

Targeted deletion of Gpbar1 protects mice from cholesterol gallstone formation

Galya Vassileva^{*1}, Andrei Golovko*, Lisa Markowitz*, Susan J Abbondanzo*, Ming Zeng*, Shijun Yang*, Lizbeth Hoos†, Glen Tetzloff†, Diane Levitan*, Nicholas J Murgolo*, Kevin Keane‡, Harry R Davis Jr†, Joseph Hedrick*, and Eric L Gustafson*

*Department of Discovery Technologies

†Department of Cardiovascular/Metabolic Diseases

‡Department of Drug Safety & Metabolism

Schering-Plough Research Institute, Kenilworth, NJ 07033

¹To whom correspondence should be addressed (email: galya.vassileva@spcorp.com)

SUPPLEMENTAL ONLINE DATA

Figure S1. Body weights of mice on lithogenic (L) diet. Individual values were measured from 22 mice per group at baseline and after 9 weeks on lithogenic diet. Error bars represent S.D. * $p < 0.05$ when compared to baseline BW.

Figure S2. Gene expression analysis. Real-time quantitative PCR analysis was performed on mRNA from livers of Gpbar1^{-/-} and Gpbar1^{+/+} littermate mice. **A.** Cholesterol, phospholipids, and fatty acids synthesis and metabolism genes. **B.** Canalicular bile secretion genes. Error bars represent S.D. Abca1, ATP-binding cassette, sub-family A, member 1; Hmgcr, 3-hydroxy-3-methylglutaryl-Coenzyme A reductase; Ldlr, low-density lipoprotein receptor; Scarb1, scavenger receptor class B, member 1; Fasn, fatty acid synthase; Lpl, lipoprotein lipase; Pctp, phosphatidylcholine transfer protein; Abcb4, ATP-binding cassette, sub-family B (MDR/TAP), member 4; Abcg5, ATP-binding cassette, sub-family G (WHITE), member 5; Abcg8, ATP-binding cassette, sub-family G (WHITE), member 8; Abcb11, ATP-binding cassette, sub-family B (MDR/TAP), member 11.

Table S1. Primers sequences for the genes involved in the synthesis and metabolism of bile acids, cholesterol, phospholipids, and fatty acids, and in the negative feedback regulation of Cyp7a1.

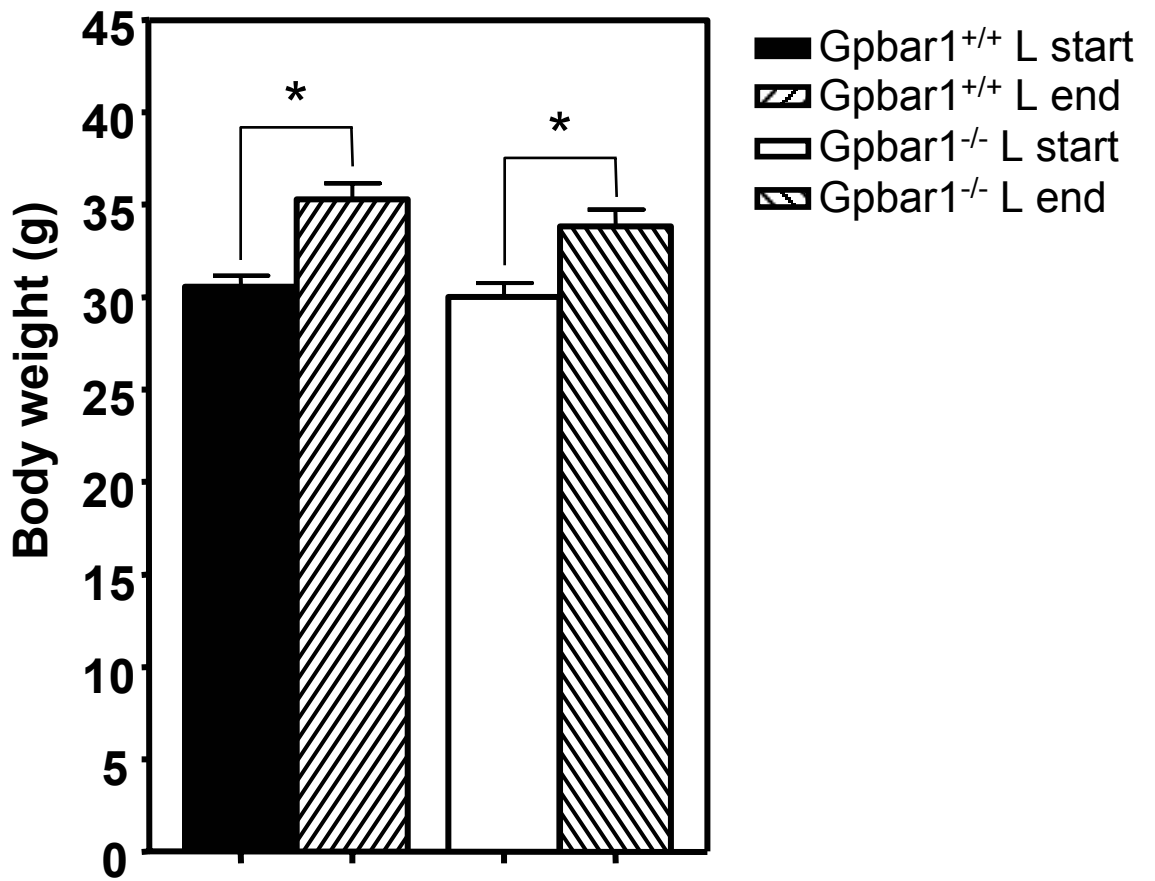


Figure S1

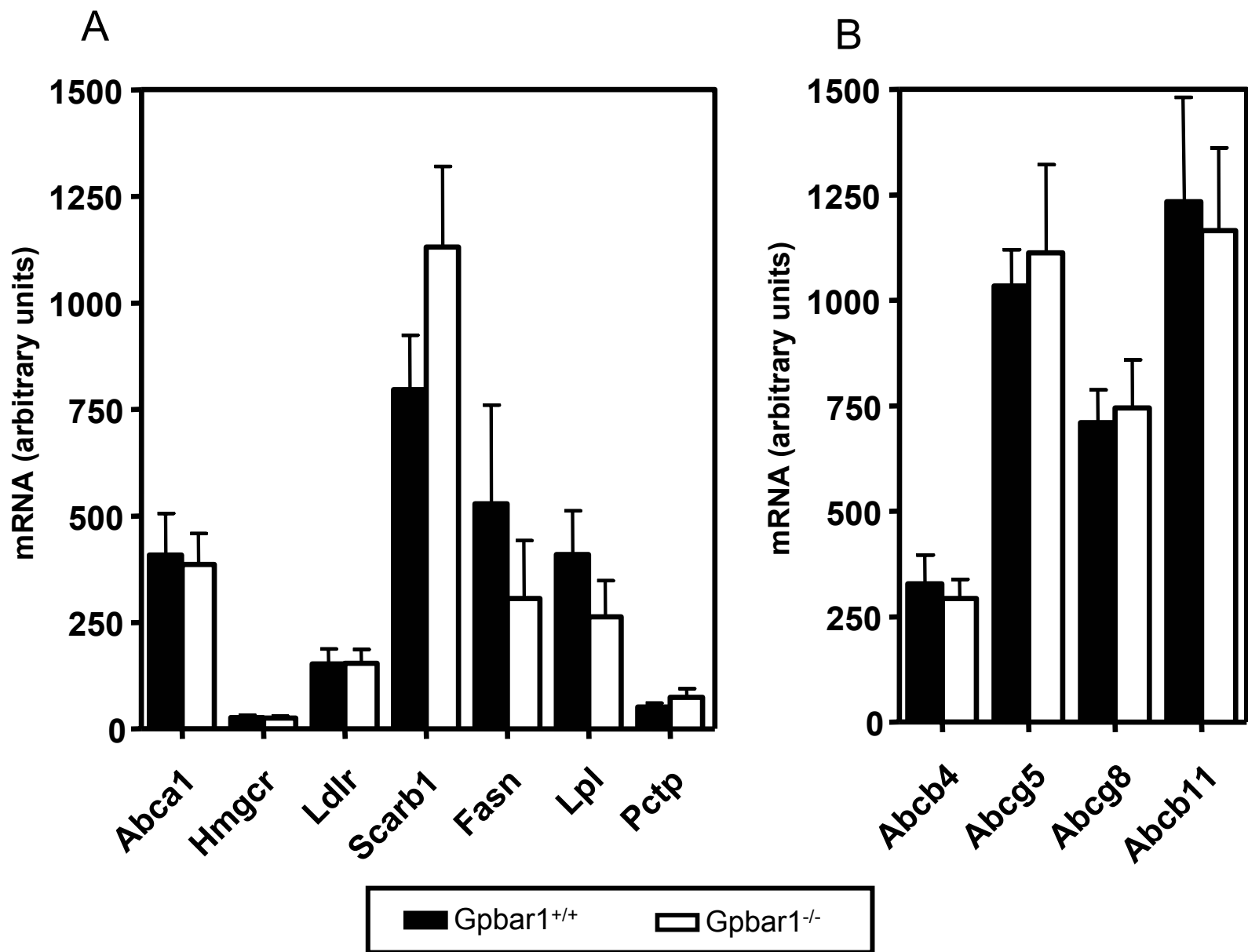


Figure S2

Gene	Sequence	Genebank Acc#
Cyp7a1	FP: 5-CCATGATGCAAAACCTCCAAT-3'	L23754
	RP: 5-ACCCAGACAGCGCTCTTTGA-3'	
	probe: 5'-TGAGACCTCCGGGCCTTCCT-3'	
Cyp8b1	FP: 5-TAGCCCTCTTTCCTCCACTCATA-3'	NM_010012
	RP: 5-GAACCGATCGAACCTAAATTCCT-3'	
Cyp27a1	FP: 5-CTGCGTCAGGCTTTGAAACA-3'	NM_024264
	RP: 5-TCGTTTAAGGCATCCGTGTAGA-3'	
FXR	FP: 5-CCACCGGCTGTCAGGATTT-3'	NM_009108
	RP: 5-GCATACCTTTAGCTGGCTTCACA-3'	
SHP	FP: 5-GCCTGGCCCGAATCCT-3'	L76567
	RP: 5-GGGTGCCTGGAATGTTCTTG-3'	
FTF	FP: 5-CGGTTTGCAACTACCCACAA-3'	NM_030676
	RP: 5-CGGGTAGCCGAAGAAGTAGCT-3'	
PXR	FP: 5-ACATTGAGTGTAGTCGGCCATATC-3'	NM_010936
	RP: 5-AGGACGGCCATGATCTTCAG-3'	
Ntcp	FP: 5-CACCGGGCCACAGAACT-3'	NM_011387
	RP: 5-TGATGAGCAGCAACATAACTACCA-3'	
Oatp1	FP: 5-CTCCCCGCAAGTCTTCATTCTAA-3'	AF148218
	RP: 5-TGGATGTCGCCAGGGAAAT-3'	
Oatp2	FP: 5-TGAAGCTCACTGCGAAGGAA-3'	NM_030687
	RP: 5-TCCATCATTCTGCATCGTAGGA-3'	
LXR	FP: 5-GTTCCACGGATGCTAATGAA-3'	NM_013839
	RP: 5-TGAATGGACGCTGCTCAAAG-3'	
Abca1	FP: 5-TCCTCATCCTCGTCATTCAA-3'	NM_013454
	GGACTTGGTAGGACGGAACCT-3'	
Hmgcr	FP: 5-GGCAGTCAGTGGGAACCTATTGC-3'	BC019782
	RP: 5-CCTCGTCCTTCGATCCAGTTT-3'	
Ldlr	FP: 5-CATAGGCTATCTGCTCTTCACCAA-3'	NM_010700
	RP: 5-GCGGTCCAGGGTTCATCTTC-3'	
Scarb1	FP: 5-CACGGCGTCCAGAATTT-3'	NM_016741
	RP: 5-GCTGAGTCCGTTCCATTTGTC-3'	
Fasn	FP: 5-CCTGGATAGCATTCCGAACCT-3'	NM_007988
	RP: 5-AGCACATCTCGAAGGCTACACA-3'	
Lpl	FP: 5-CCAGGATGCAACATTGGAGAA-3'	NM_008509
	RP: 5-CCACGTCTCCGAGTCTCTCT-3'	
Pctp	FP: 5-TGGCATACTGGGAAGTGAAGTAC-3'	NM_008796
	RP: 5-GGCGGGTGTAGACGTAATCTC-3'	
Abcb4	FP: 5-GGATCTTGAGGCAGCGAGAA-3'	NM_008830
	RP: 5-GGTTGCTGATGCTGCCTAGTT-3'	
Abcg5	FP: 5-CCCATACACCGGCATGCT-3'	NM_031884
	RP: 5-GGTCGCTGACGGCTCTCA-3'	
Abcg8	FP: 5-CCGTCGTCAGATTTCCAATGA-3'	NM_026180
	RP: 5-GGCTTCCGACCCATGAATG-3'	
Abcb11	FP: 5-AAGCTGCCAAGGATGCTAATG-3'	NM_021022
	RP: 5-CTCCAAGTGGGTGTCAAATTGC-3'	
Klb	FP: 5-TGCCACTGGGCAGAACCT-3'	NM_031180
	RP: 5-GCTCGGCTGCCTTCCA-3'	

Table S1