

1 **Cholesterol induces lipoprotein lipase expression in a tree shrew (*Tupaia***

2 ***belangeri chinensis*) model of non-alcoholic fatty liver disease**

3 Linqiang Zhang<sup>1,2\*</sup>, Zhiguo Zhang<sup>1,2\*</sup>, Yunhai Li<sup>1\*</sup>, Shasha Liao<sup>1,3</sup>, Xiaoyun Wu<sup>1</sup>, Qing

4 Chang<sup>1</sup>, Bin Liang<sup>1#</sup>

5 1, Key Laboratory of Animal Models and Human Disease Mechanisms of Chinese  
6 Academy of Science & Yunnan province, Kunming Institute of Zoology, Chinese  
7 Academy of Sciences, Kunming, Yunnan 650223, China

8 2, Kunming College of Life Science, University of Chinese Academy of Sciences,  
9 Kunming, Yunnan 650204, China

10 3, School of Life Sciences, Anhui University, Hefei, Anhui 230601, China.

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12 \*: Equal contribution

13 #: Correspondence should be addressed to

14 Bin Liang

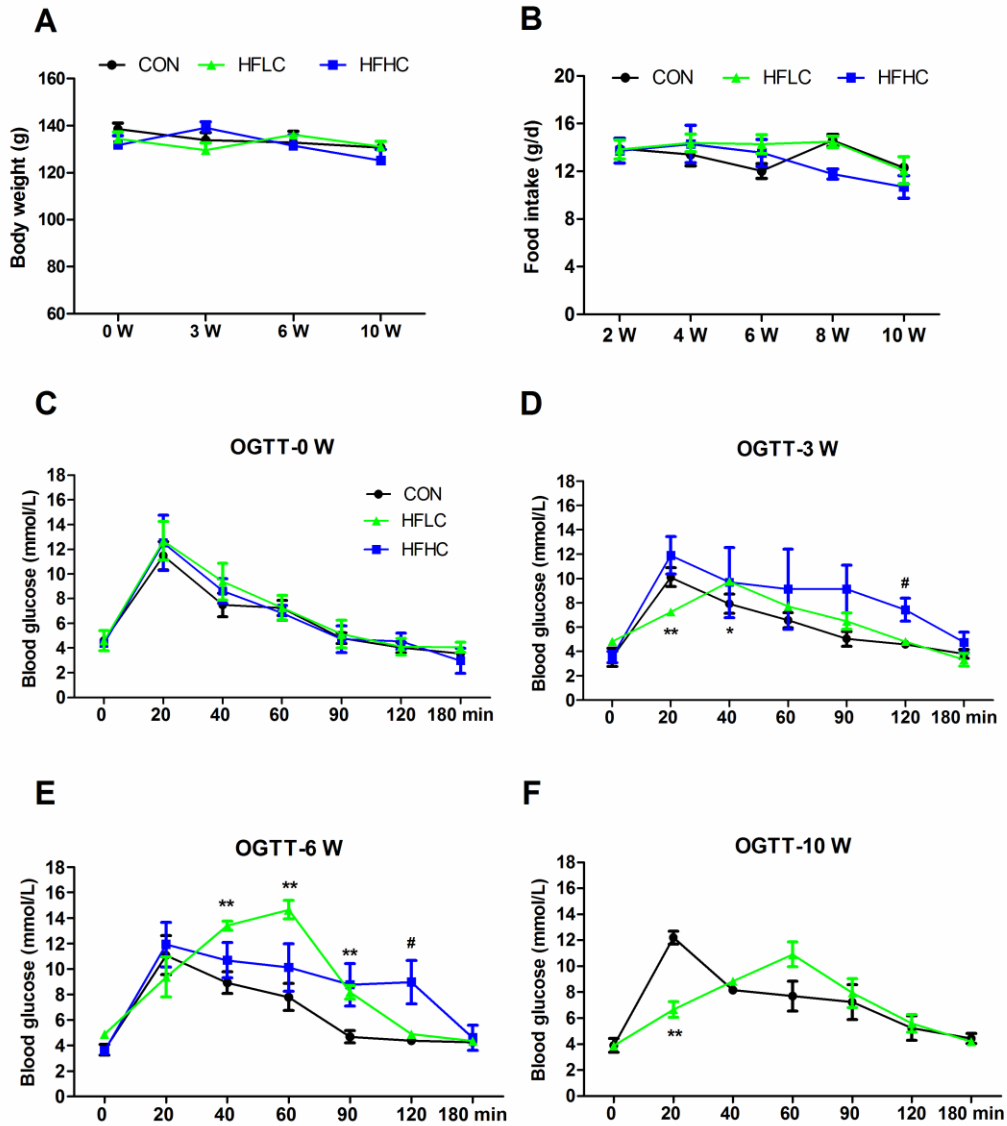
15 Tel: 086-871-65181927

16 E-mail: [liangb@mail.kiz.ac.cn](mailto:liangb@mail.kiz.ac.cn)

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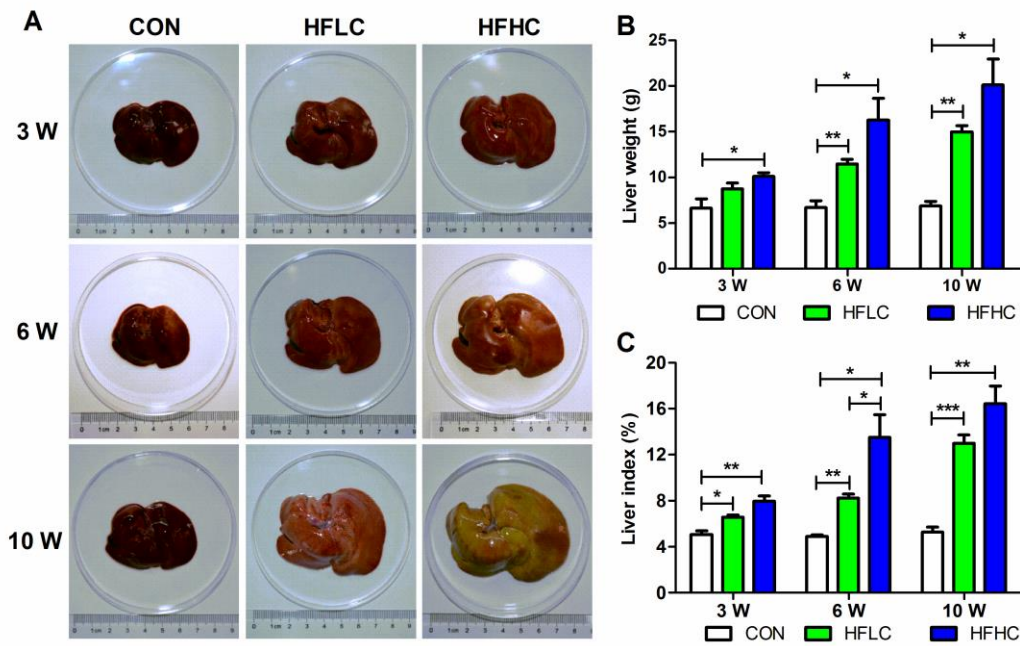
19 **Supplementary figures and legends**



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21 **Figure S1. Body weight, food intake and oral glucose tolerance test (OGTT) in**  
 22 **tree shrew.** Compared to control diet, both HFLC and HFHC diet did not change  
 23 body weight (A) and food intake (B). OGTT at 0 week (C) (n=4 for each group), 3  
 24 weeks (D) (n=4, 4, 5 for CON, HFLC and HFHC, respectively), 6 weeks (E) (n=4, 4,  
 25 3 for CON, HFLC and HFHC, respectively), and 10 week (F) (n=3, 3 for CON and  
 26 HFLC, respectively). Data were presented as mean  $\pm$  SEM. Significant difference  
 27 between two groups, \*: P<0.05, \*\*: P<0.01.

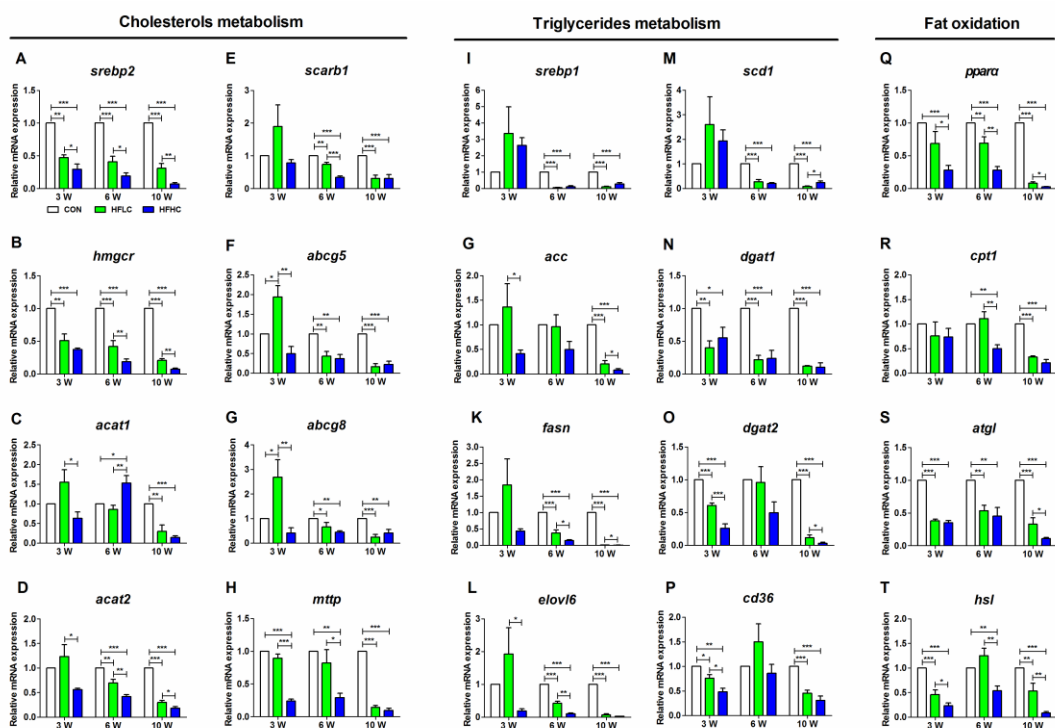
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31 **Figure S2. Liver morphology, liver weight and liver index.** A: liver morphology of  
 32 represented animal. Liver weight (B) and liver index (C) were significantly increased  
 33 in a time-dependent manner in both HFLC and HFHC group compared to control  
 34 group (CON). Data were presented as mean  $\pm$  SEM of 3-4 animals. Significant  
 35 difference between two groups, \*:  $P < 0.05$ , \*\*:  $P < 0.01$ , \*\*\*:  $P < 0.001$ .

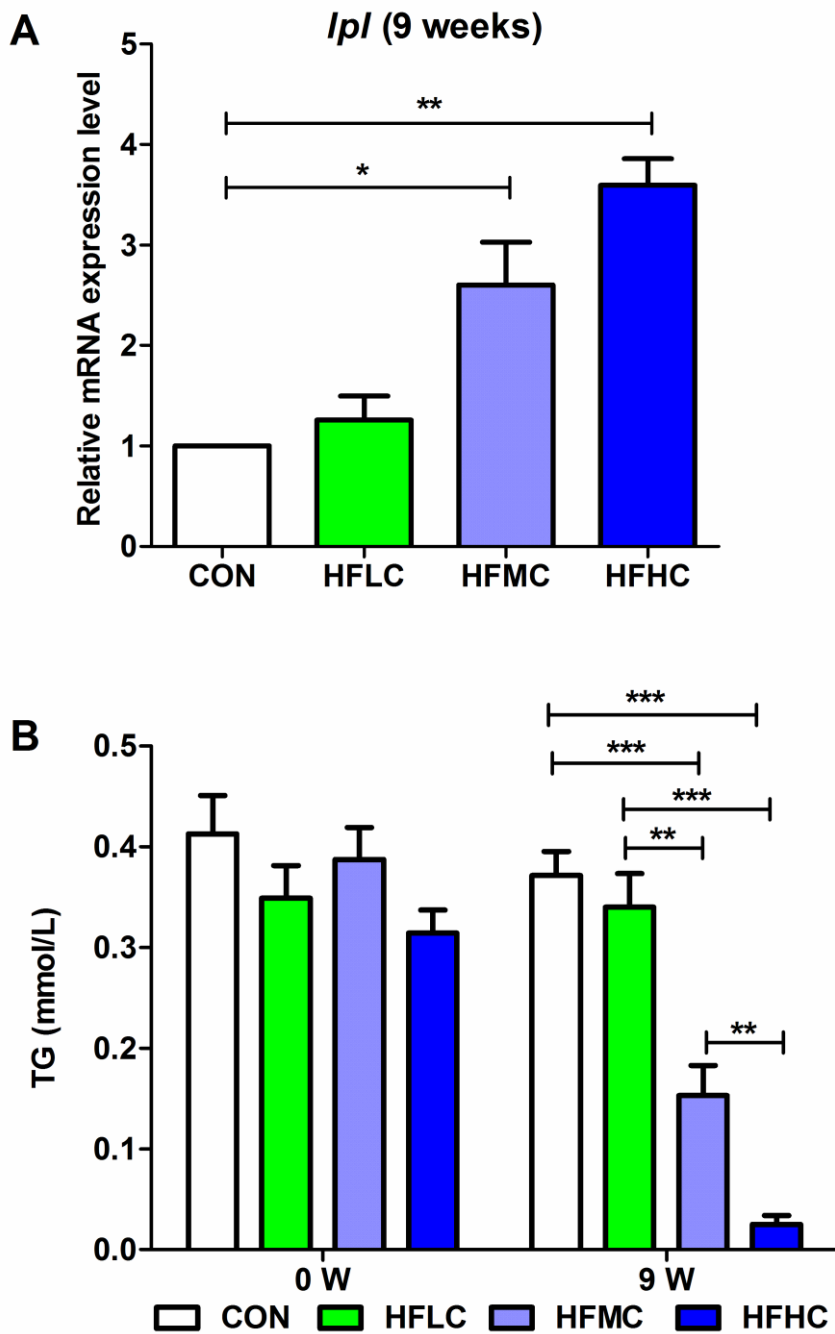
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39 **Figure S3.** The mRNA expression of genes involved in cholesterol, triglycerides  
 40 metabolism and fat oxidation. A-H: Relative mRNA expression of *srebp2*, *hmgcr*,  
 41 *acat1*, *acat2*, *scarb1*, *abcg5*, *abcg8* and *mttp* involved in cholesterol metabolism. I-P:  
 42 Relative mRNA expression of *srebp1*, *acc*, *fas*, *elovl6*, *scd1*, *dgat1*, *dgat2* and *cd36*  
 43 involved in triglycerides metabolism. Q-T: Relative mRNA expression of *ppara*, *cpt1*,  
 44 *atgl* and *hsl* involved in fat oxidation. Data were presented as mean  $\pm$  SEM of  
 45 3-4 animals. Significant difference between two groups, \*:  $P < 0.05$ , \*\*:  $P < 0.01$ , \*\*\*:  
 46  $P < 0.001$ . **Abbreviations:** SREBP: Sterol regulatory element binding protein;  
 47 HMGCR: 3-hydroxy-3-methyl-glutaryl-CoA reductase; ACAT: Acyl-coenzyme A  
 48 cholesterol acyltransferase; SCARB: Scavenger receptor class B member; ABCG:  
 49 ATP-binding cassette sub-family G member; MTP: Microsomal triglyceride transfer  
 50 protein; ACC: Acetyl-CoA carboxylase; FASN: Fatty acid synthase; ELOVL6: Family  
 51 member 6, elongation of long-chain fatty acids; SCD: Stearoyl-CoA desaturase; DGAT:  
 52 Diacylglycerol acyltransferase; CD-36: Cluster differentiation protein-36, fatty acid  
 53 translocase; CPT-1: Carnitine palmitoyltransferase-1; ATGL: Adipose triacylglycerol  
 54 lipase; HSL: Hormone-sensitive lipase.

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57 **Figure S4. The mRNA expression of *lpl* and plasma TG level.** A: The mRNA  
 58 expression of hepatic *lpl* among different diet groups at 9 weeks. HFMC: high fat  
 59 (20.2%), medium cholesterol (0.5%) diet (#D12107C). B: Plasma TG level in  
 60 different diet groups at 9 weeks. Data were presented as mean  $\pm$  SEM of 3-4 animals  
 61 for hepatic *lpl*, 6-8 animals for plasma TG, respectively. Significant difference  
 62 between two groups, \*\*:  $P < 0.01$ , \*\*\*:  $P < 0.001$ .

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64 **Supplementary table**

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	CON		HFHC		HFHC+P-407	
	0 W	3 W	0 W	3 W	0 W	3 W
	(n=6)	(n=6)	(n=5)	(n=5)	(n=6)	(n=3)
Body weight (g)	136.0±2.6	137.8±2.7	131.0±3.1	123.9±6.0	130.0±5.1	120.2±7.4 b*
AST(U/L)	177.8±45.6	133.0±19.4	113.2±35.5	304.6±42.6 a† d†	145.7±32.3	55.3±43.8 c†
ALT(U/L)	127.8±25.8	109.8±17.1	140.6±70.3	409.4±84.8 a† d*	124.7±38.4	45.33±2.4 c†
TC(mmol/L)	2.03±0.14	1.71±0.09	2.03±0.09	7.80±0.51 a† d†	2.01±0.17	31.15±0.47 b† c† d†
TG(mmol/L)	0.44±0.02	0.47±0.04	0.45±0.03	0.28±0.04 a* d*	0.40±0.05	4.20±0.70 b* c* d*
HDL-c(mmol/L)	1.21±0.10	0.98±0.09	1.18±0.07	2.78±0.17 a† d†	1.23±0.10	6.48±2.82 b† c* d*
LDL-c(mmol/L)	0.22±0.05	0.28±0.03	0.17±0.02	2.29±0.43 a† d†	0.19±0.03	18.77±0.58 b† c† d†
FBG(mmol/L)	4.17±0.30	4.28±0.29	4.34±0.46	4.58±0.26	4.07±0.40	5.57±0.24 b* d*
HbA1c(%)	4.65±0.08	4.06±0.19 d*	4.58±0.06	4.54±0.07 a*	4.25±0.17 b†	3.17±0.12 b† c† d†

66 **Table S1. Body weight, food intake, and blood biochemical parameters of tree shrew treated**  
67 **with P-407.** Data are presented as mean±SEM. a, b, c: indicated a significant difference of  
68 comparison between groups at same time point (\*P<0.05, †P<0.01). a: CON versus HFHC, b:  
69 CON versus HFHC+P-407, c: HFHC versus HFHC+P-407.d: indicated a significant difference of  
70 comparison in same diet group at different time point (\*P<0.05, †P<0.01). d: 0 W versus 3 W.

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