Haploinsufficiency of Lipin3 leads to hypertriglyceridemia and obesity via disrupting the expression and nucleocytoplasmic localization of Lipin1

Short title: Haploinsufficiency of Lipin3 leads to HTG

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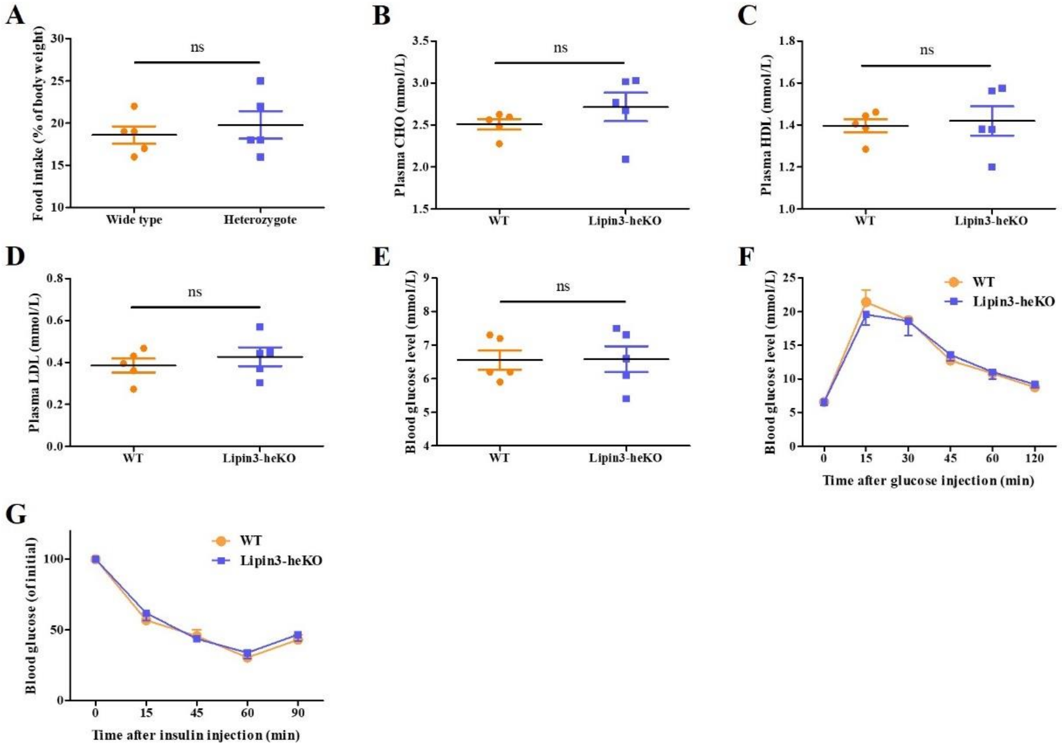
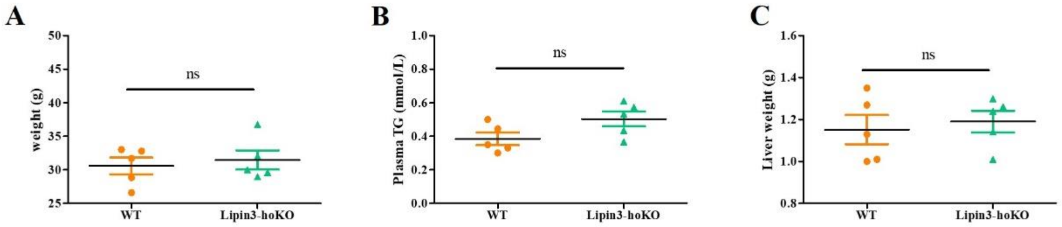
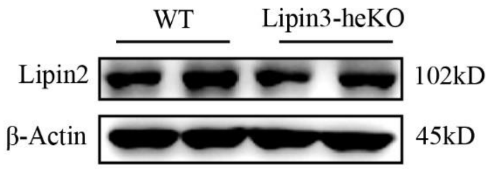


Supplementary Figure 1. (A) The food intake analysis of WT and Lipin3-heKO mice. The plasma (B) total cholesterol, (C) high-density lipoprotein, (D) low-density lipoprotein and (E) blood glucose levels of WT and Lipin3-heKO mice. The glucose tolerance test (F) and insulin tolerance test (G) of WT and Lipin3-heKO mice. n = 5. ns, no significant difference.



Supplementary Figure 2. (A) Body weight of WT mice and Lipin3-hoKO mice. (B) Peripheral blood TG levels of WT mice and Lipin3-hoKO mice. (C) Weight of liver tissue in WT mice and Lipin3-hoKO mice. n = 5. ns, no significant difference.



Supplementary Figure 3. WB analysis revealed the expression of Lipin2 in the primary hepatocytes of WT and Lipin3-heKO.

Supplementary Table 1. The gene list of Sanger sequencing validation and co-segregation analysis.

CHR	POS	RB	AB	Gene	AAChange	SIFT	Polyphen2	MutationTaster	OMIM clinical phenotype	ToppGene function
1	1153002	C	T	SDF4	NM_016176:exon7:c.G979A:p.D327N	0,D	1.0,D	1.000,D	-	cerebellum development
2	228563809	TTA	T	SLC19A3	NM_025243:exon3:c.620_621del:p.I207fs	-	-	-	AR, thiamine metabolism dysfunction syndrome	thiamine transport
5	139751139	T	A	SLC4A9	NM_001258427:exon18:c.T2411A:p.I804N	0,D	0.972,D	1.000,D	-	regulation of cellular pH
8	125072864	T	C	FER1L6	NM_001039112:exon24:c.T3061C:p.C1021R	0,D	0.999,D	1.000,D	-	-
9	95005518	T	G	IARS	NM_002161:exon28:c.A2980C:p.I994L	0.05,D	0.607,P	1.000,D	AR, growth retardation	regulation of translational fidelity
9	130162257	CGTCGG	C	SLC2A8	NM_001271712:exon2:c.10_14del:p.V4fs	-	-	-	-	galactose transmembrane transport
12	69964192	C	T	FRS2	NM_001278357:exon4:c.C148T:p.R50C	0,D	0.963,D	1.000,D	-	optic placode formation
14	76639894	C	G	GPATCH2L	NM_017972:exon4:c.C910G:p.H304D	0.01,D	0.99,D	1.000,D	-	-

15	75014801	T	C	CYP1A1	NM_000499:exon2:c.A638G:p.E213G	0.01,D	0.9,P	1.000,D	-	ethylene metabolic process
16	417709	G	A	MRPL28	NM_006428:exon6:c.C737T:p.P246L	0.01,D	0.579,P	1.000,D	-	mitochondrial translation
16	49670226	C	T	ZNF423	NM_001271620:exon4:c.G2657A:p.R886Q	0,D	0.998,D	0.999,D	AR, Joubert syndrome	regulation of BMP signaling pathway
19	55526100	G	GAAGC	GP6	NM_001083899:exon8:c.1212_1213insGCTT:p.L405fs	-	-	-	AR, bleeding disorder	collagen-activated signaling pathway
20	39985711	A	T	LPIN3	NM_001301860:exon15:c.A1838T:p.D612V	0,D	0.959,D	1.000,D	-	triglyceride process
22	43219699	G	A	ARFGAP3	NM_001142293:exon7:c.C503T:p.S168F	0.01,D	0.988,D	1.000,D	-	golgi transport vesicle coating
X	129168574	C	G	BCORL1	NM_001184772:exon8:c.C4450G:p.P1484A	0.01,D	0.998,D	1.000,D	Shukla-Vernon syndrome	-

CHR = Chromosome; POS = position; RB = reference sequence base; AB = alternative base identified; D= damaging; P= probably damaging; AR= autosomal recessive; BP=Benign Supporting; PP= Pathogenicity Supporting; PS= Pathogenicity Strong.