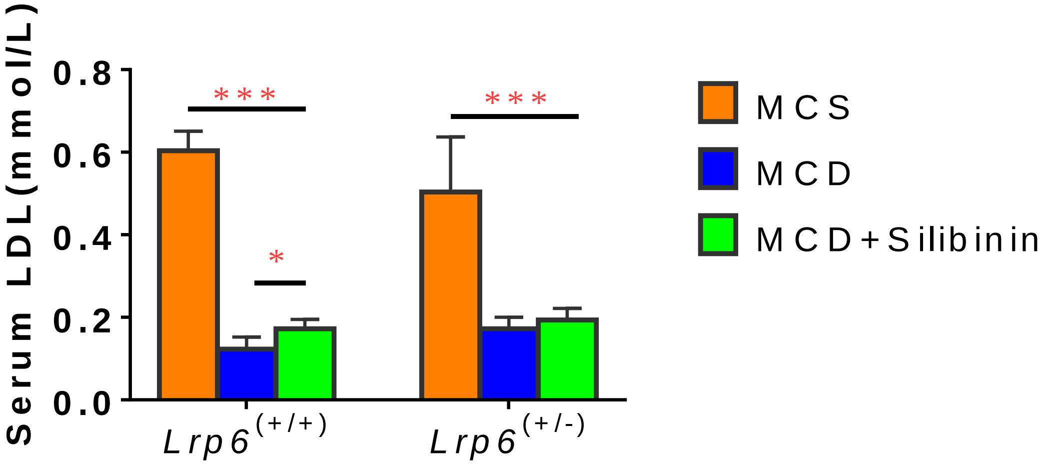

Figure S4. Changes in the LDL level during NAFLD moulding with and without the treatment of silibinin between the *Lrp6*$^{(+/+)}$ and the *Lrp6*$^{(+/-)}$ mice groups.

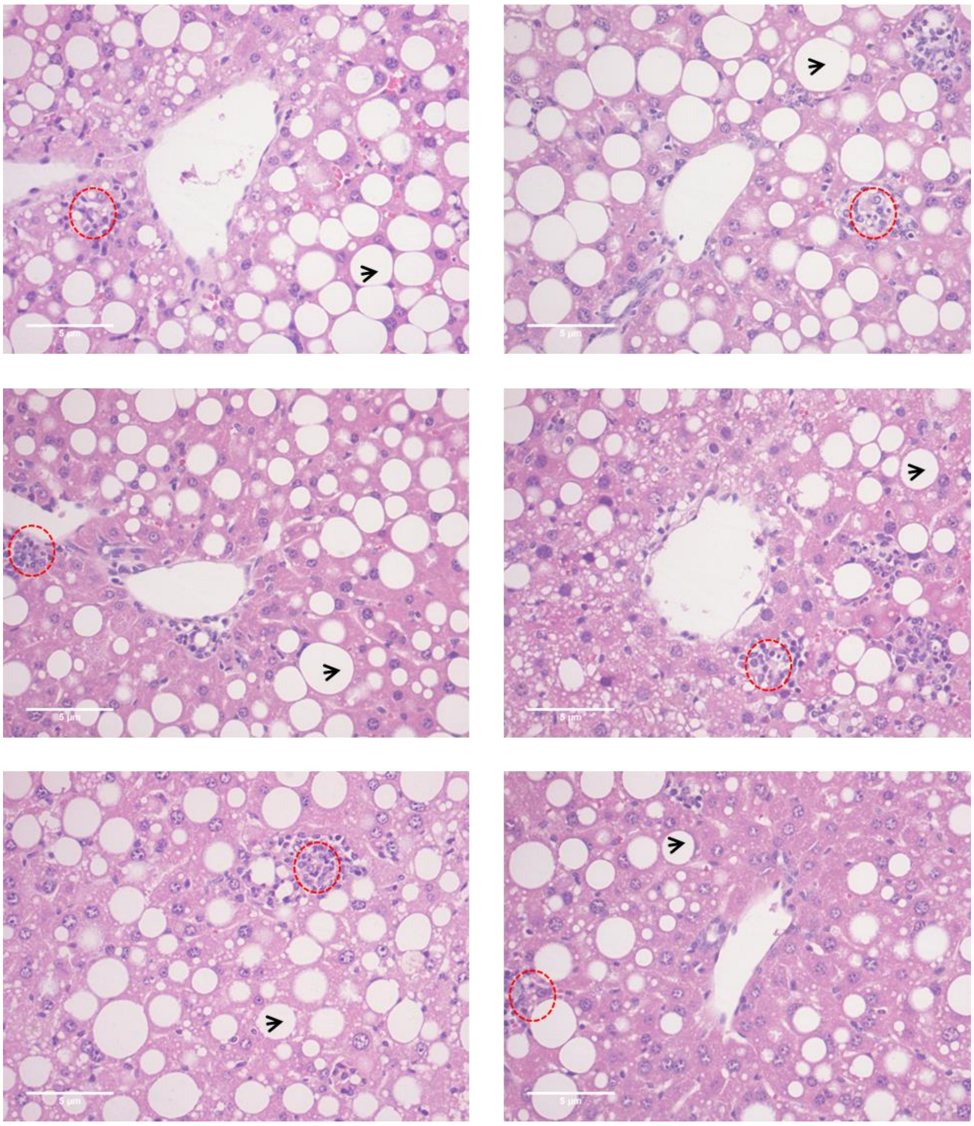

Figure S5. Additional H&E figures for inflammatory and fibrotic phenotypes of MCD-induced NAFLD mice model. Macrovesicular steatosis indicated with arrow and necroinflammatory foci indicated with circular broken lines (Scale bar, 5μm).