

SLC39A5-Y47X

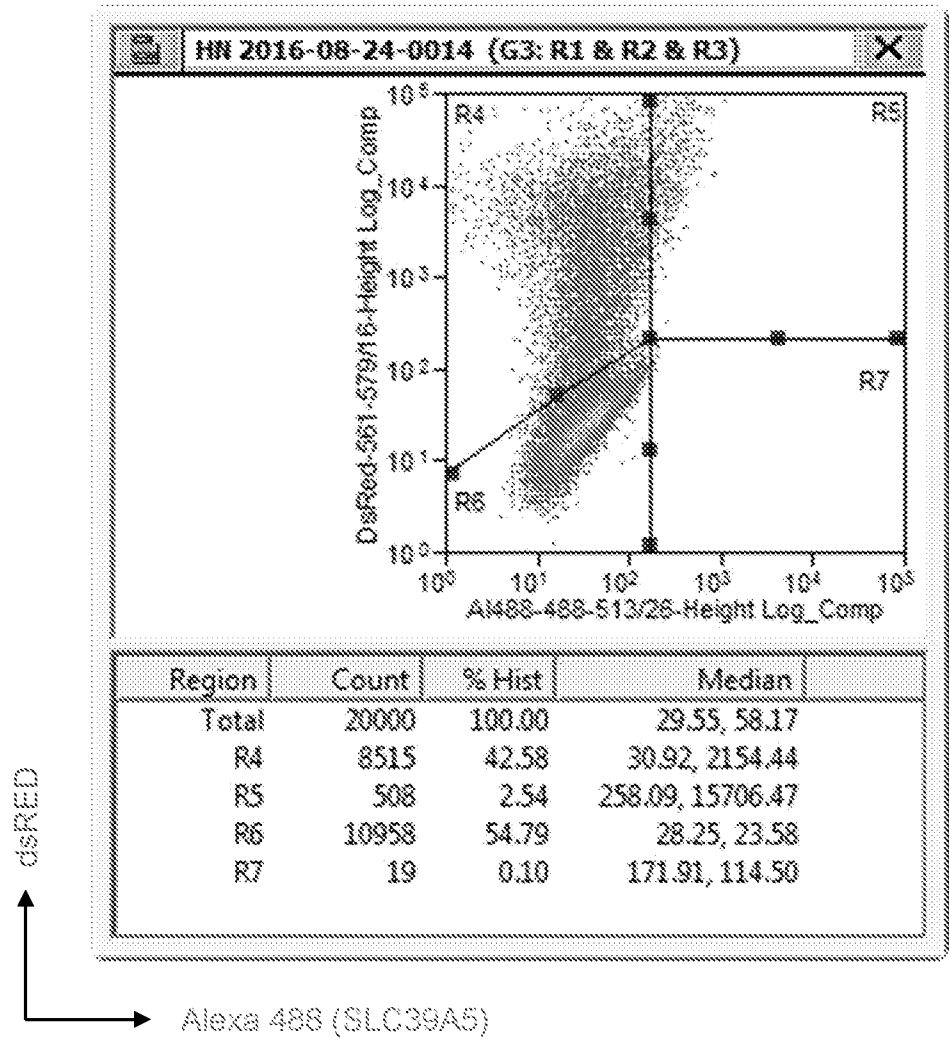


Figure 1A

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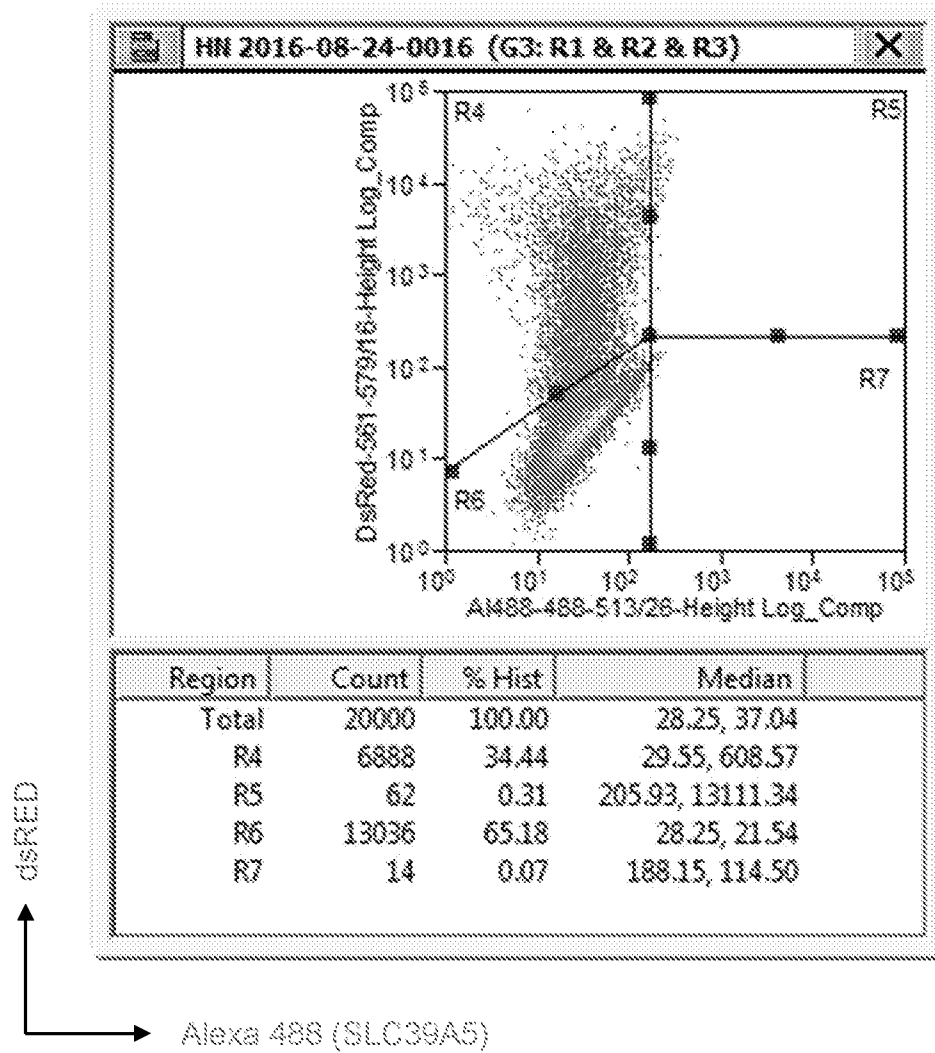
SLC39A5-R311X

Figure 1A (cont.)

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SLC39A5-R322X

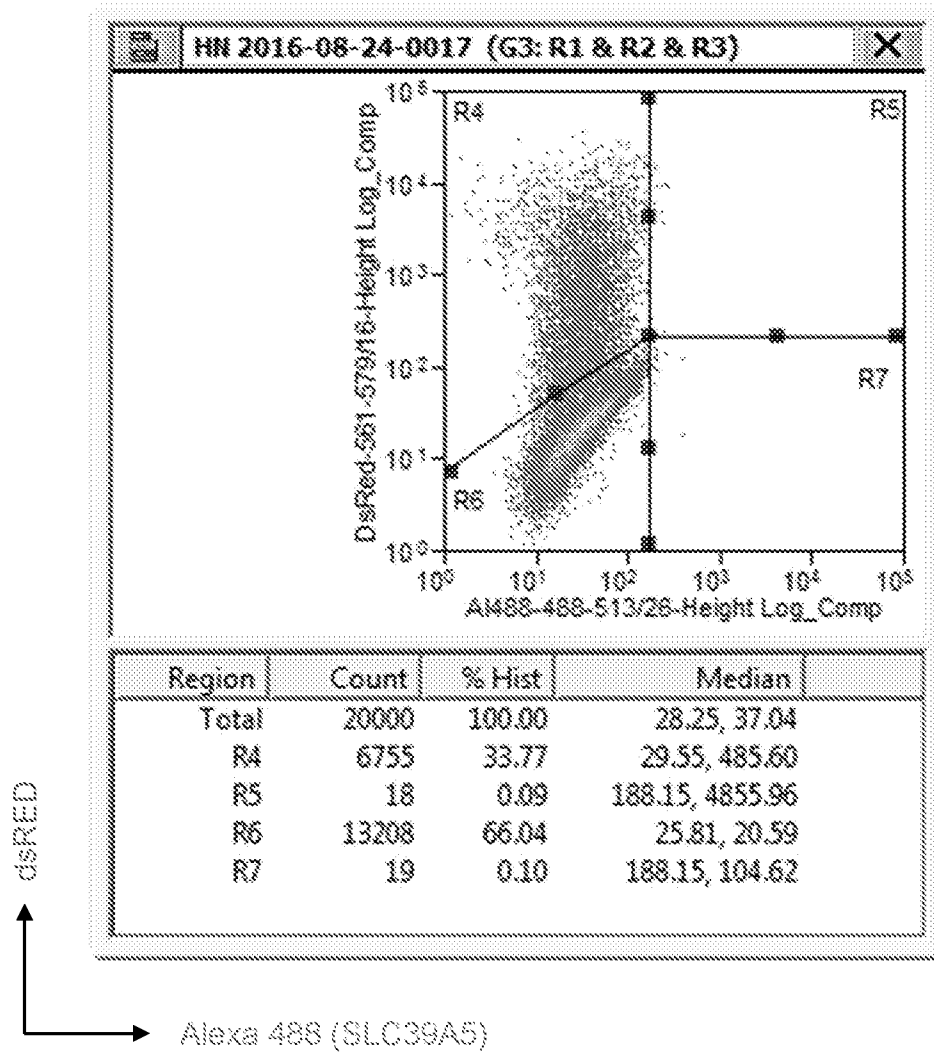


Figure 1A (cont.)

SLC39A5-M304T

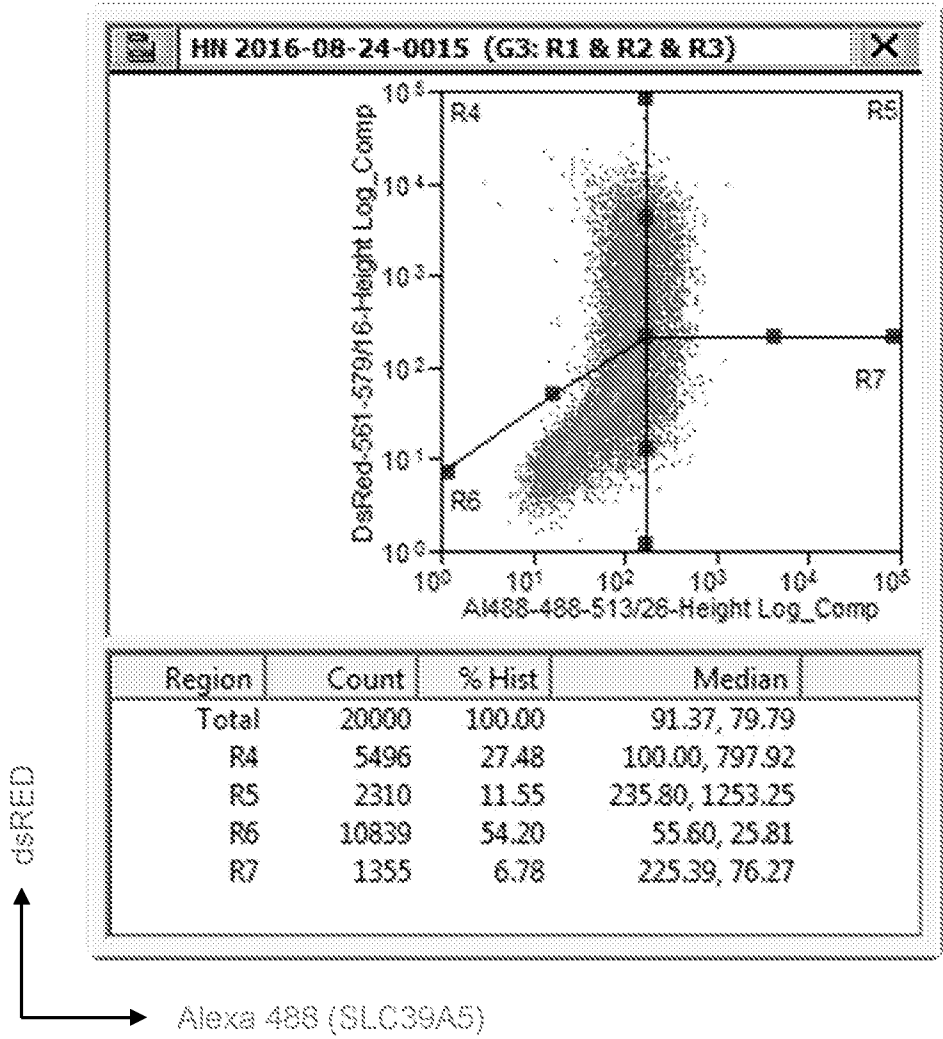


Figure 1A (cont.)

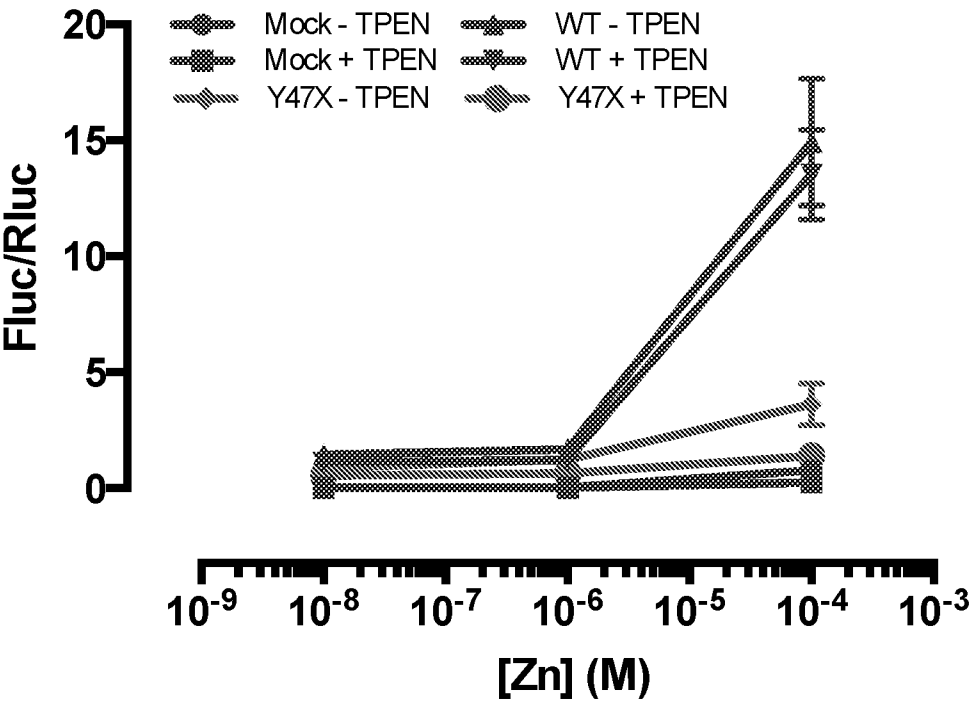
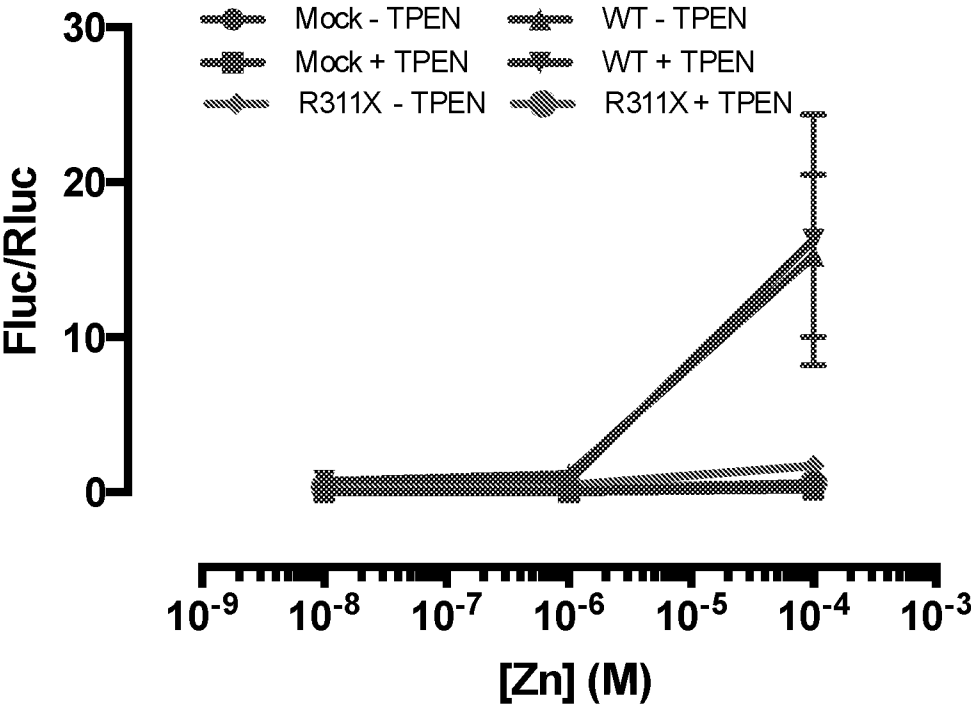


Figure 1B

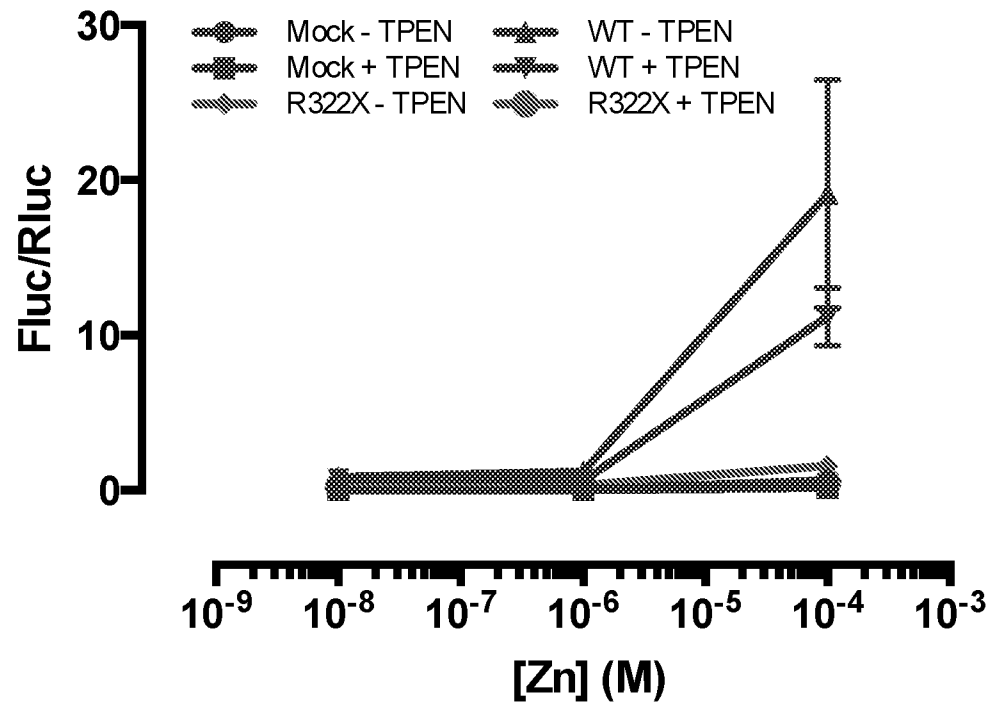
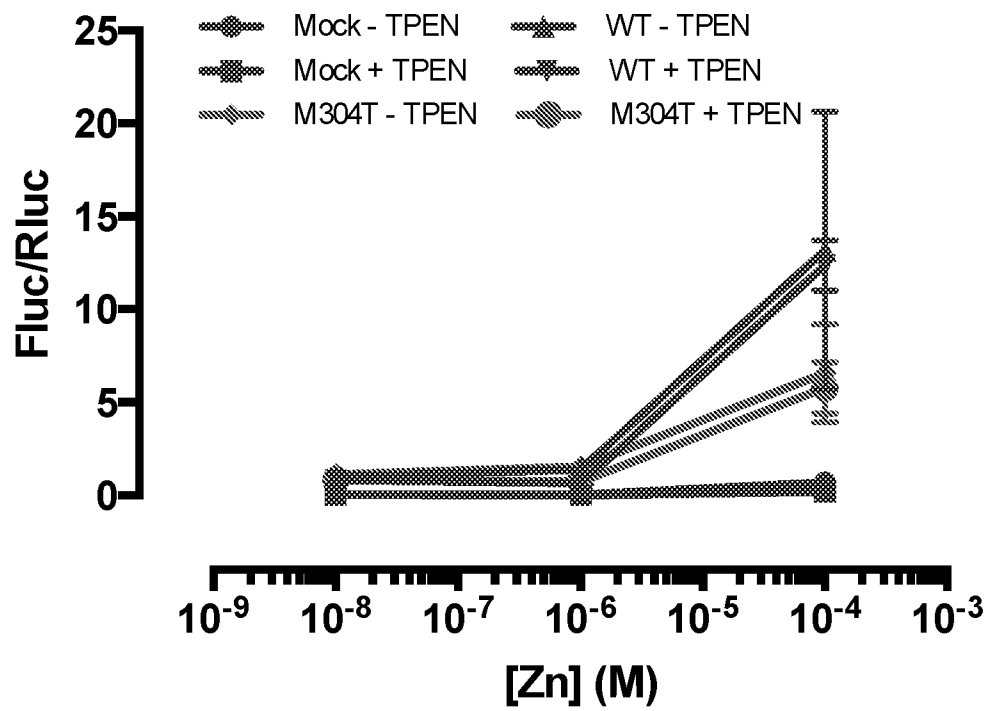


Figure 1B (cont.)

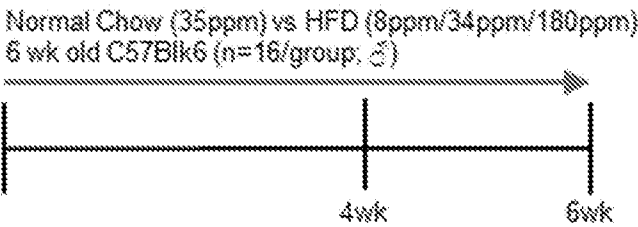


Figure 2A

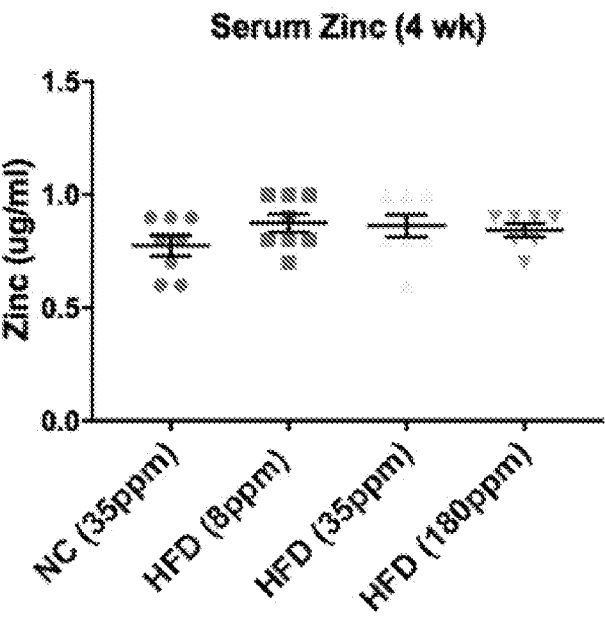


Figure 2B

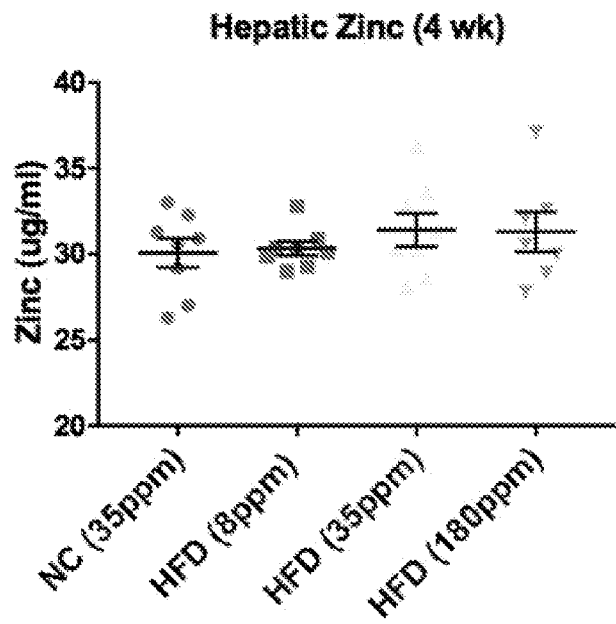


Figure 2C

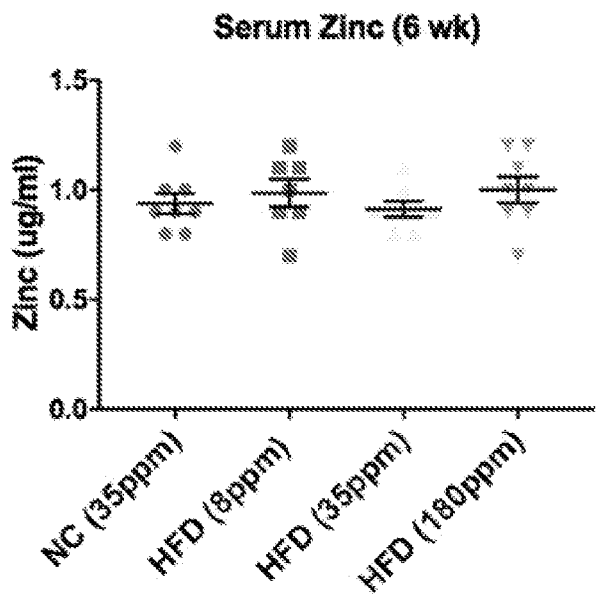


Figure 2D

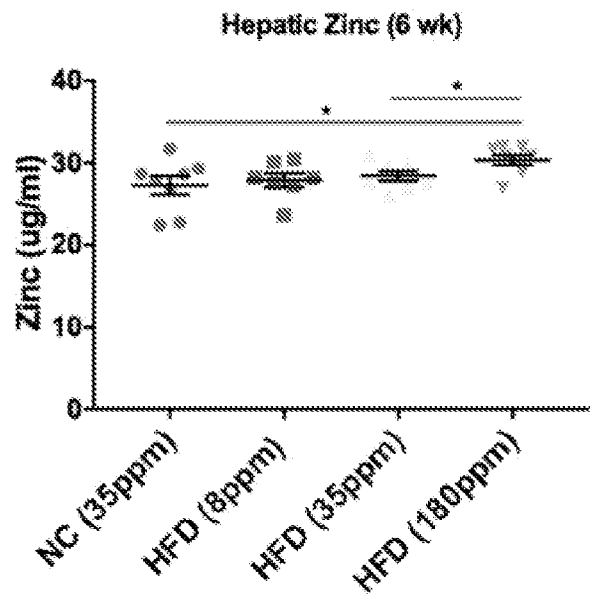


Figure 2E

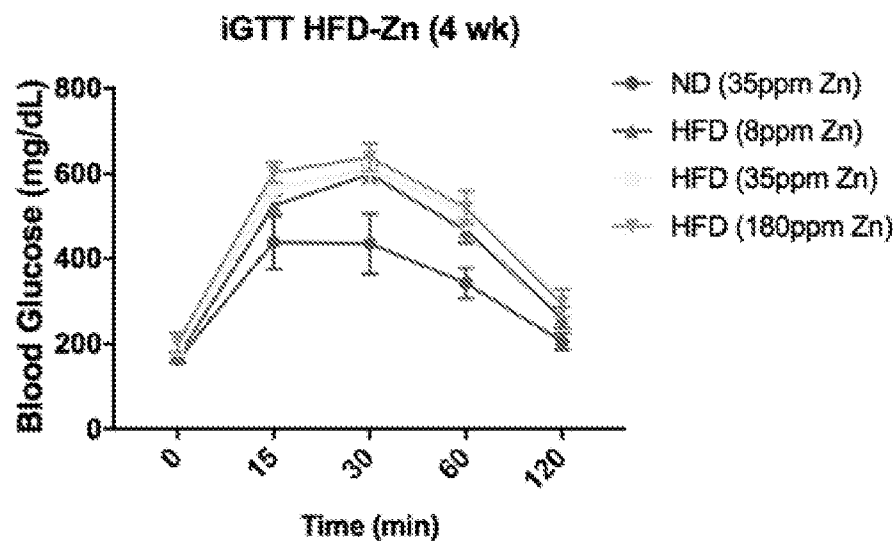


Figure 3A

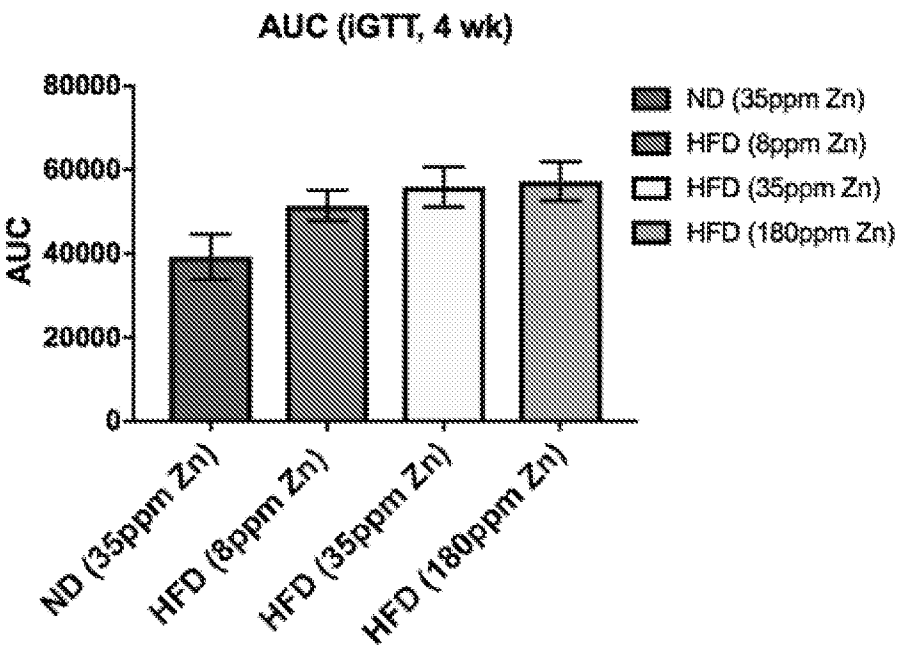


Figure 3B

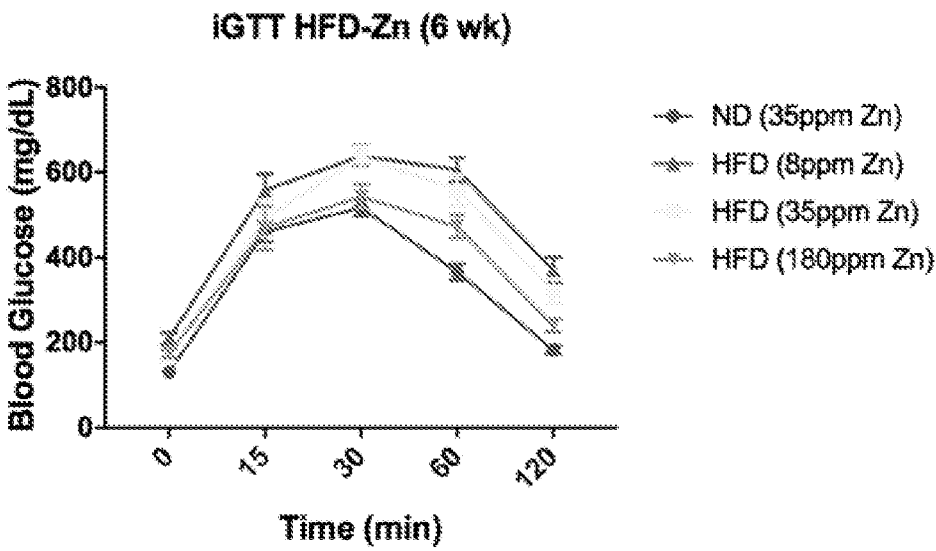


Figure 3C

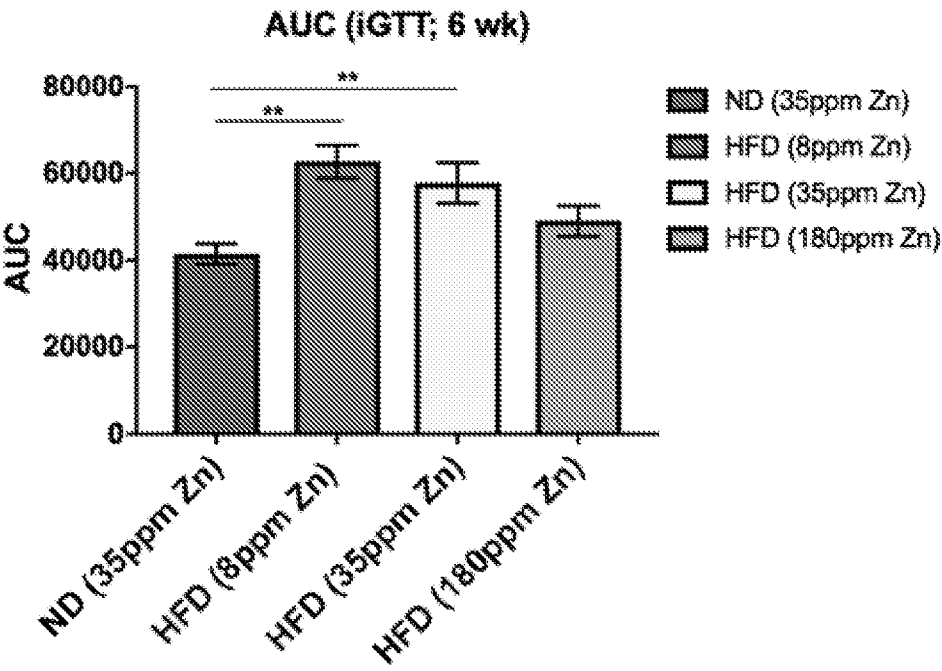


Figure 3D

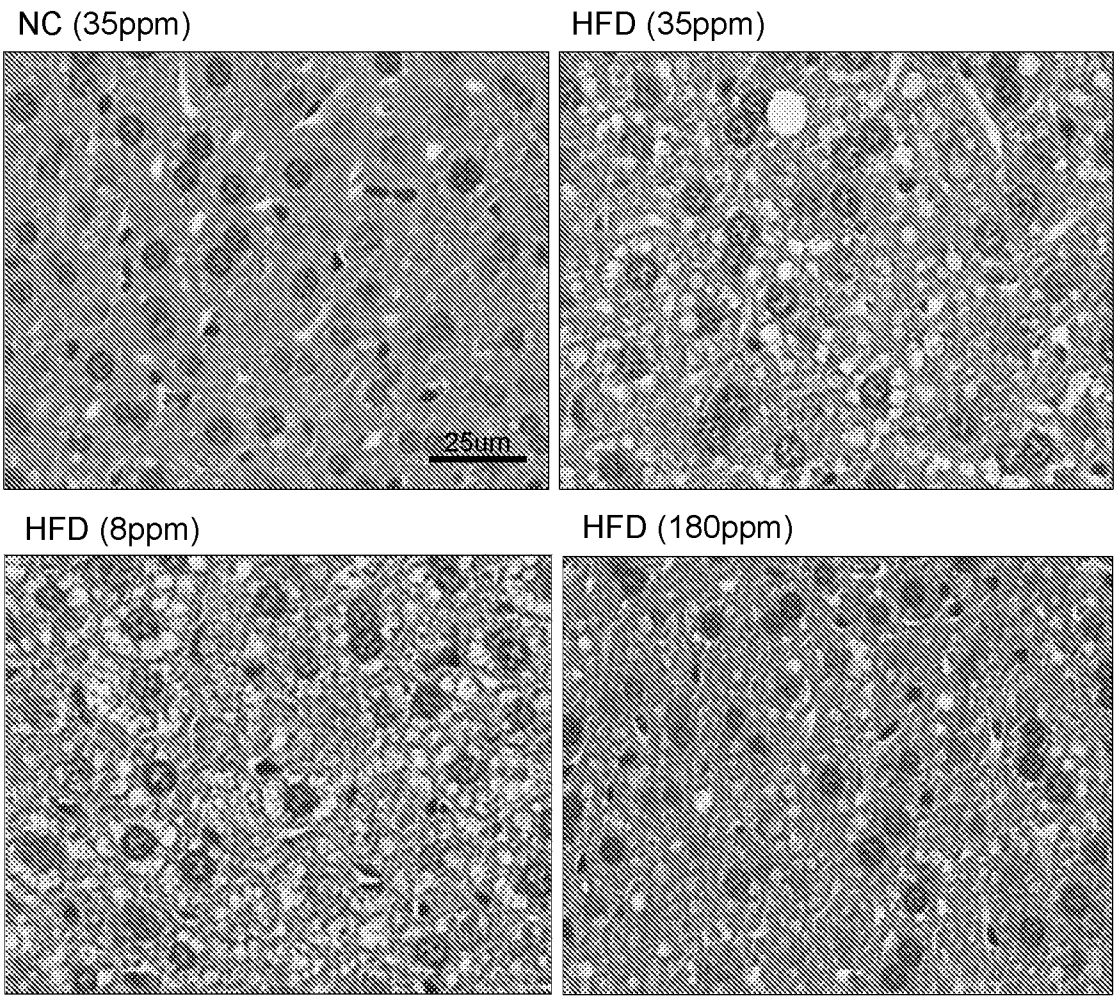


Figure 4

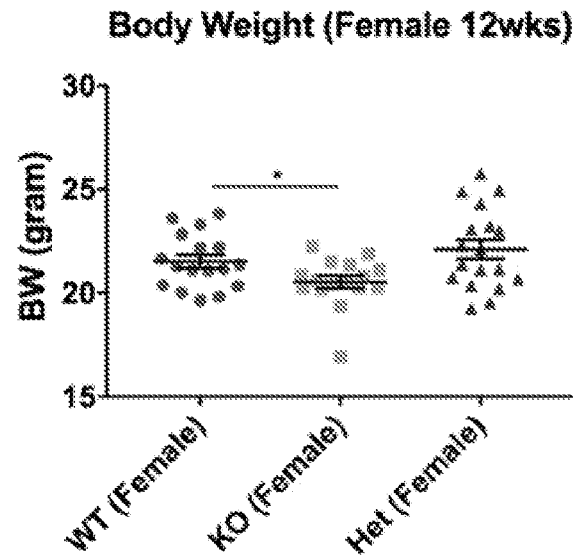


Figure 5A

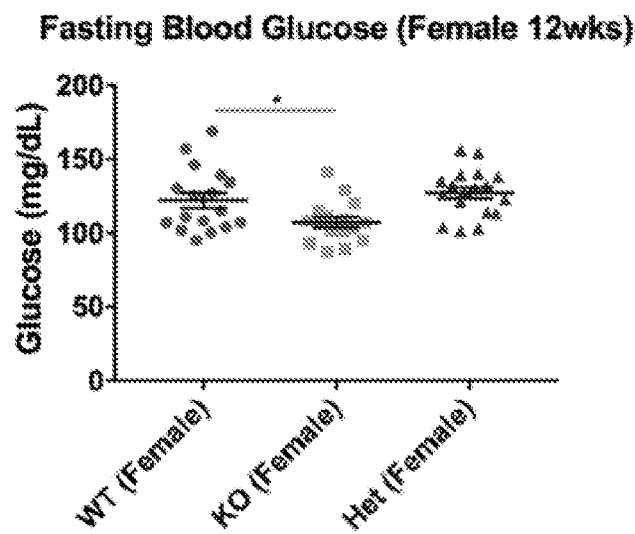


Figure 5B

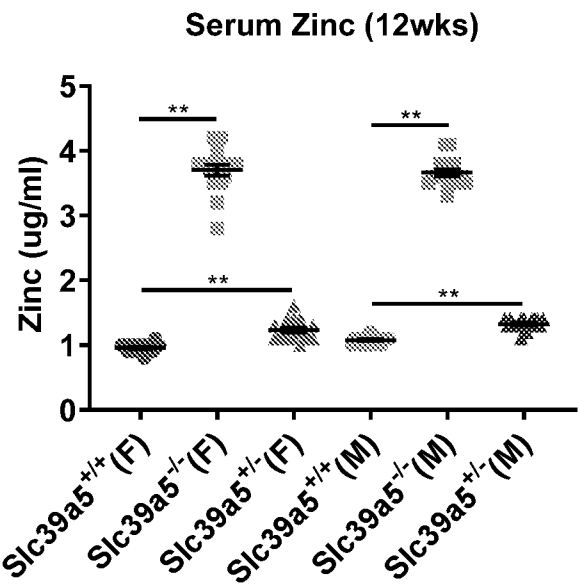


Figure 5C



Figure 5D

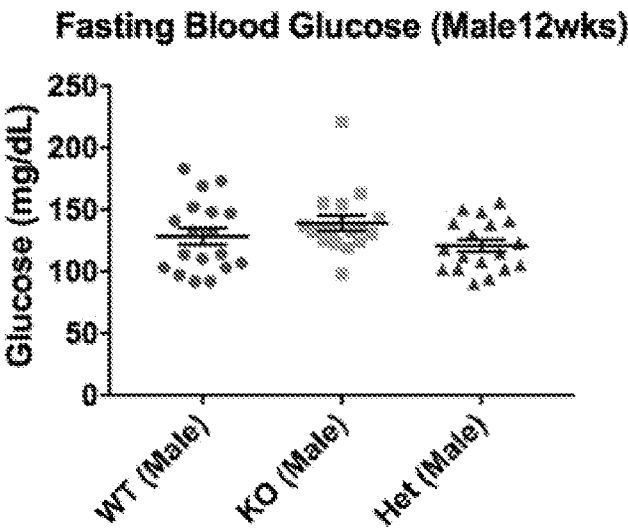


Figure 5E

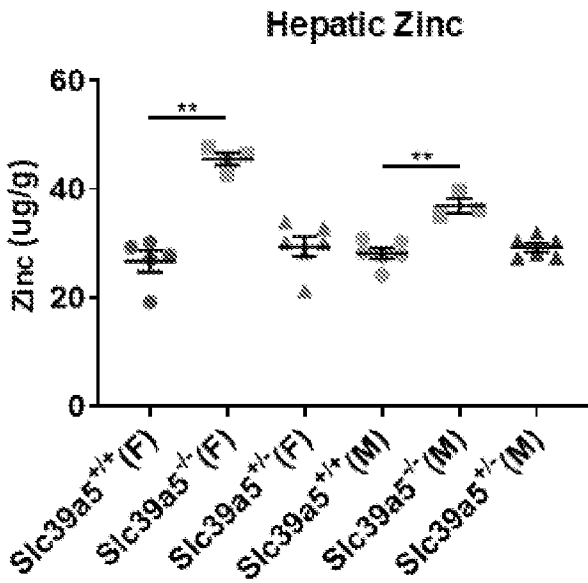


Figure 5F

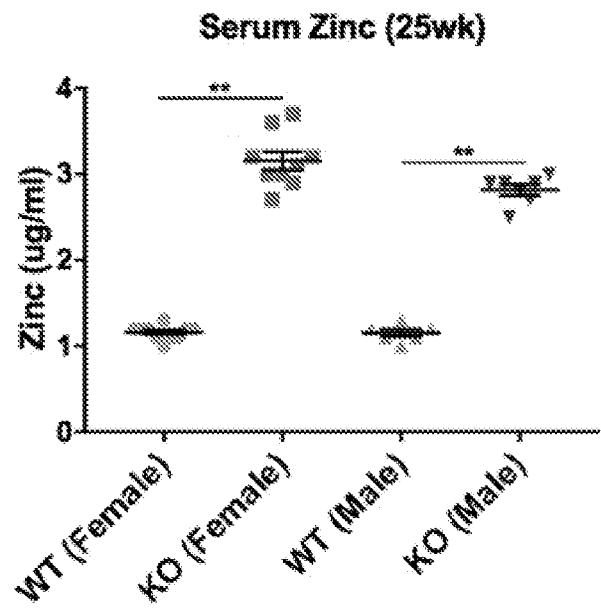


Figure 6A

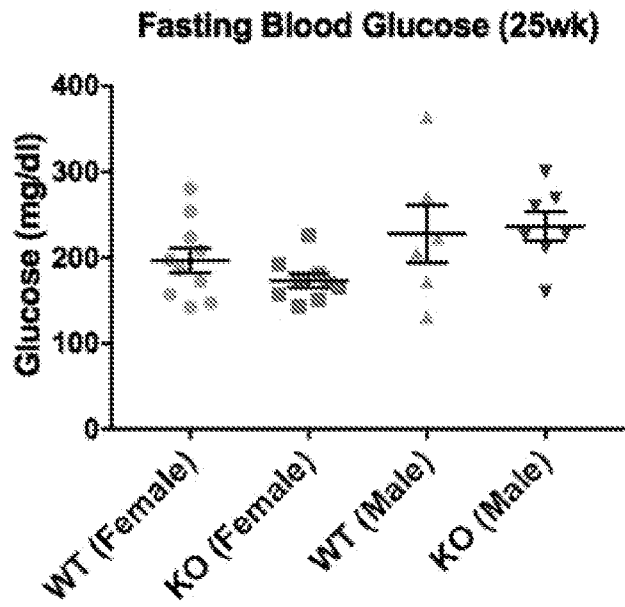


Figure 6B

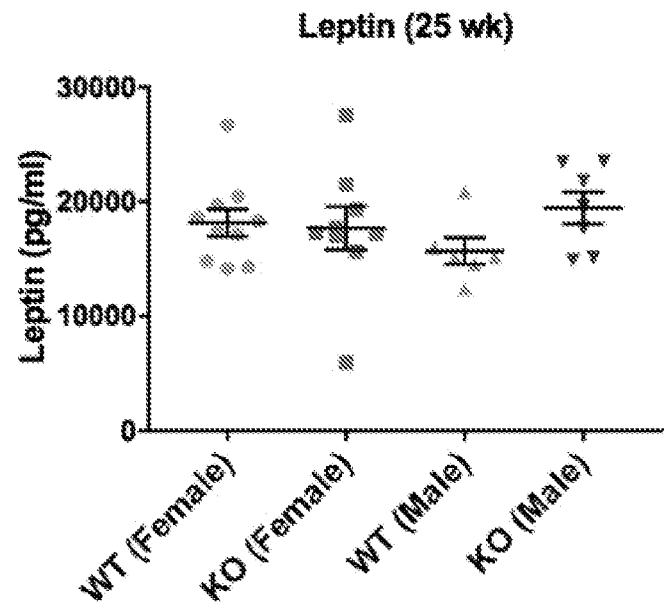


Figure 6C

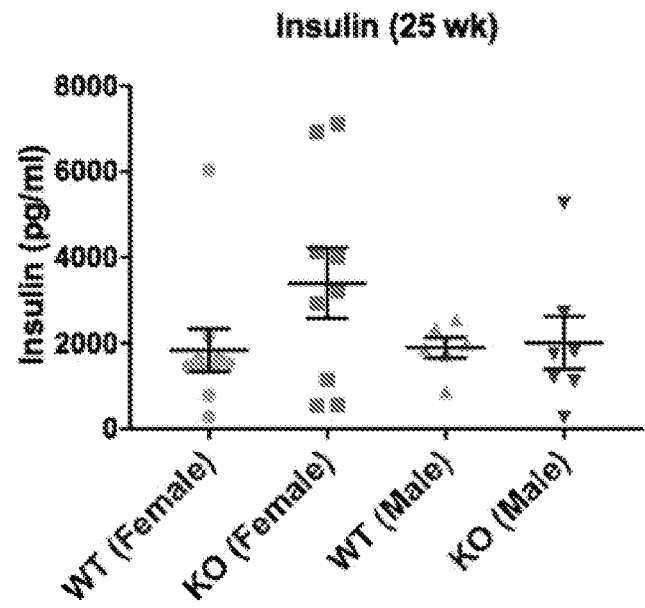


Figure 6D

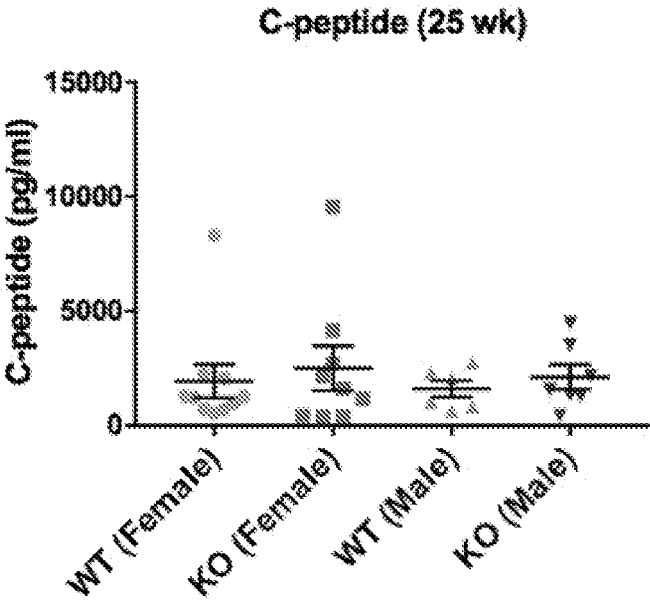


Figure 6E

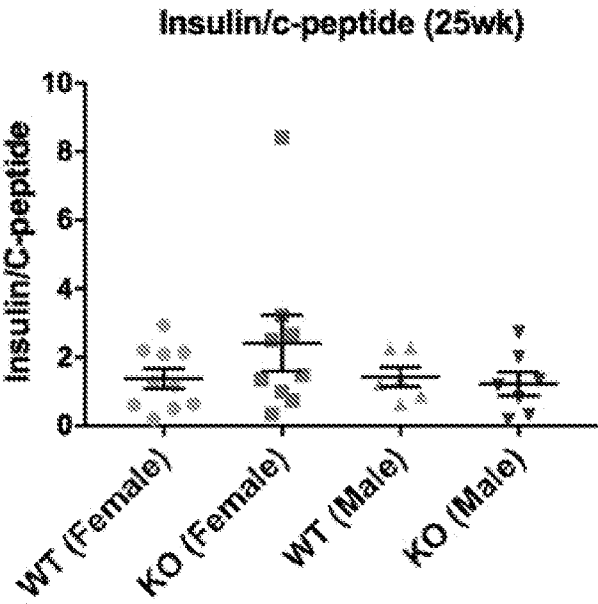


Figure 6F

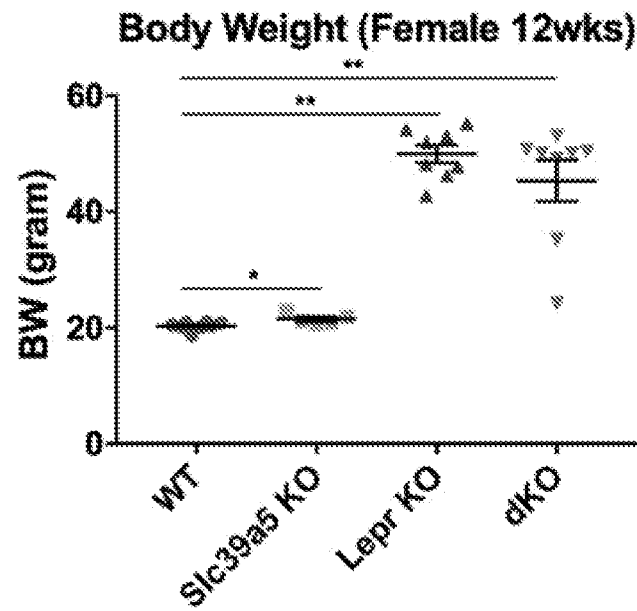


Figure 7A

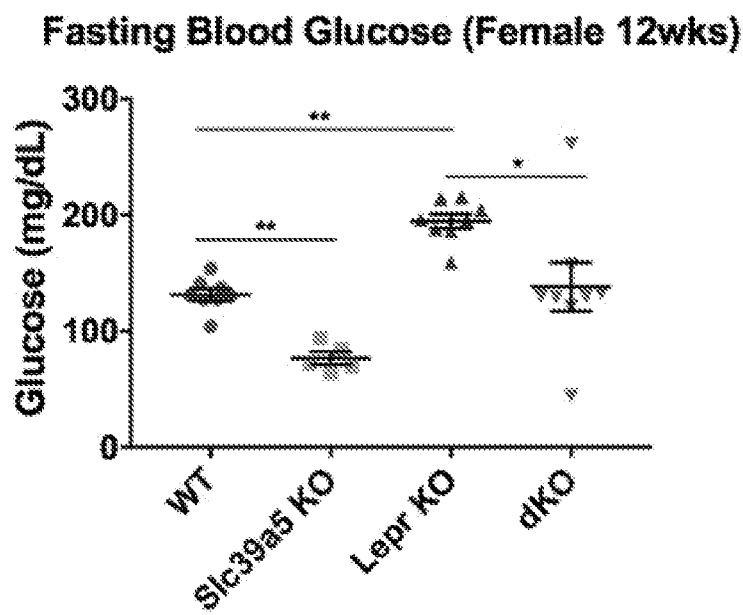


Figure 7B

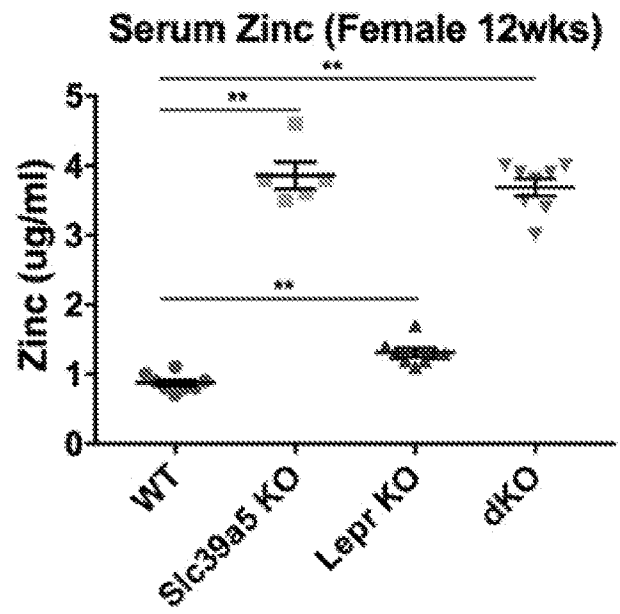


Figure 7C

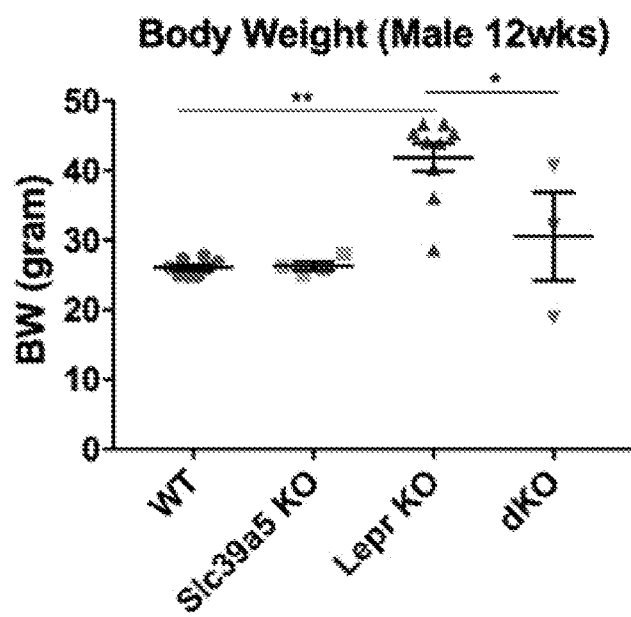


Figure 7D

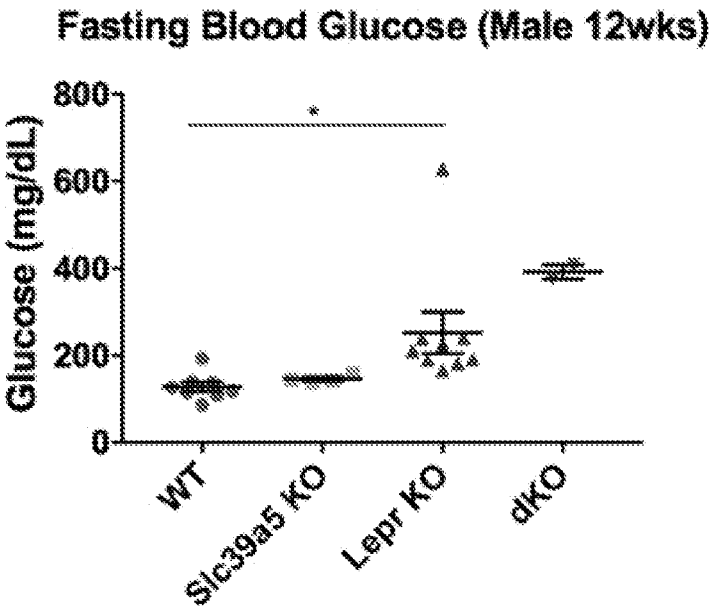


Figure 7E

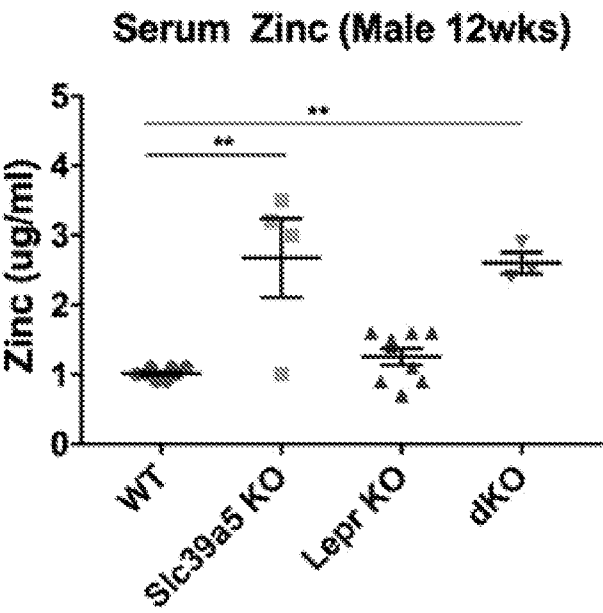


Figure 7F

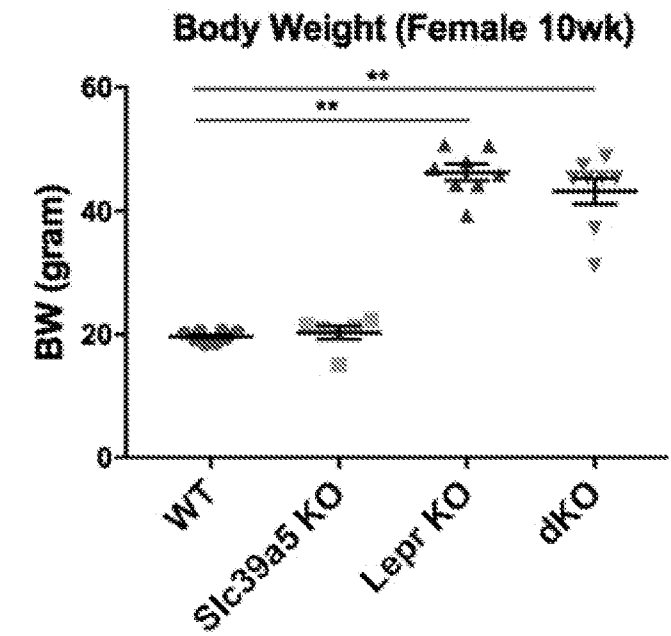


Figure 8A

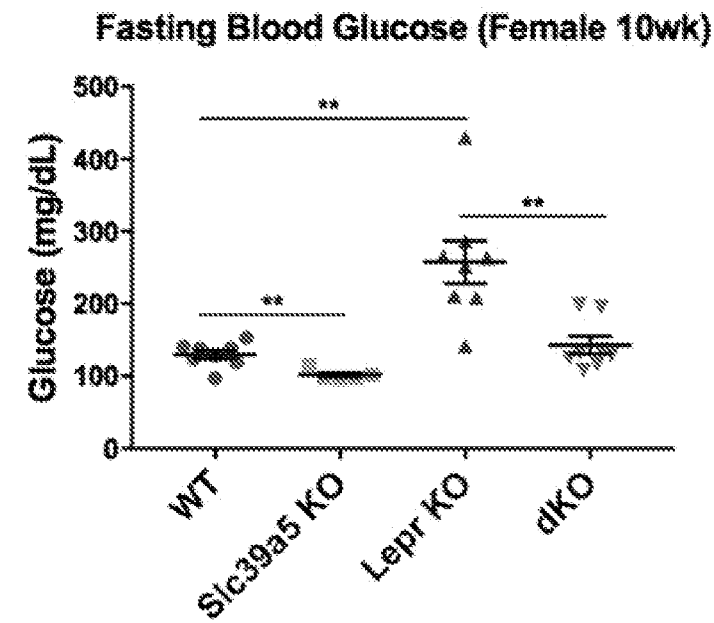


Figure 8B

β -hydroxybutyrate (Female 10wk)

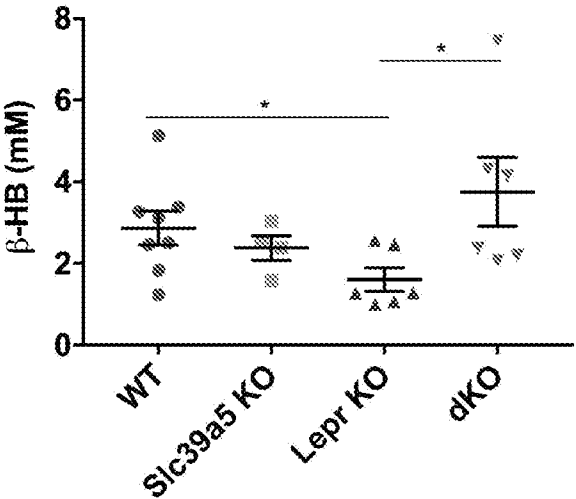


Figure 8C

Body Weight (Male 10wk)

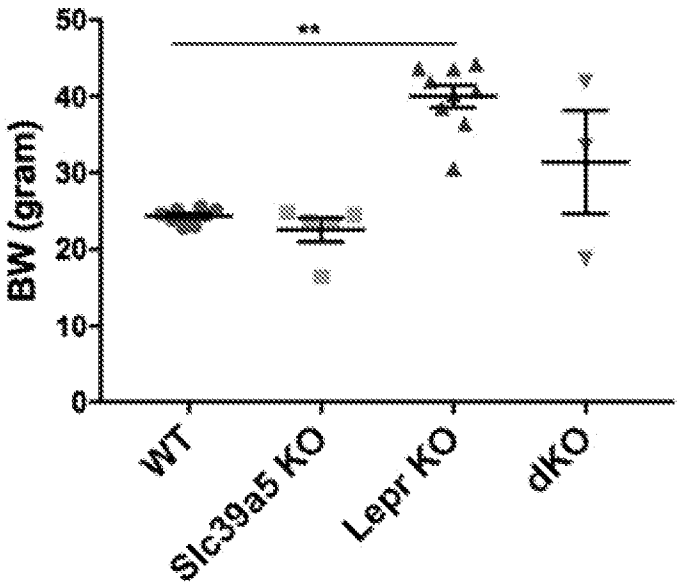


Figure 8D

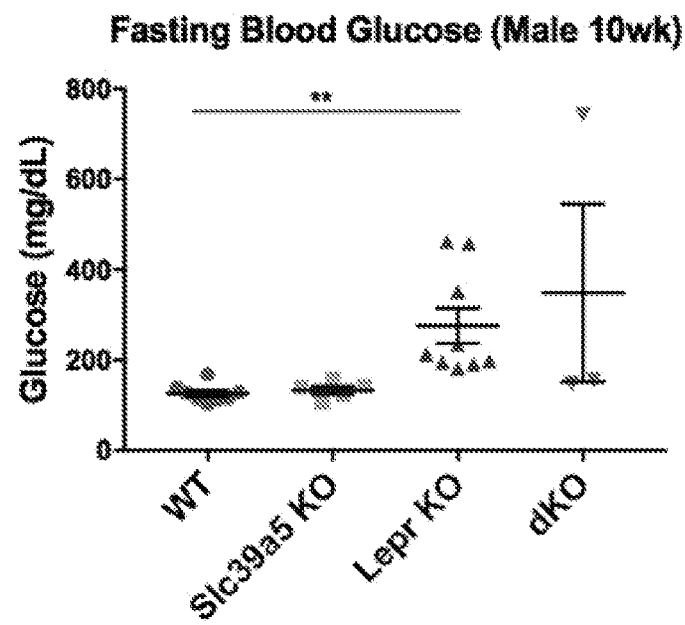


Figure 8E

IPGTT: Mean blood glucose concentration (week 14)

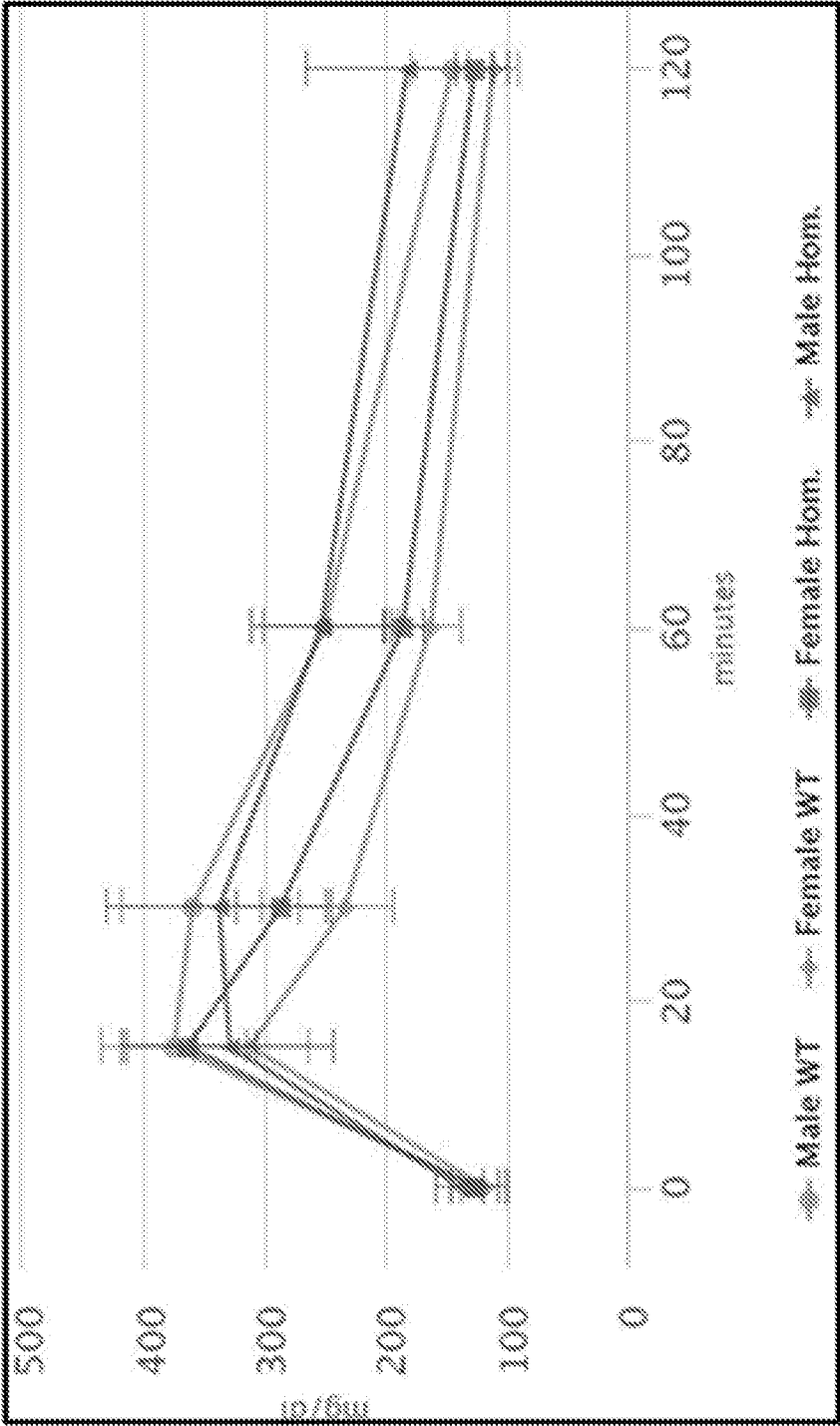


Figure 9A

Insulin Blood Level (non-fasting/terminal; week 16)

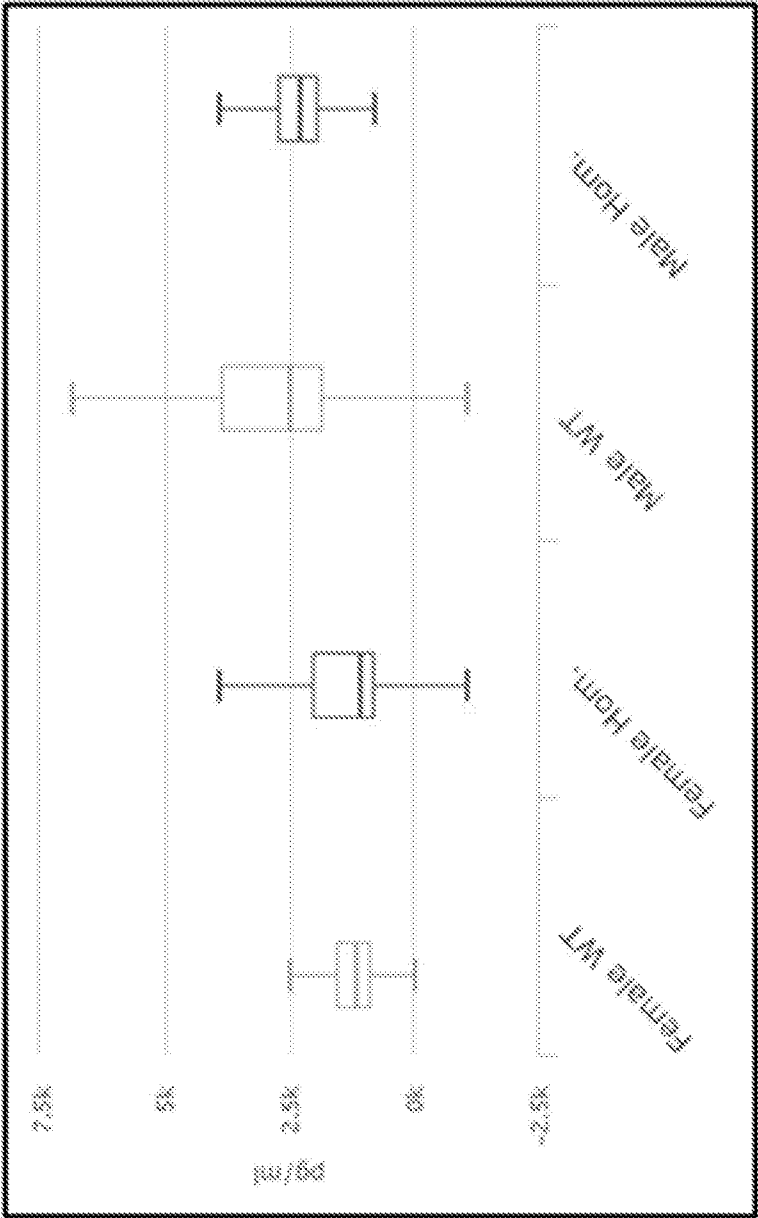
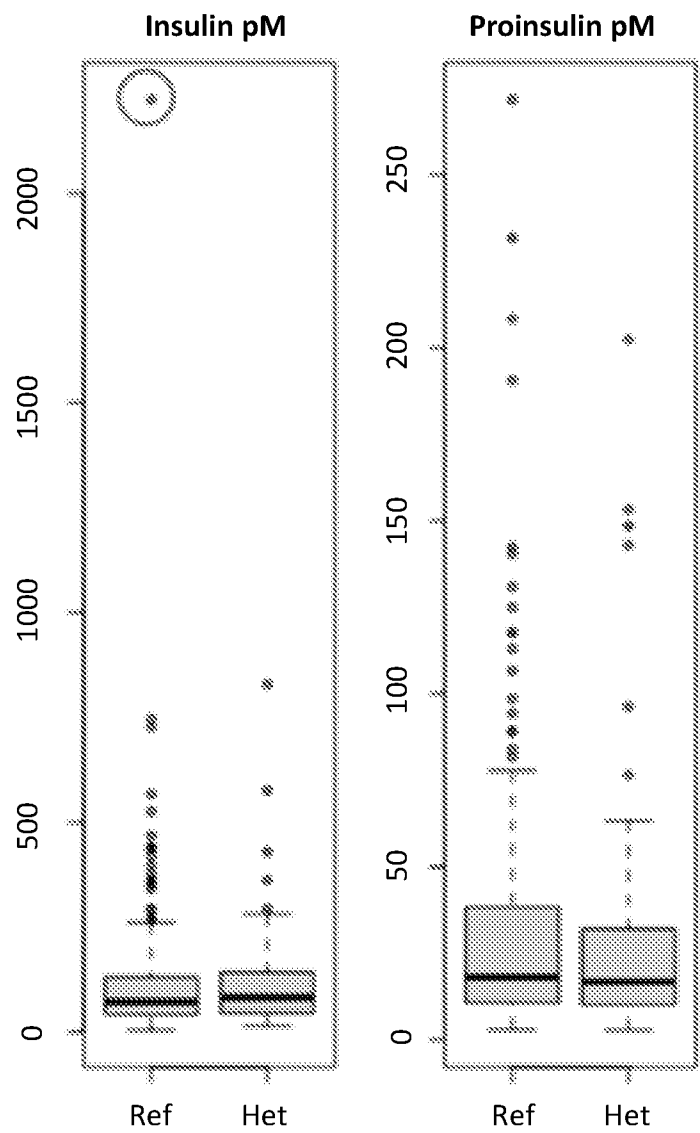


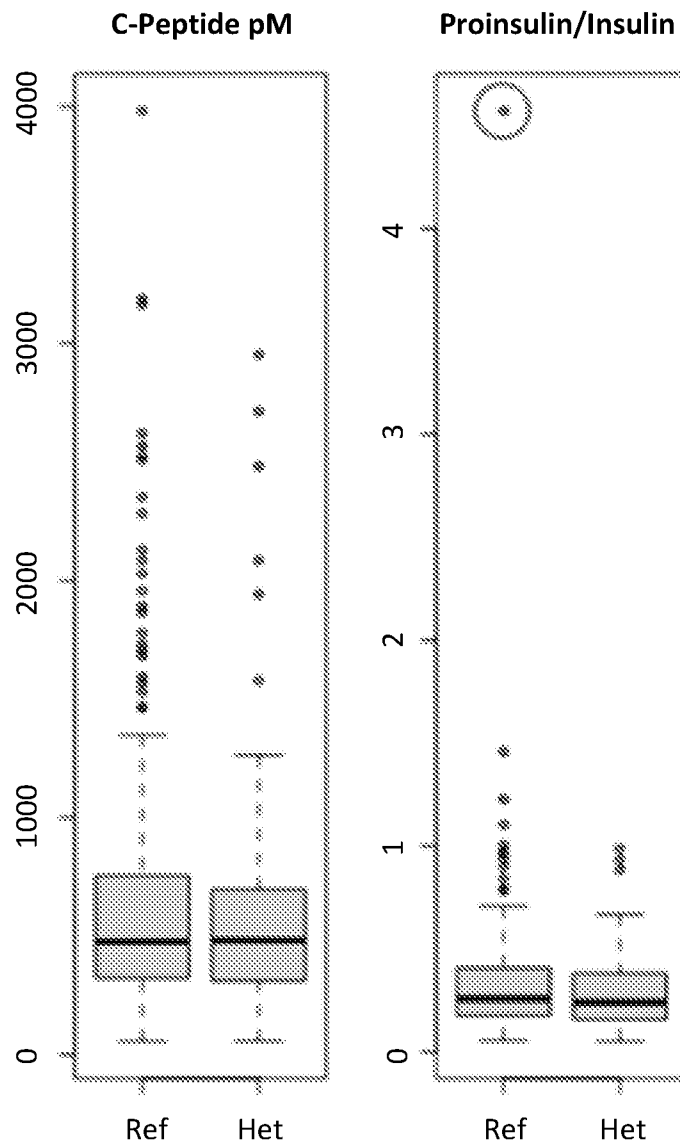
Figure 9B



Measure	Insulin pM		Proinsulin, pM	
SLC39A5LOF	Ref	Het	Ref	Het
Mean	121.1	118.7	30.95	28.65
Median	71.1	82.05	18	16.7
N	247	86	253	91

Figure 10

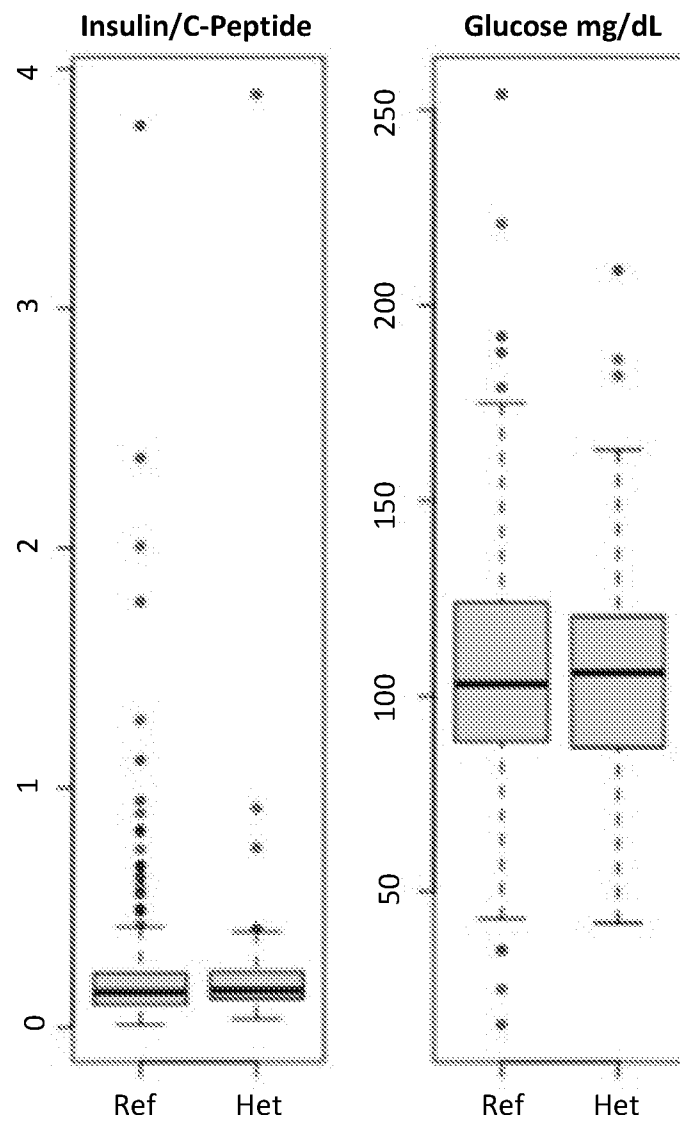
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Measure	C-Peptide pM		Proinsulin/ Insulin	
SLC39A5LOF	Ref	Het	Ref	Het
Mean	661.8	629.6	0.3394	0.2895
Median	475.1	480.6	0.258	0.239
N	253	91	247	86

Figure 10 (cont.)

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Measure	Insulin/C-Peptide		Glucose	
SLC39A5LOF	Ref	Het	Ref	Het
Mean	0.2331	0.2336	106.6	106.6
Median	0.145	0.154	103	106
N	247	86	247	87

Figure 10 (cont.)

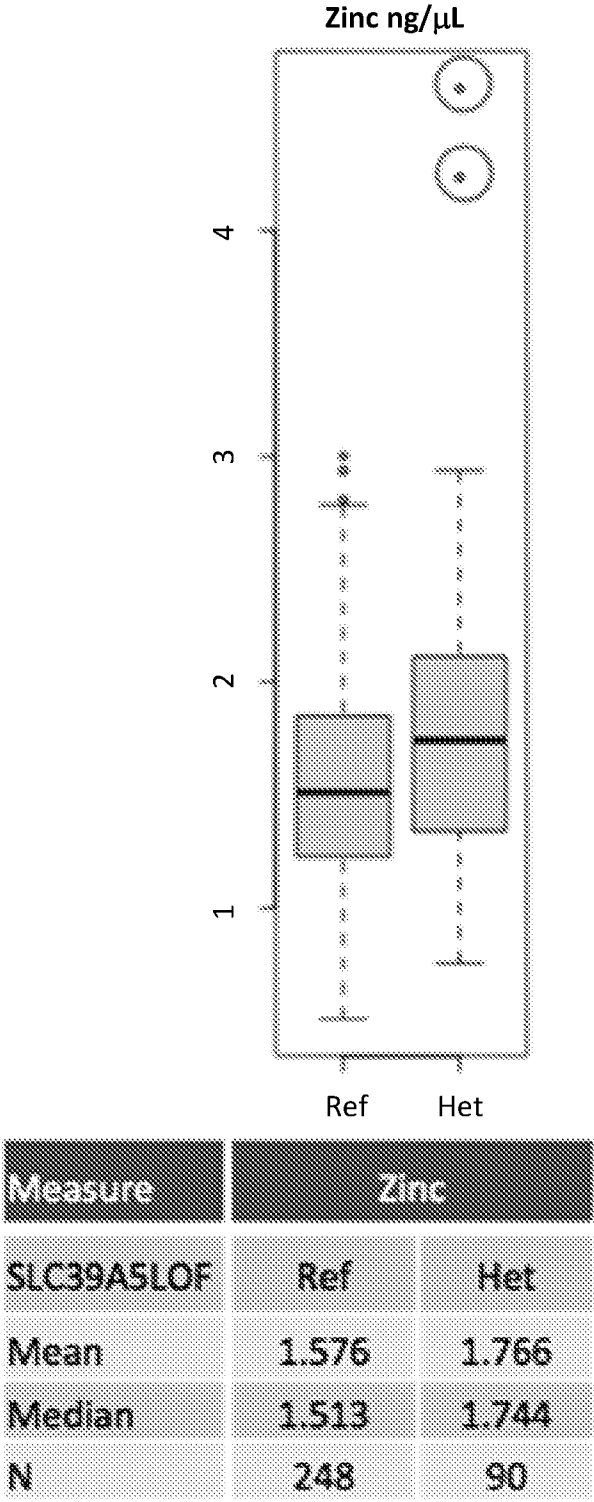


Figure 10 (cont.)

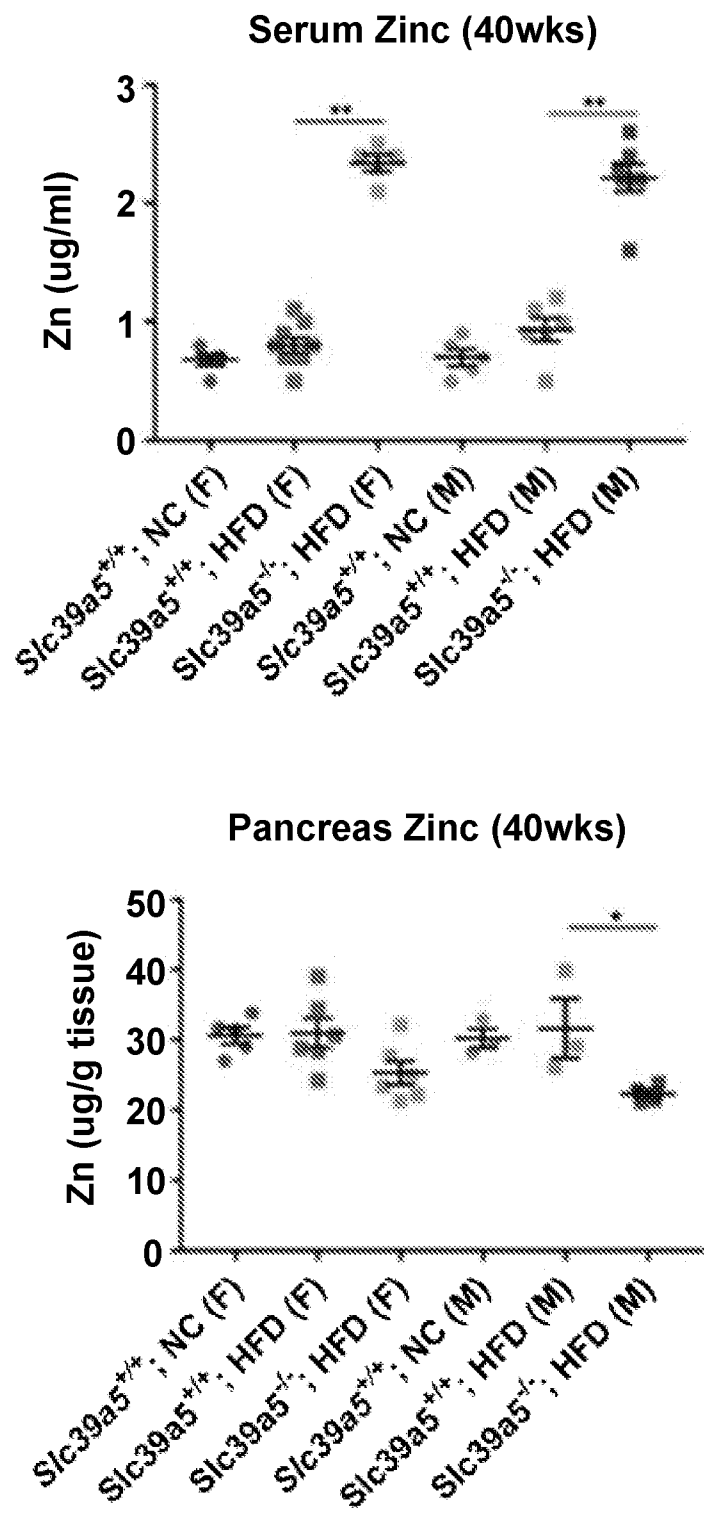


Figure 11

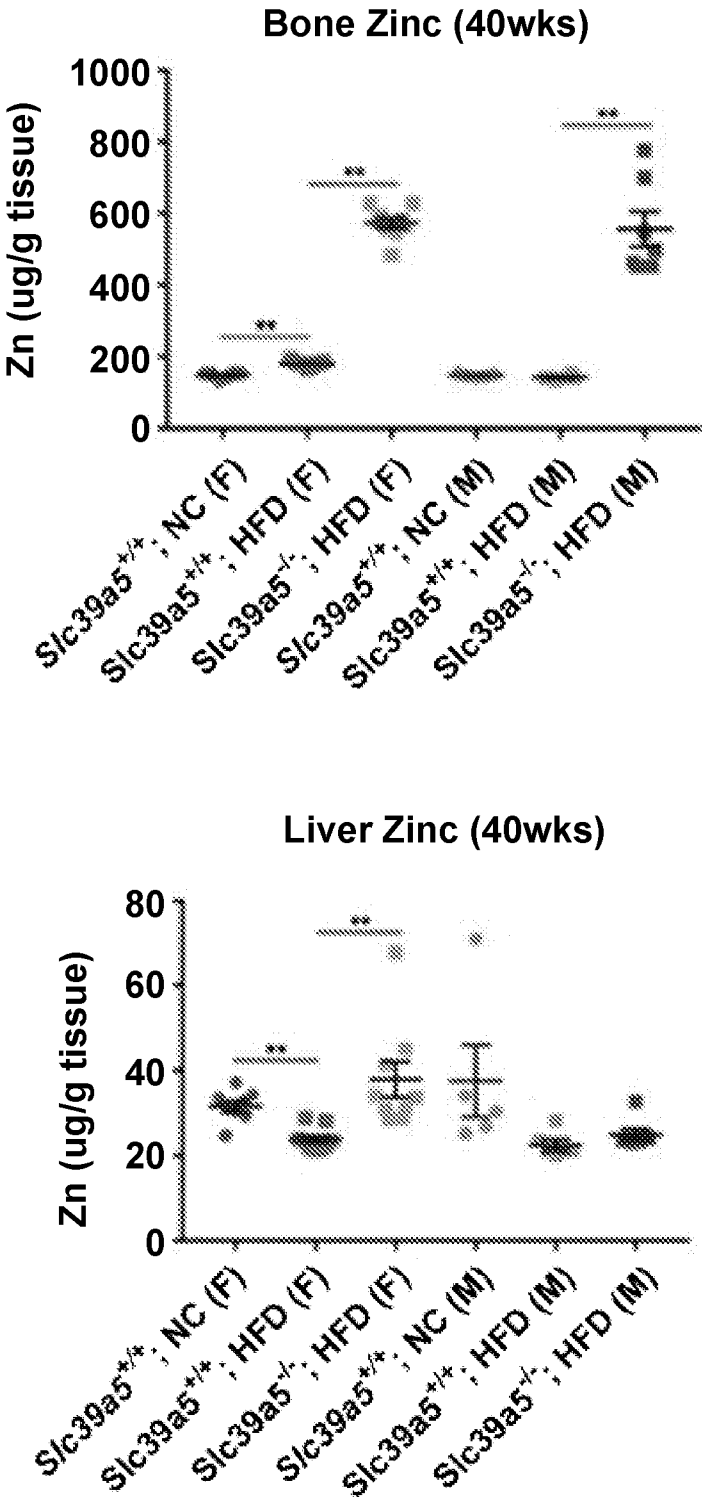


Figure 11 (cont.)

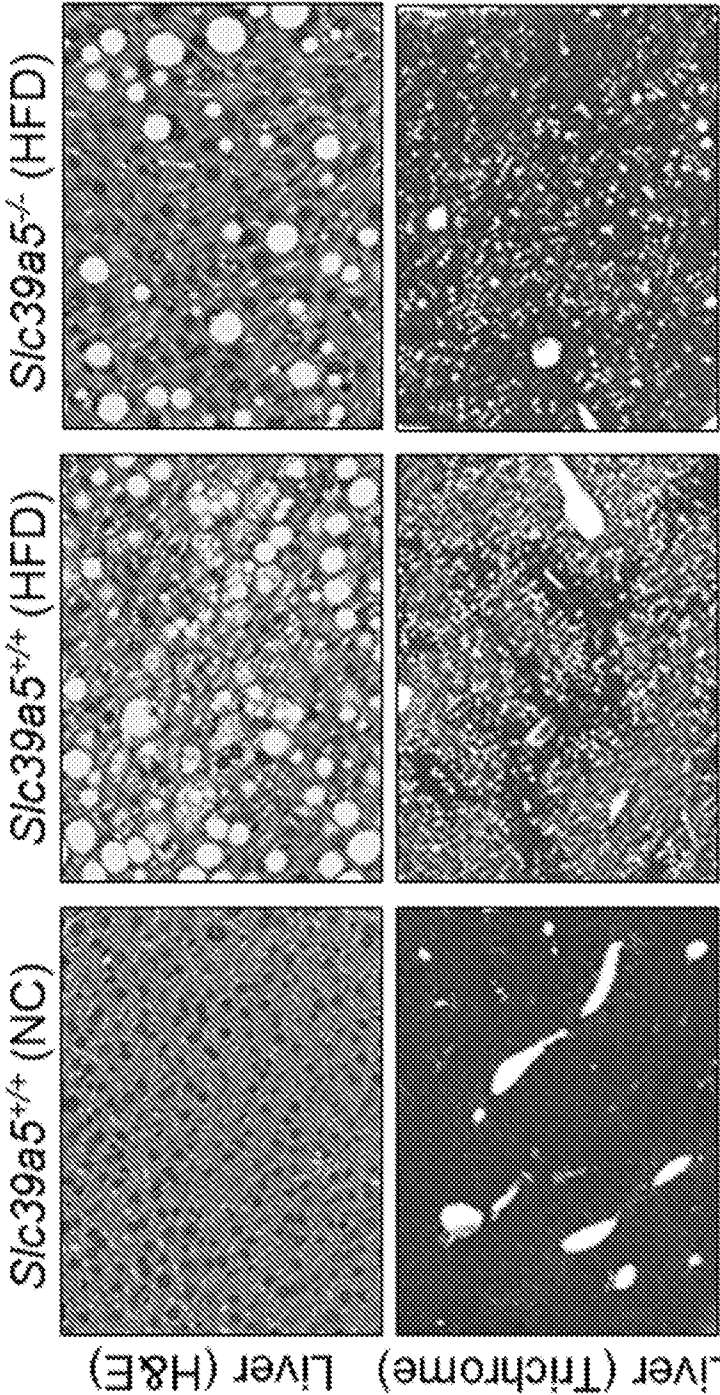


Figure 12

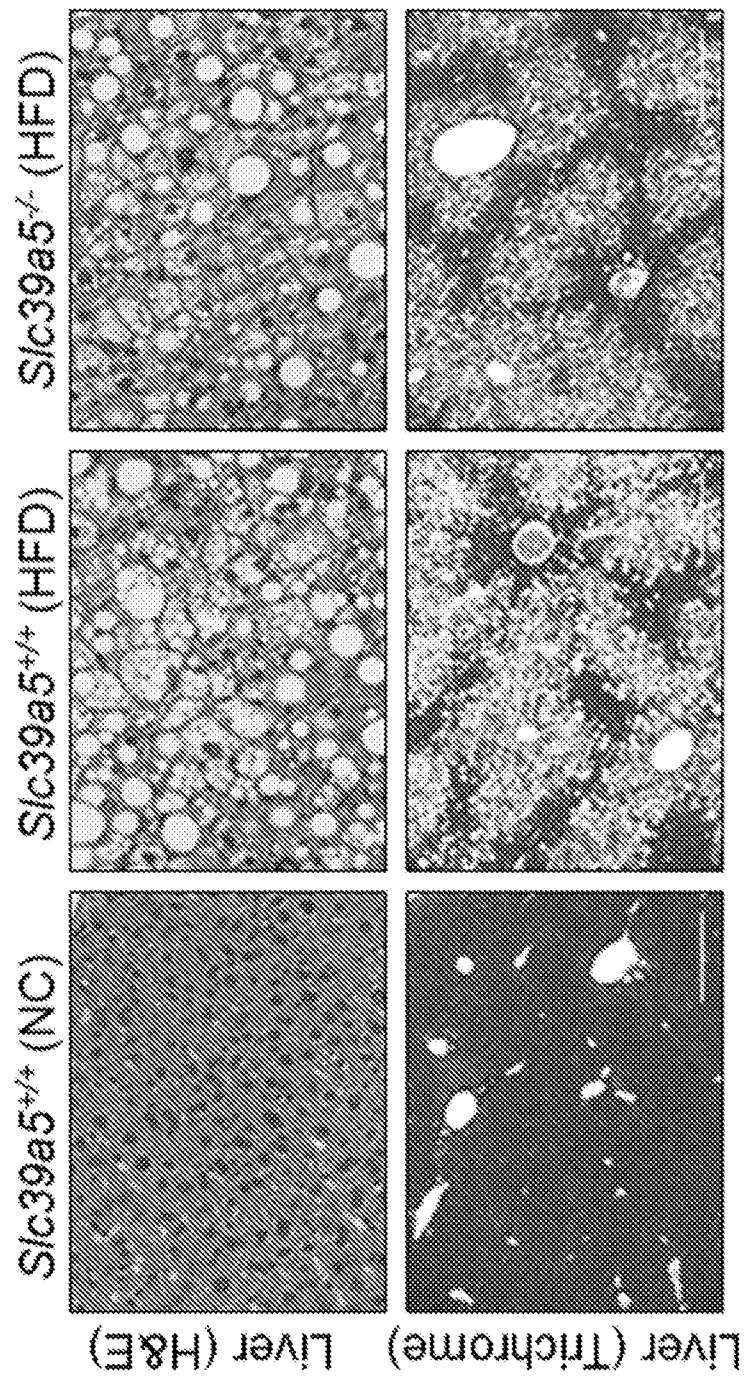


Figure 12 (cont.)

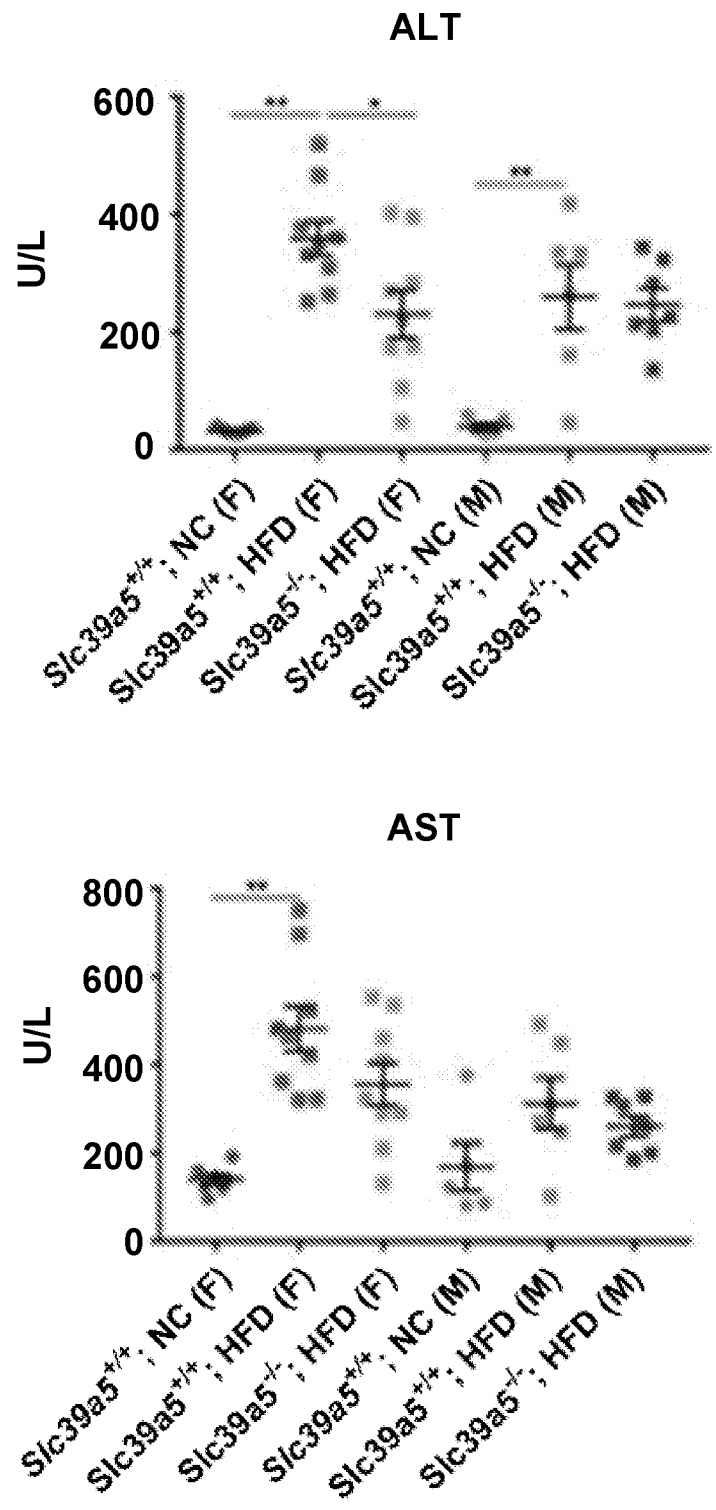


Figure 13

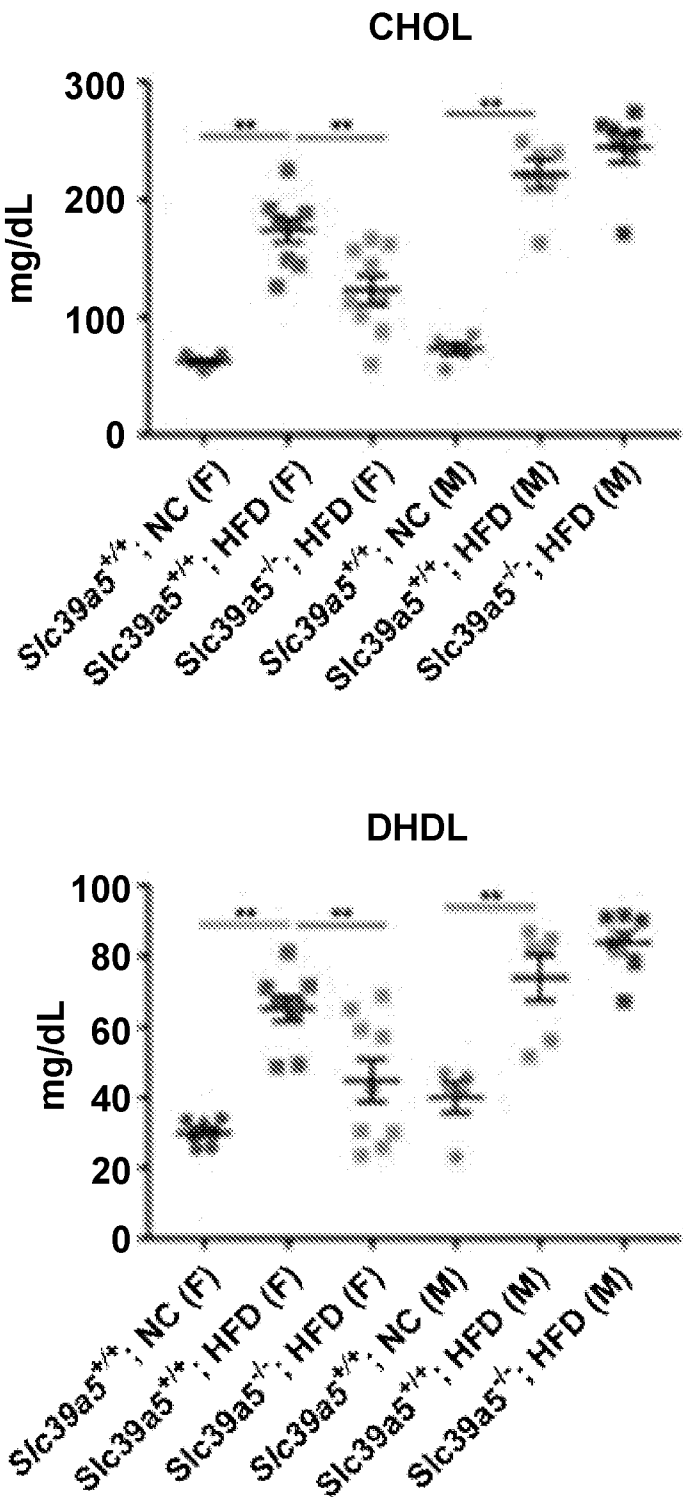


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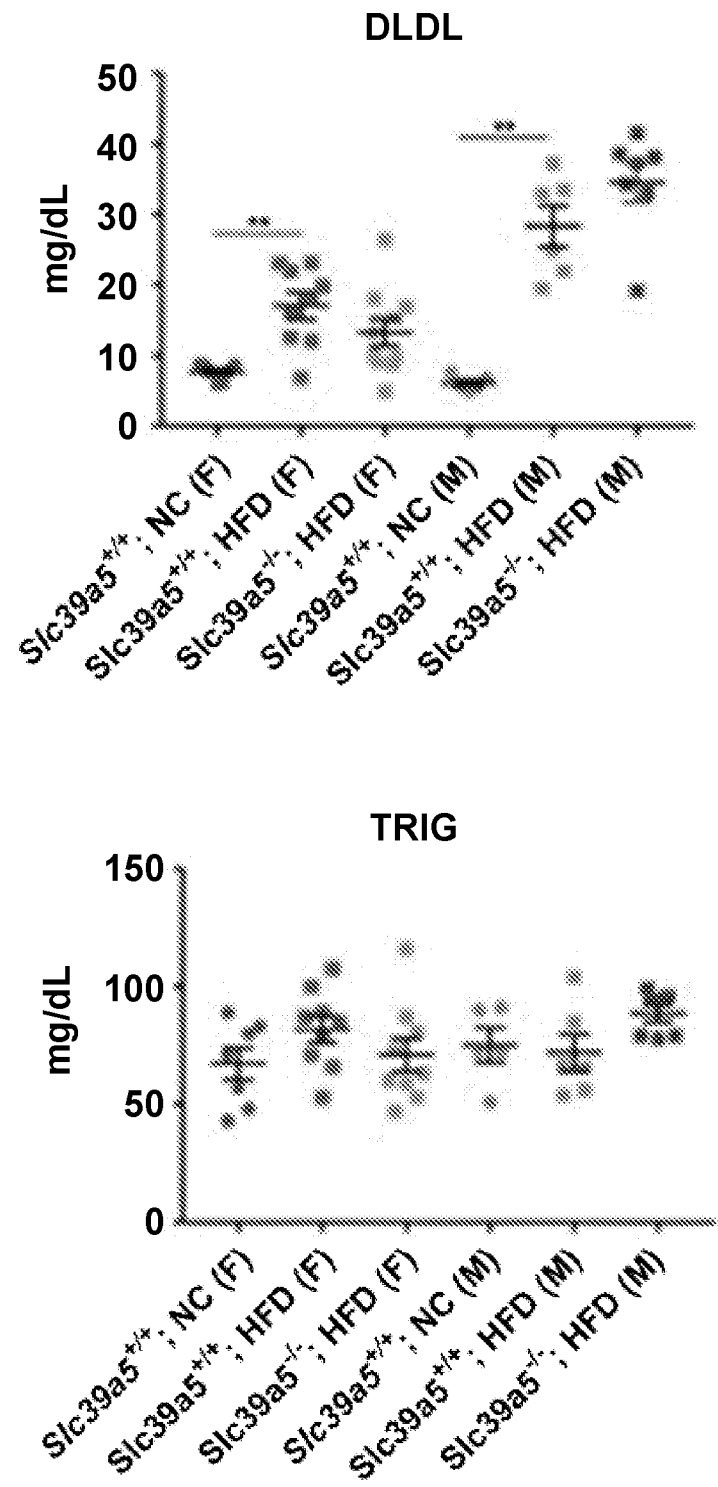


Figure 13 (cont.)

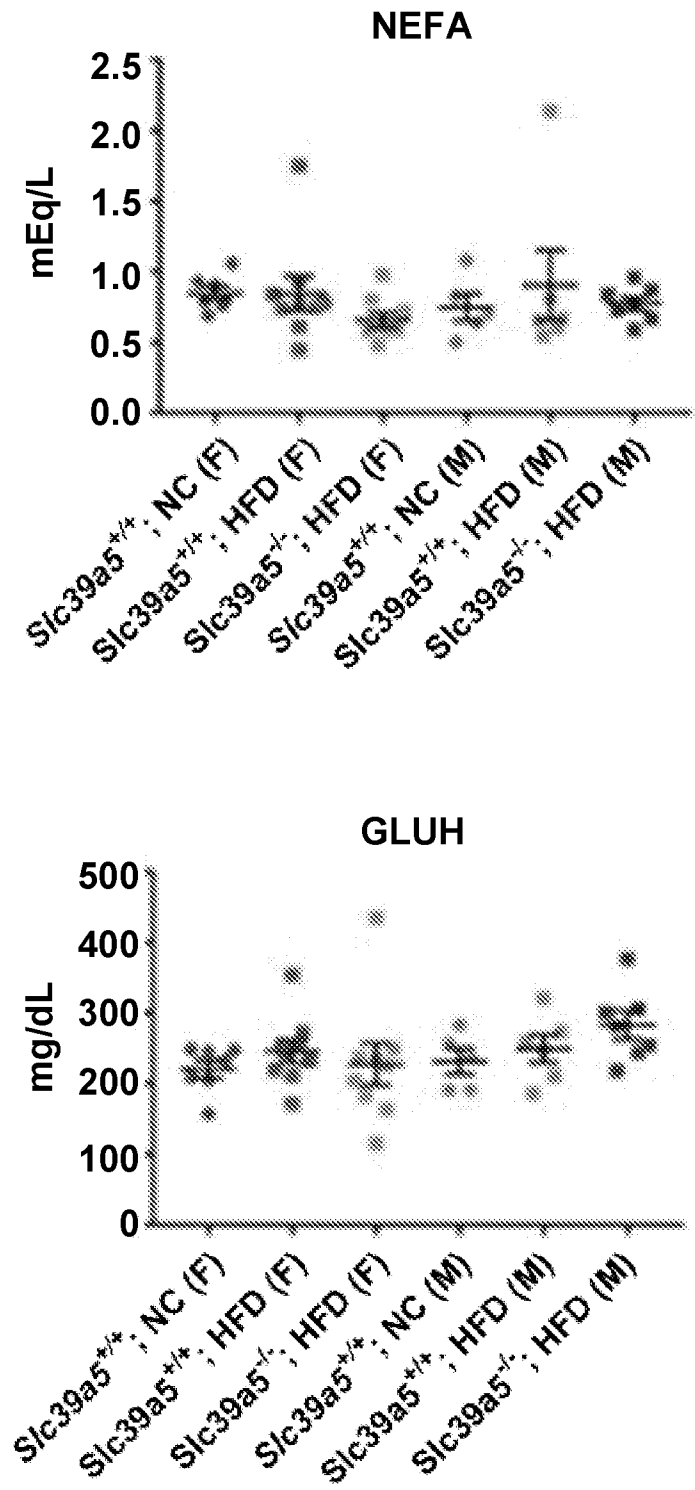


Figure 13 (cont.)

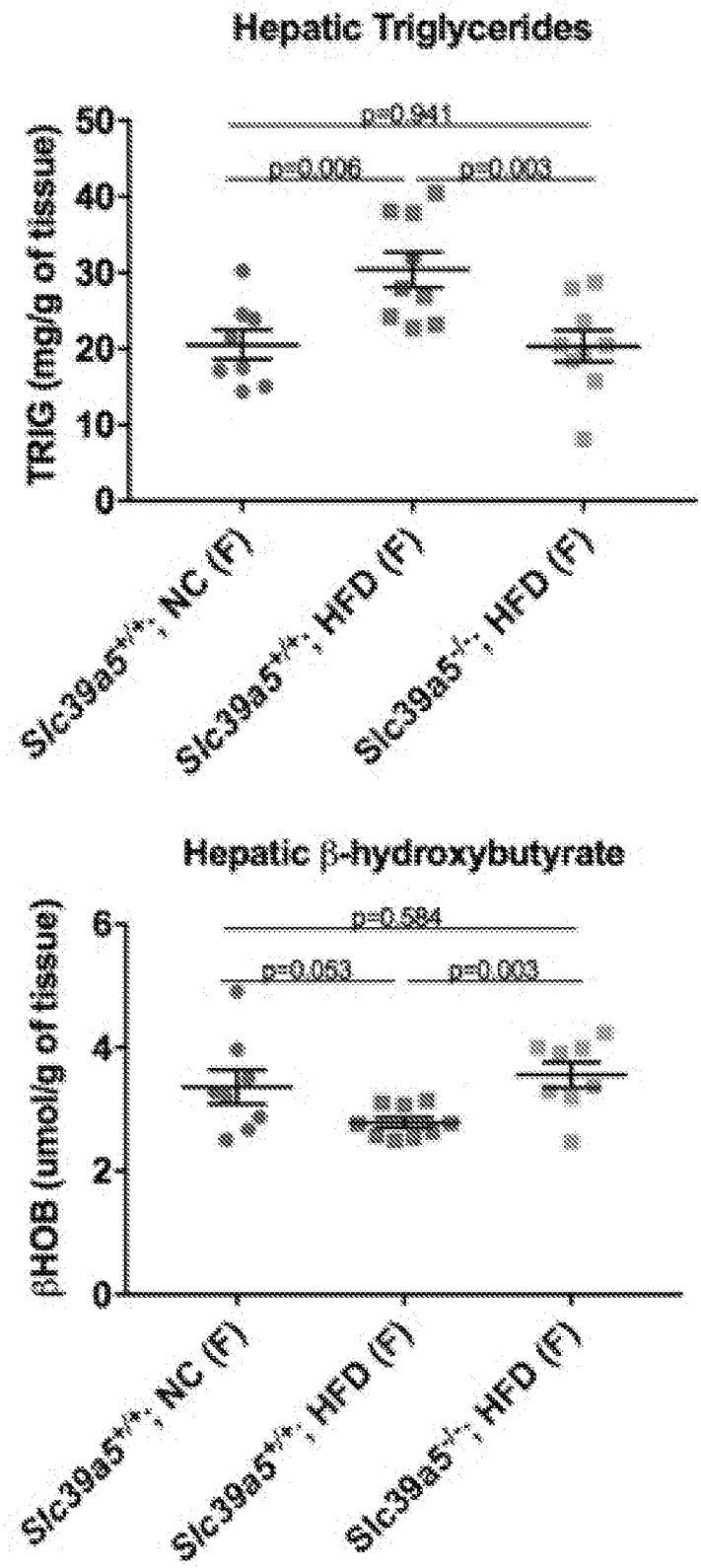


Figure 14

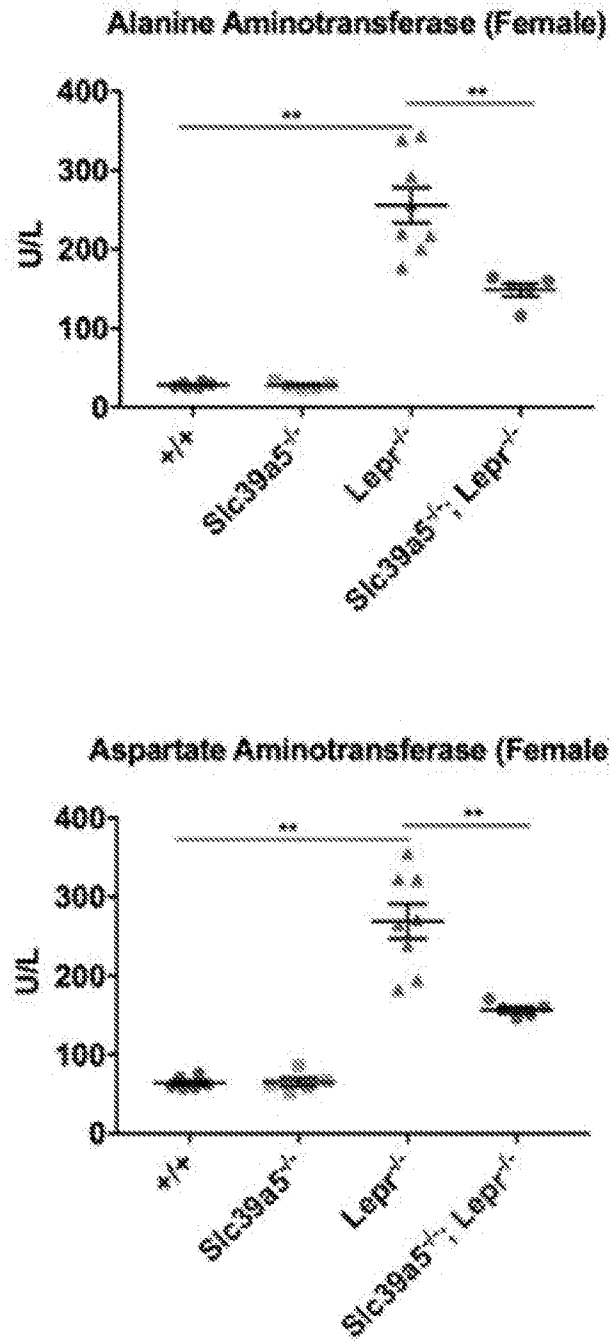


Figure 15

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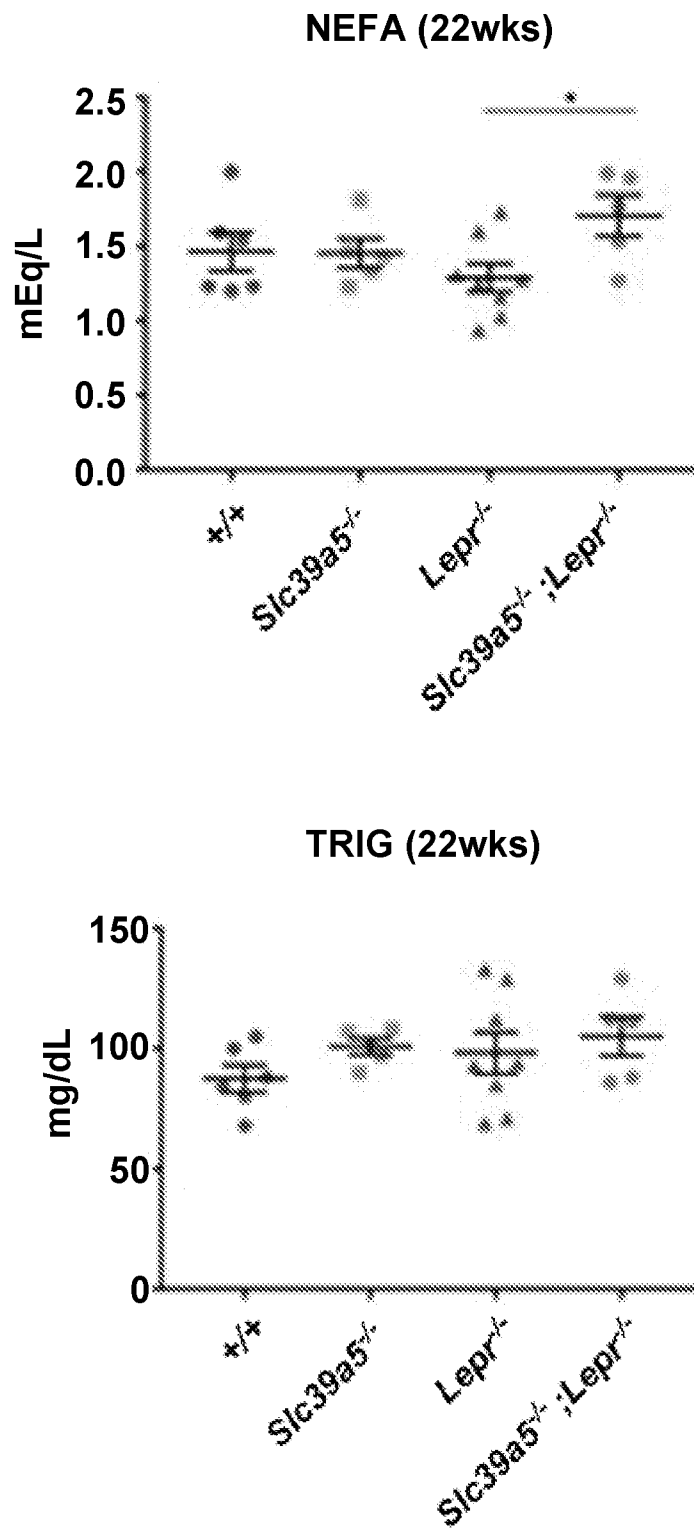


Figure 15 (cont.)

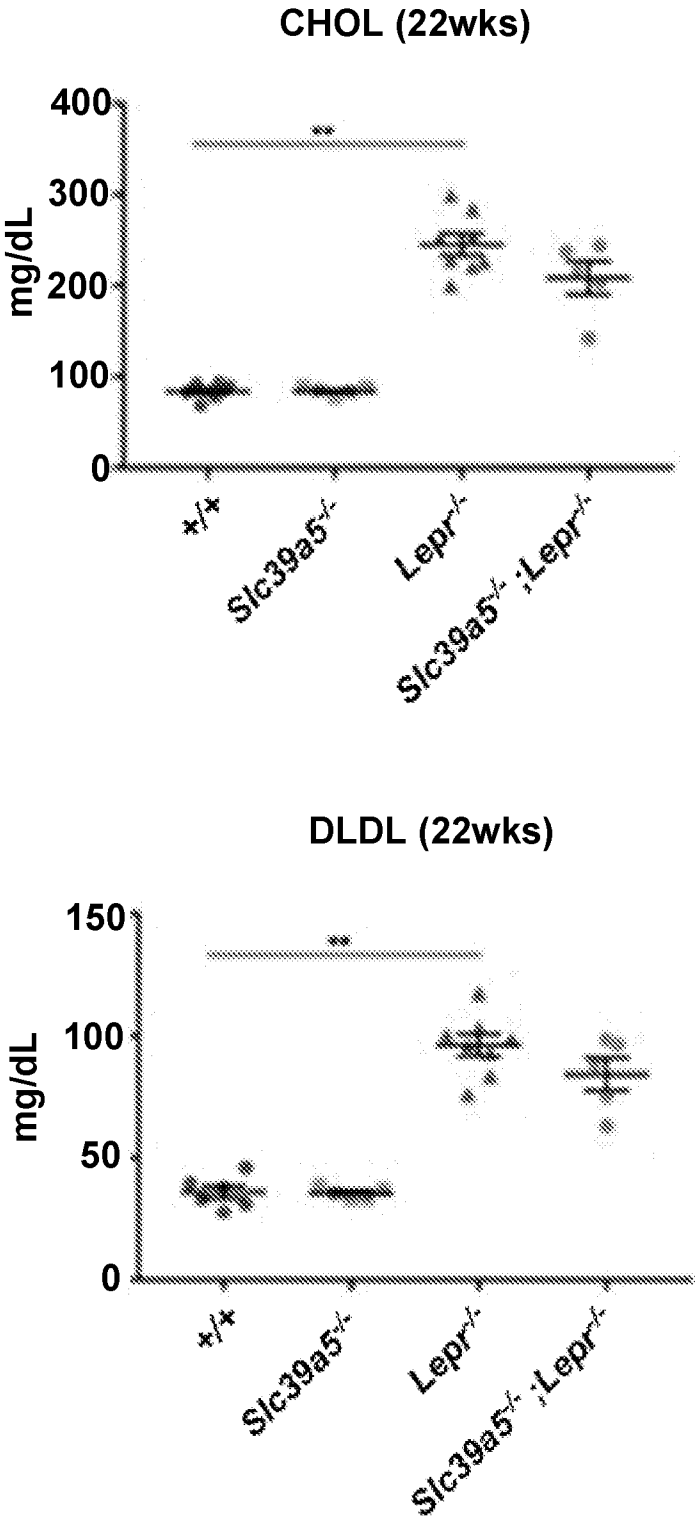


Figure 15 (cont.)

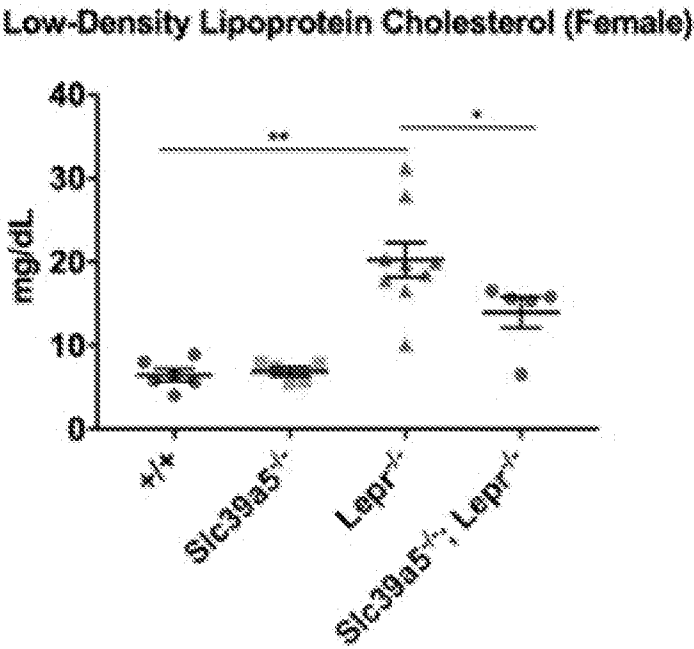


Figure 15 (cont.)

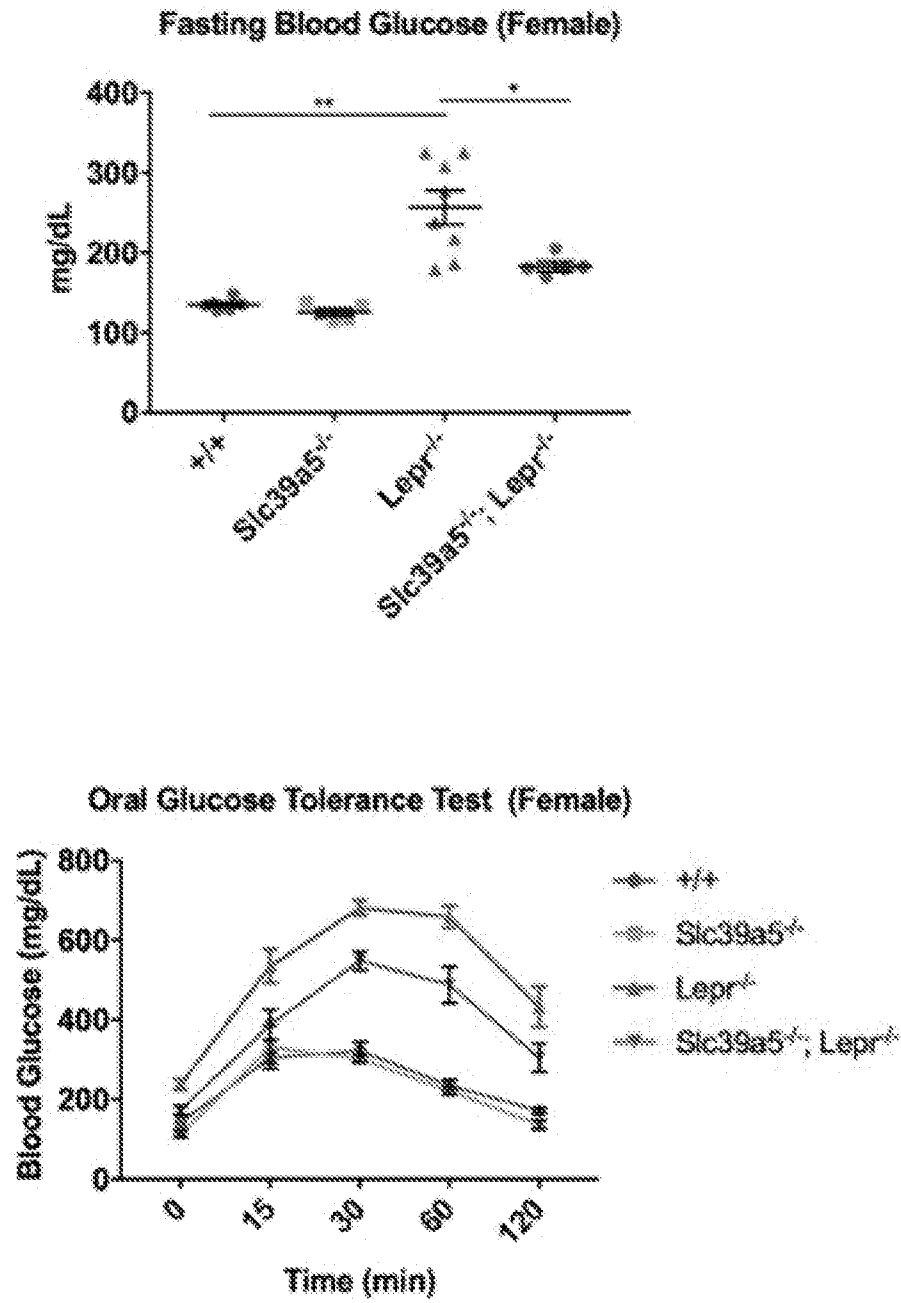


Figure 16

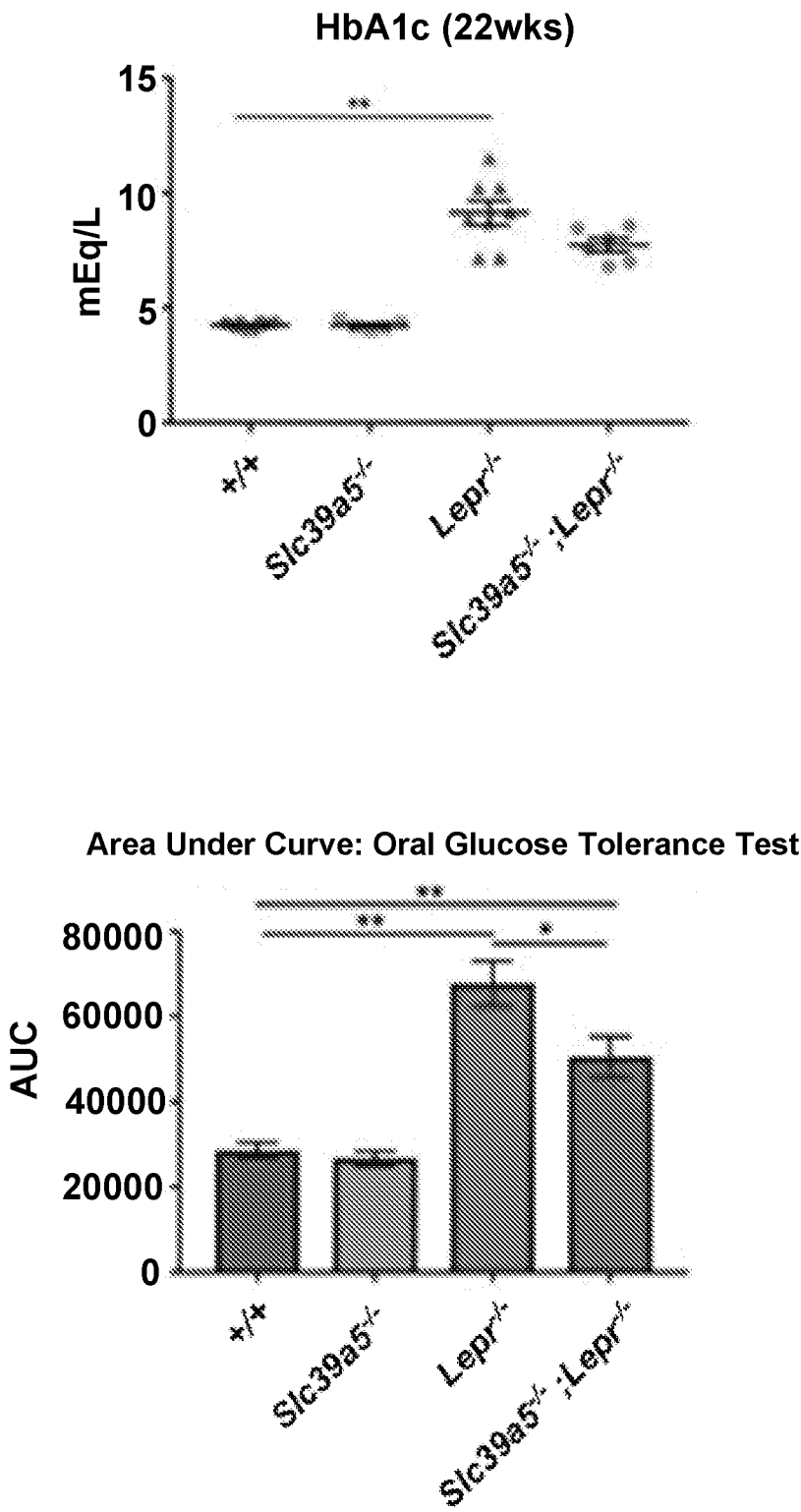


Figure 16 (cont.)

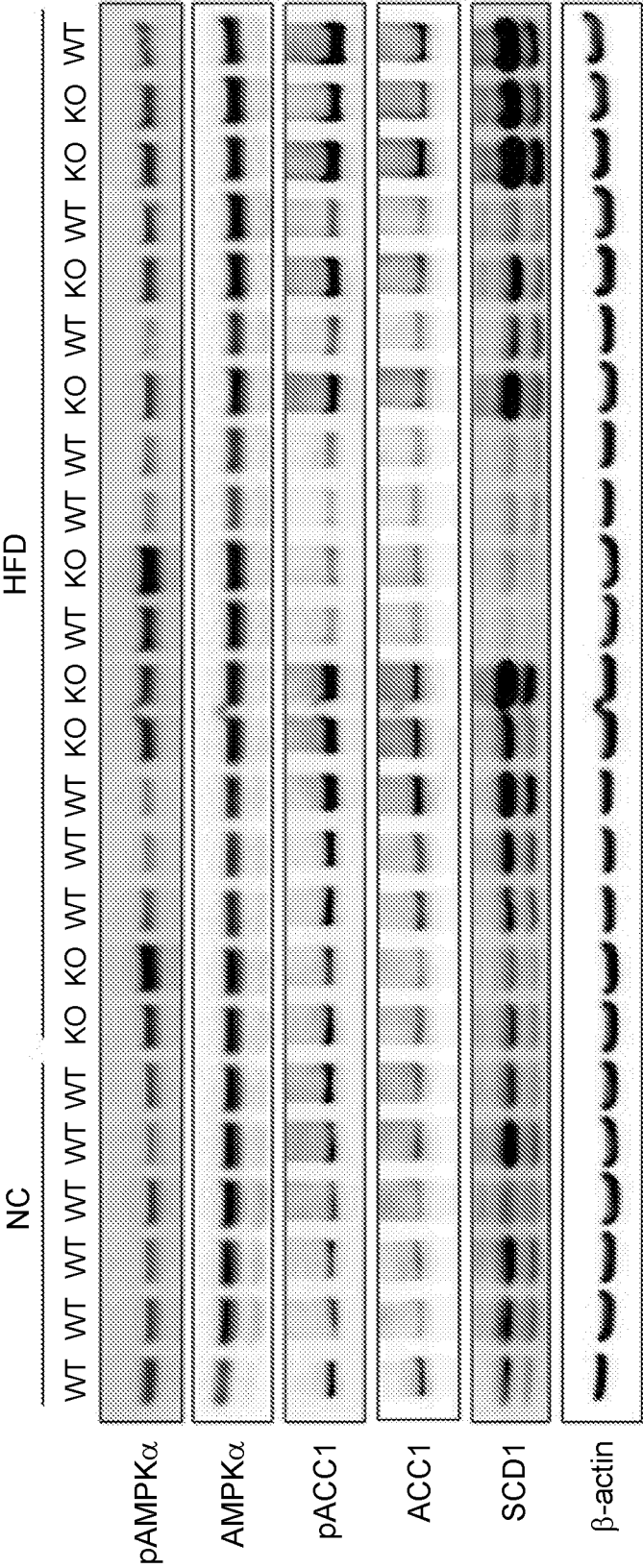


Figure 17

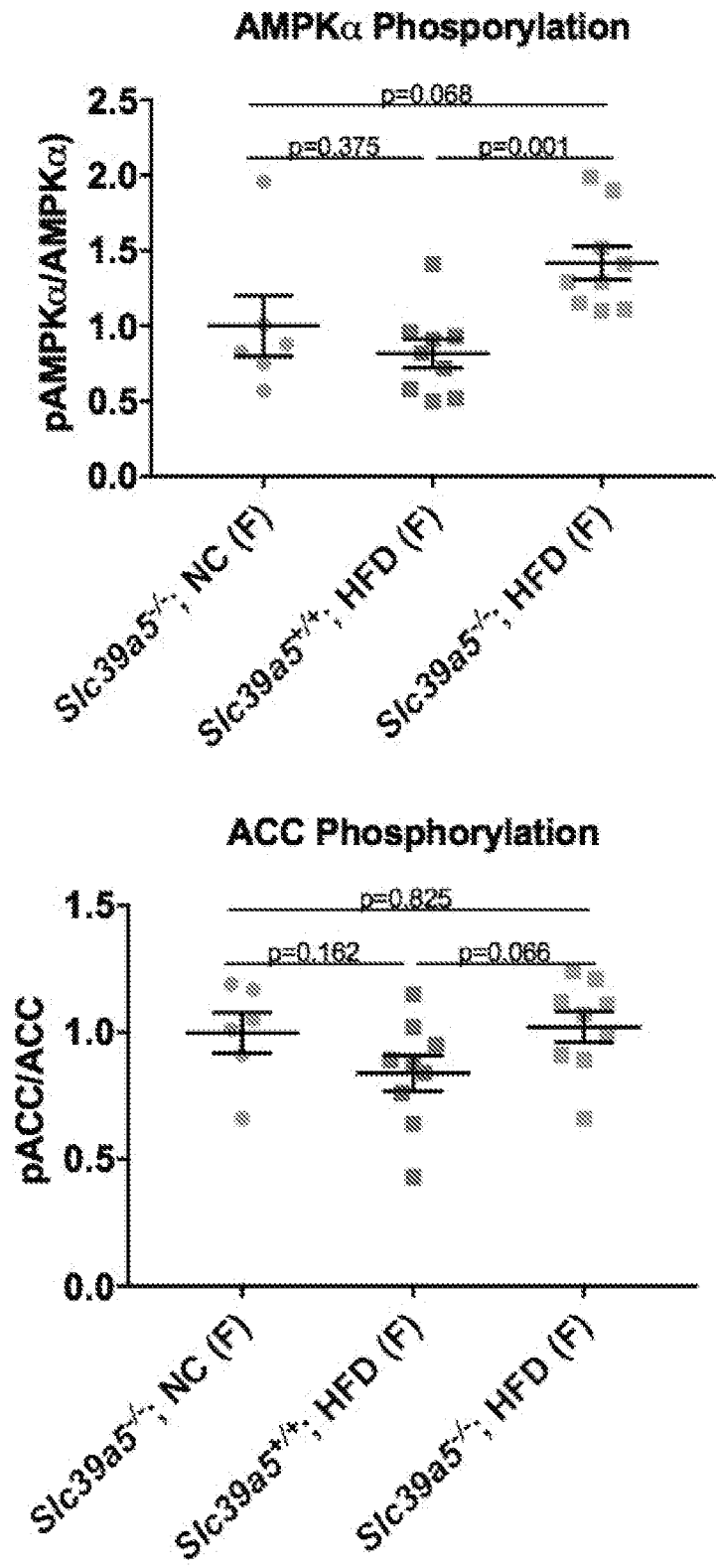


Figure 17 (cont.)

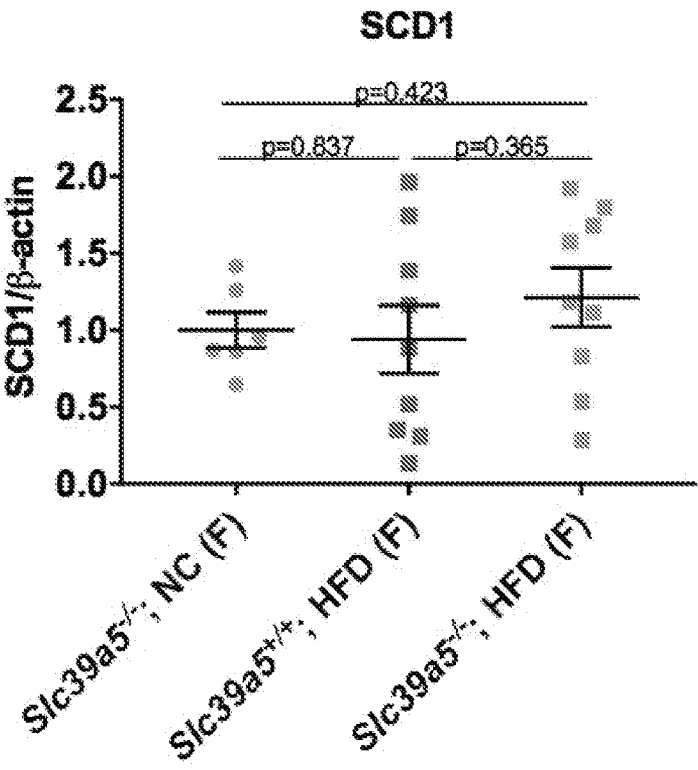


Figure 17 (cont.)

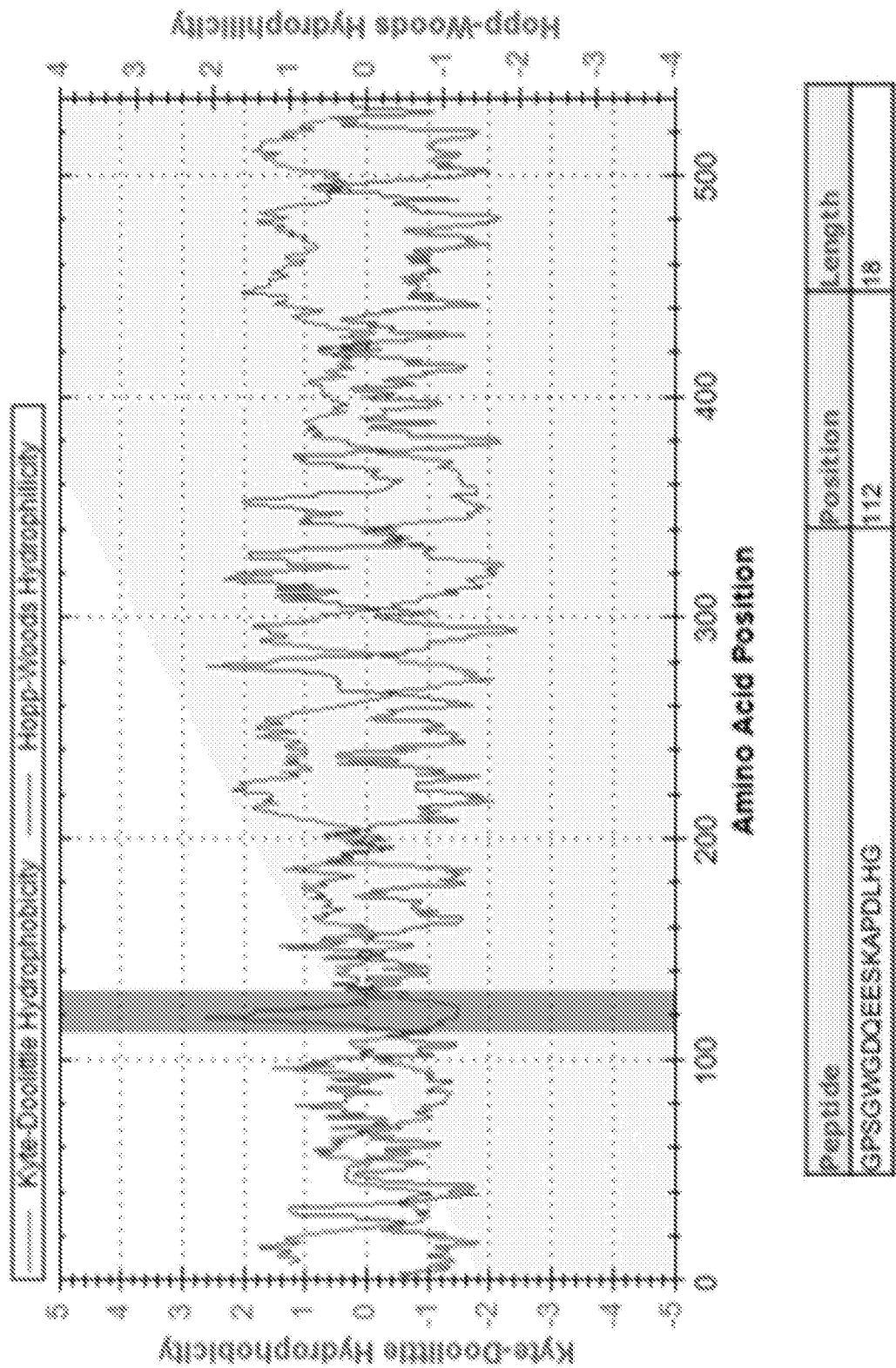
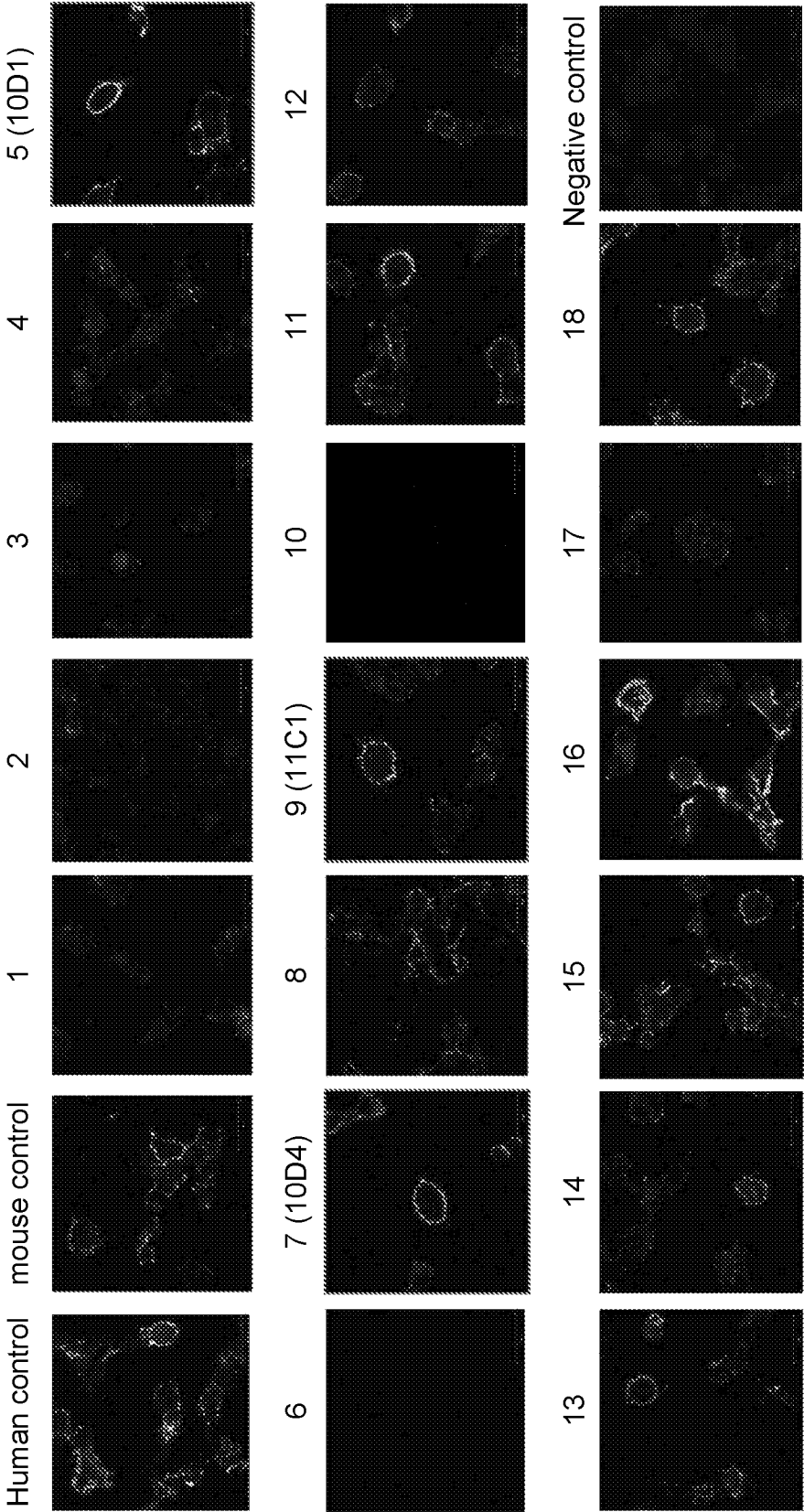


Figure 18

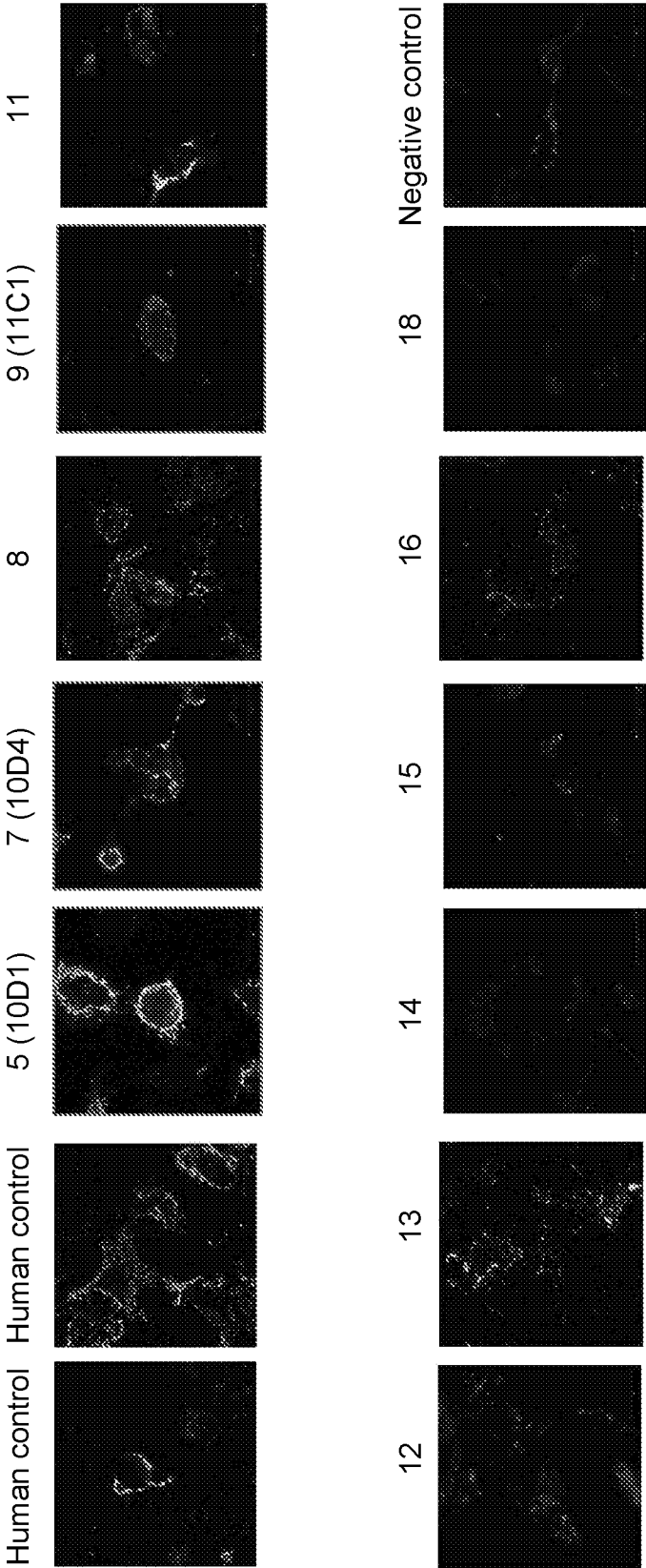
Slc39a5 mAb screening: HEK overexpressing mSlc39a5



Mouse supernatants 1:50; Control: SAB1408465 N-term -SLC39A5

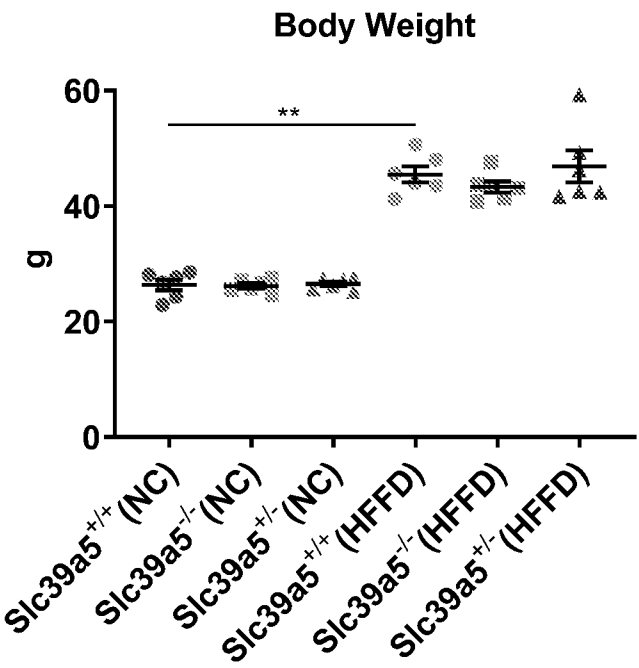
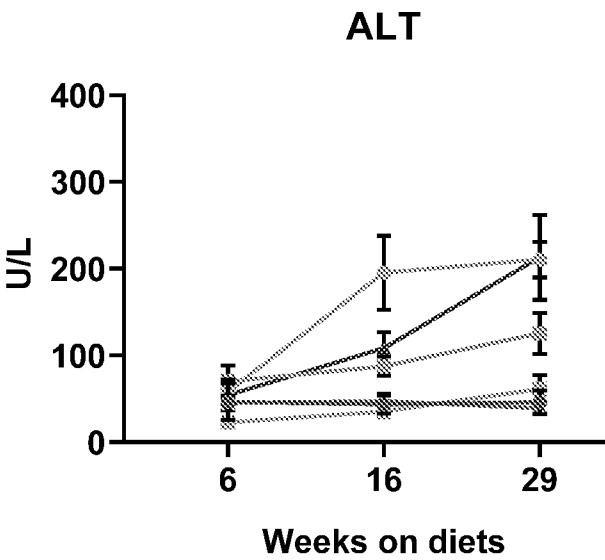
Figure 19

Slc39a5 mAb screening: HEK overexpressing hSLC39A5



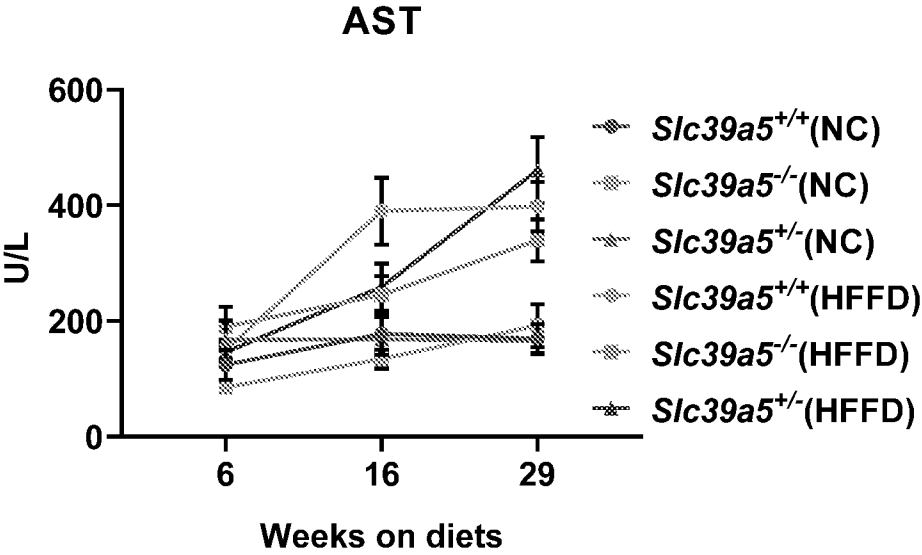
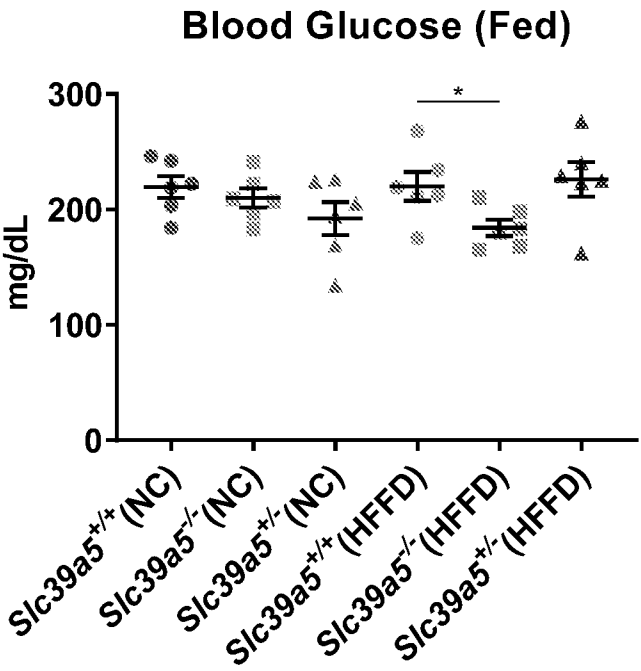
Mouse supernatants 1:50; Control: SAB1408465 N-term -SLC39A5

Figure 20



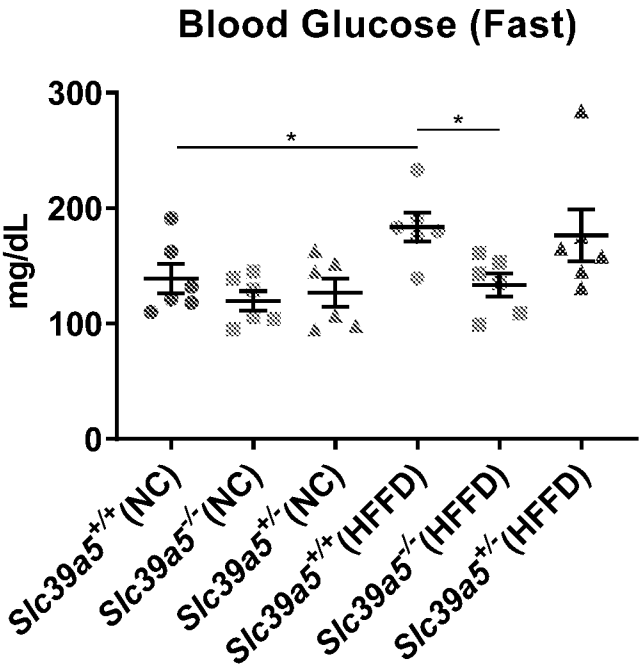
Normal chow; Zinc 87ppm; oGTT (20wk) after 16hr fast – 2mg/g body weight; *p<0.05, **p<0.01; Error bars: SEM

Figure 21



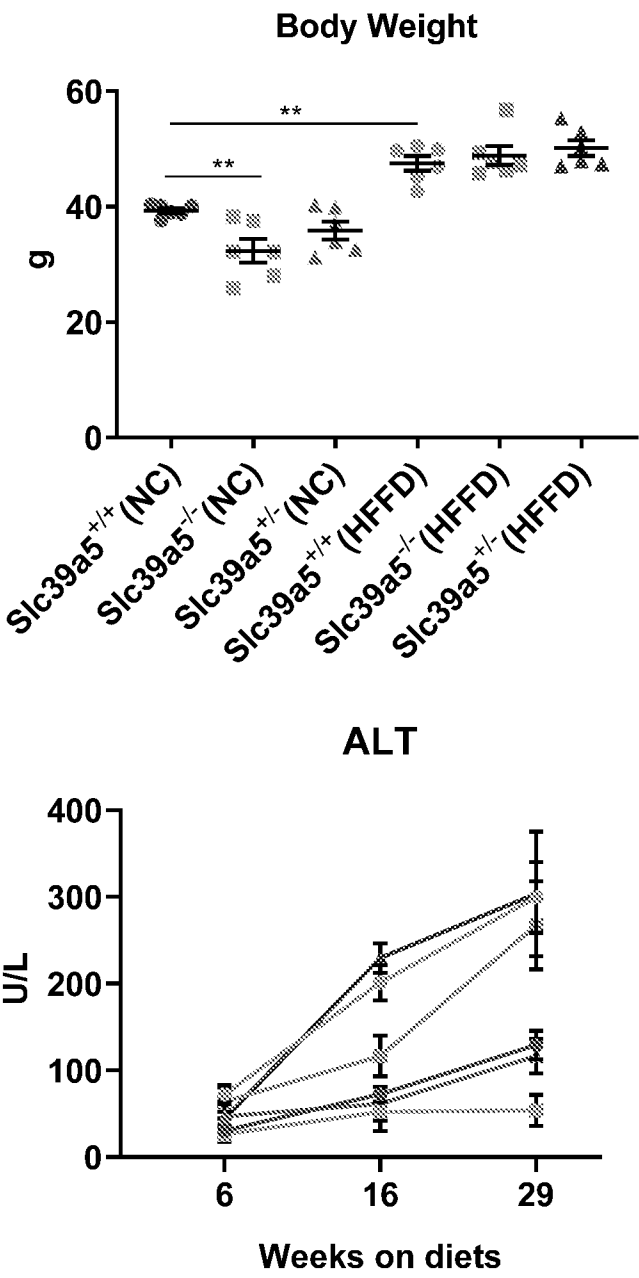
Normal chow; Zinc 87ppm; oGTT (20wk) after 16hr fast – 2mg/g body weight; *p<0.05, **p<0.01; Error bars: SEM

Figure 21 (cont.)



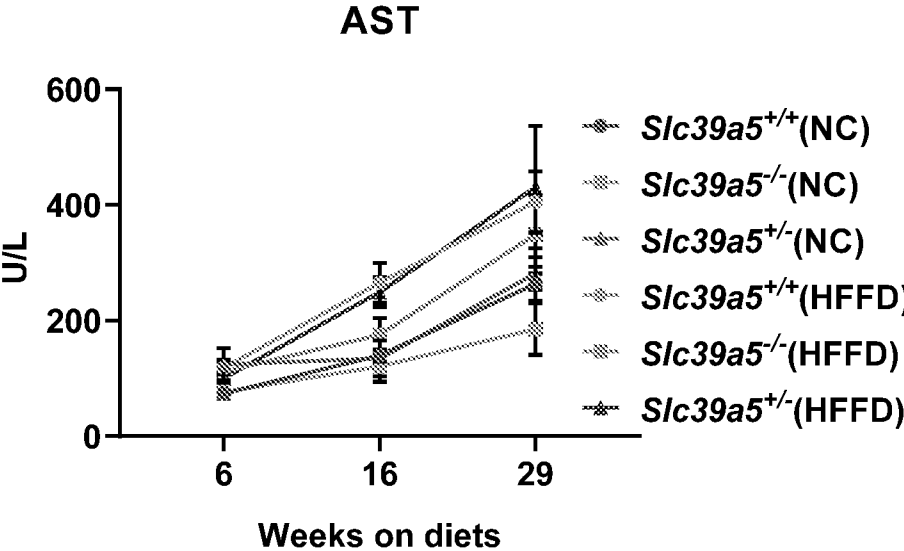
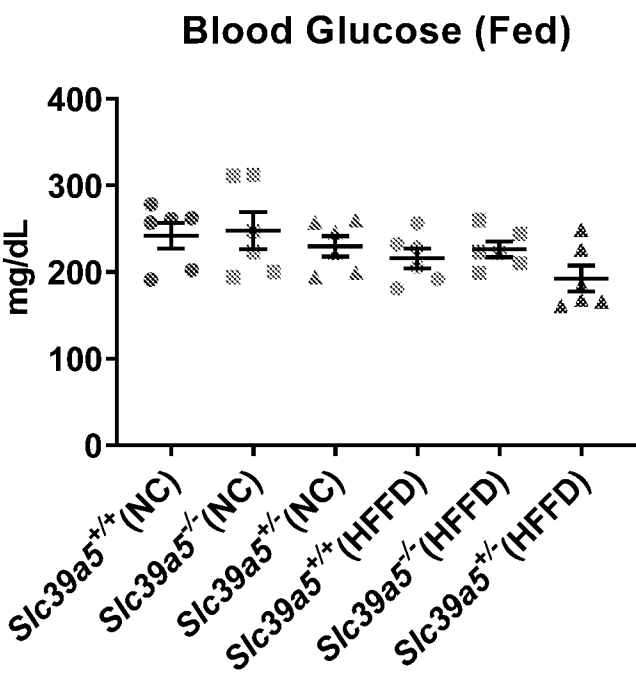
Normal chow; Zinc 87ppm; oGTT (20wk) after 16hr fast – 2mg/g body weight; *p<0.05, **p<0.01; Error bars: SEM

Figure 21 (cont.)



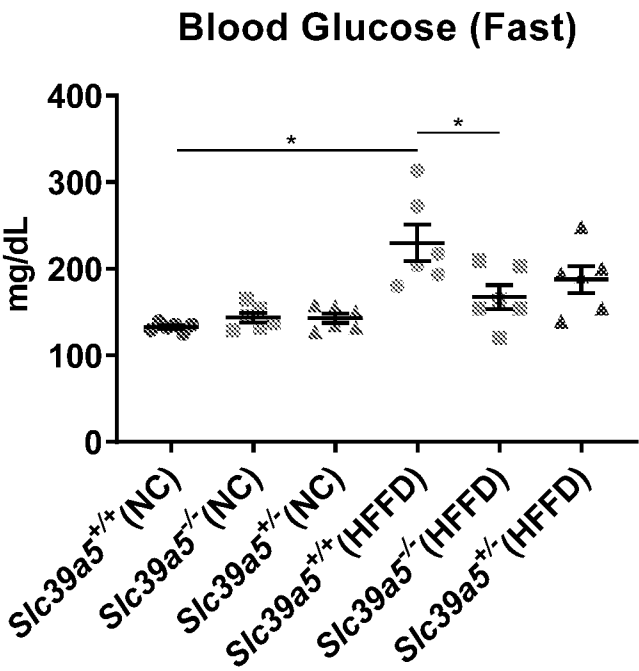
Normal chow; Zinc 87ppm; oGTT (20wk) after 16hr fast – 2mg/g body weight; *p<0.05, **p<0.01; Error bars: SEM

Figure 21 (cont.)



Normal chow; Zinc 87ppm; oGTT (20wk) after 16hr fast – 2mg/g body weight; *p<0.05, **p<0.01; Error bars: SEM

Figure 21 (cont.)



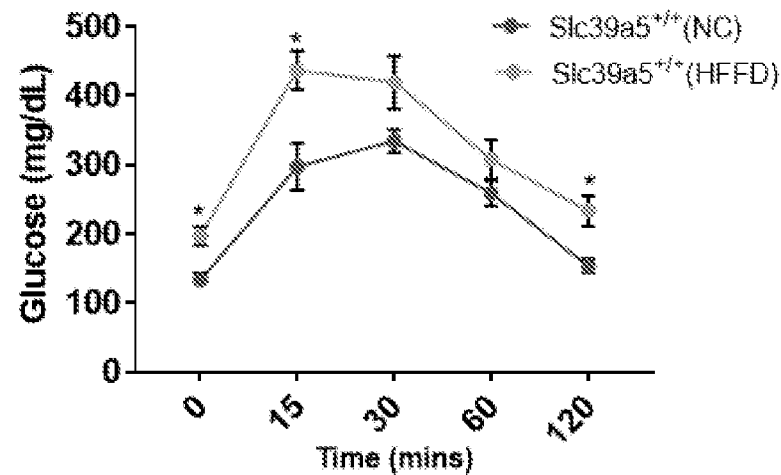
Normal chow; Zinc 87ppm; oGTT (20wk) after 16hr fast – 2mg/g body weight; *p<0.05, **p<0.01; Error bars: SEM

Figure 21 (cont.)

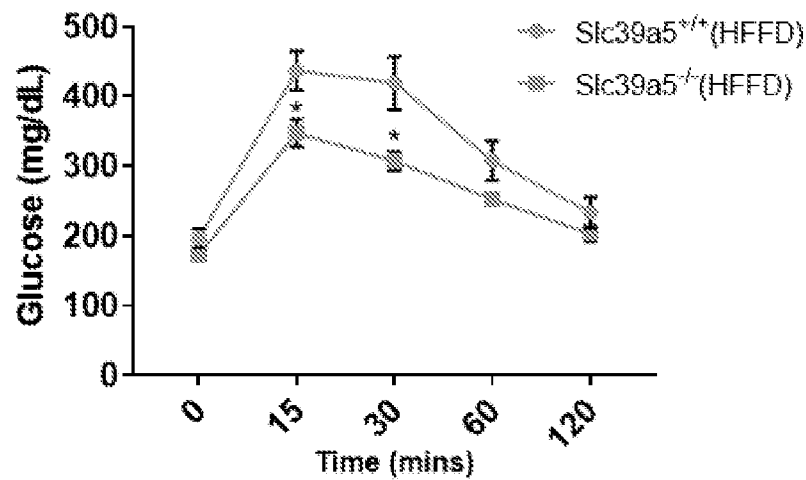


Oral glucose tolerance test

GTT (WT NC vs WT HFFD)



GTT (HFFD: WT vs KO)

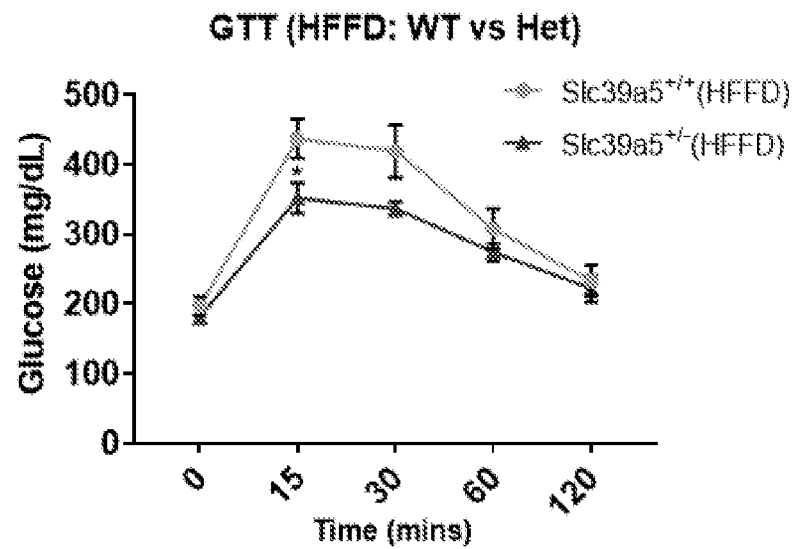


High fat high fructose (HFFD) or Normal Chow (NC) for 18weeks; Zinc 34ppm;
oGTT after 16hr fast, 2mg/g body weight; *p<0.05, **p<0.01

Figure 22



Oral glucose tolerance test



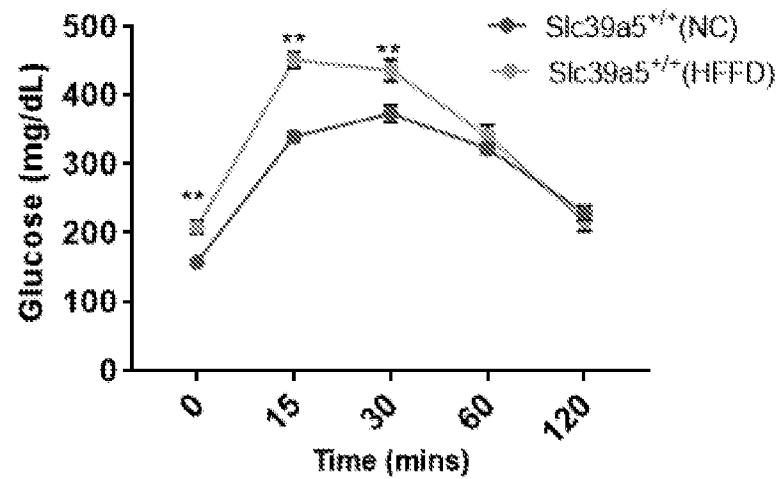
High fat high fructose (HFFD) or Normal Chow (NC) for 18weeks; Zinc 34ppm;
oGTT after 16hr fast, 2mg/g body weight; *p<0.05, **p<0.01

Figure 22 (cont.)

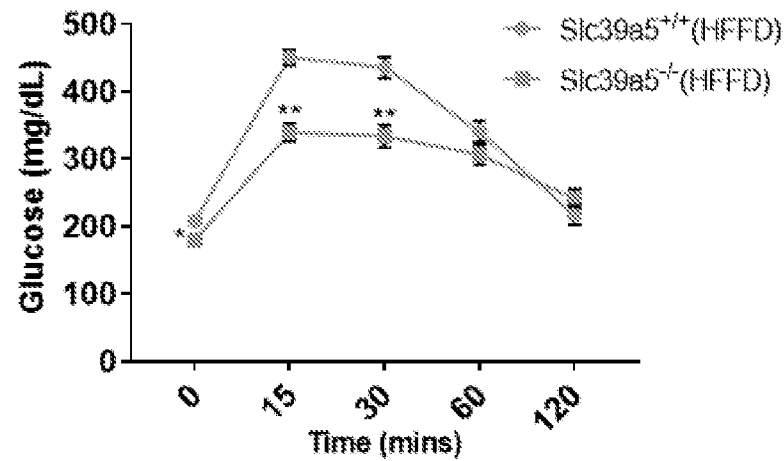


Oral glucose tolerance test

GTT (WT NC vs WT HFFD)



GTT (HFFD: WT vs KO)

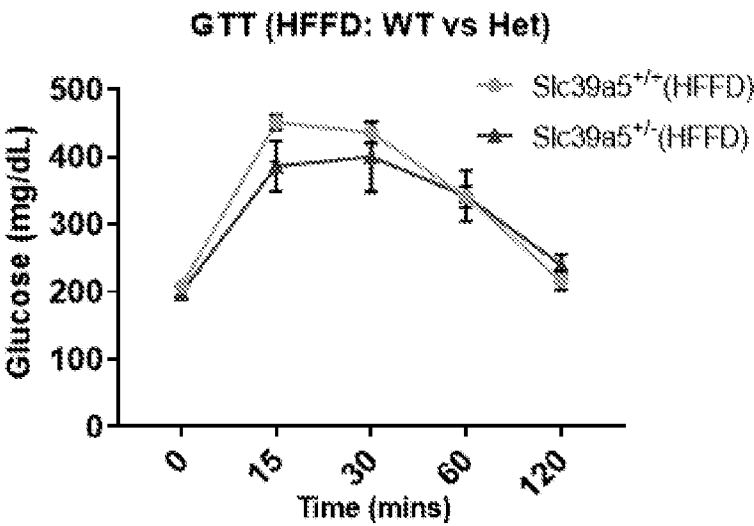


High fat high fructose (HFFD) or Normal Chow (NC) for 18weeks; Zinc 34ppm;
oGTT after 16hr fast, 2mg/g body weight; *p<0.05, **p<0.01

Figure 22 (cont.)

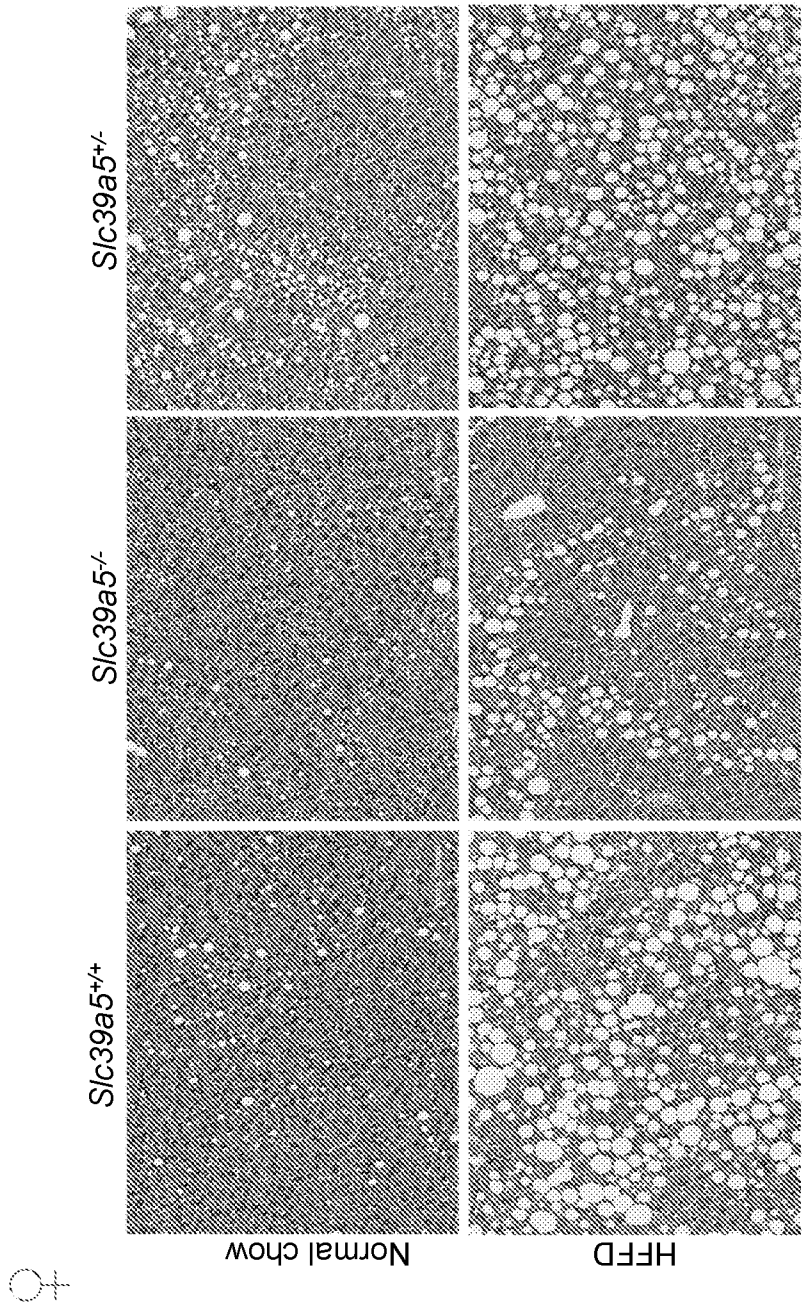


Oral glucose tolerance test



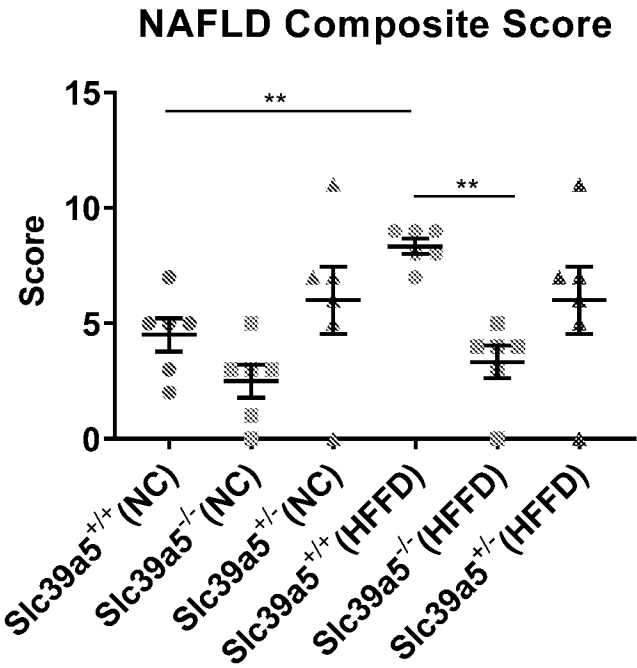
High fat high fructose (HFFD) or Normal Chow (NC) for 18weeks; Zinc 34ppm;
oGTT after 16hr fast, 2mg/g body weight; *p<0.05, **p<0.01

Figure 22 (cont.)



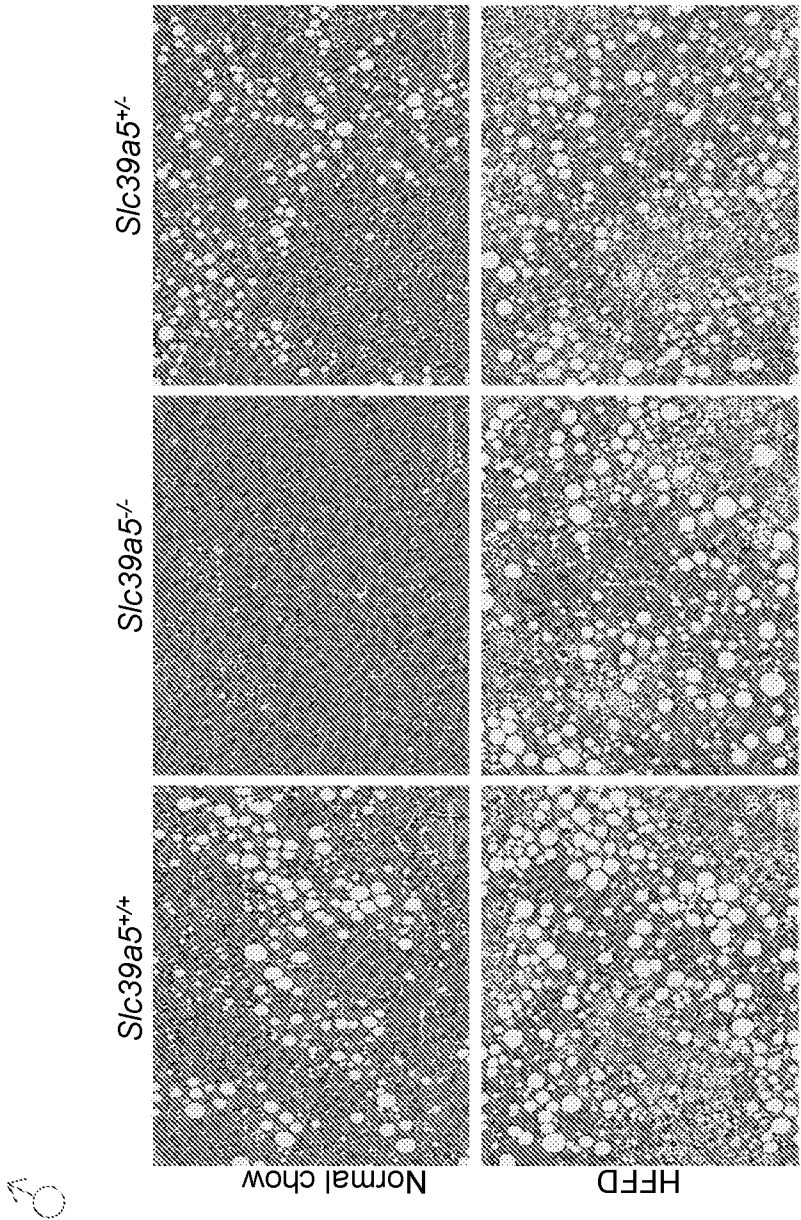
Liver histology – 29 weeks; NAFLD Composite Score: Macrovesicular Steatosis, Microvesicular Steatosis, Hepatocellular Hypertrophy, Inflammation, Fibrosis; * $p<0.05$, ** $p<0.01$; Error bars: SEM

Figure 23



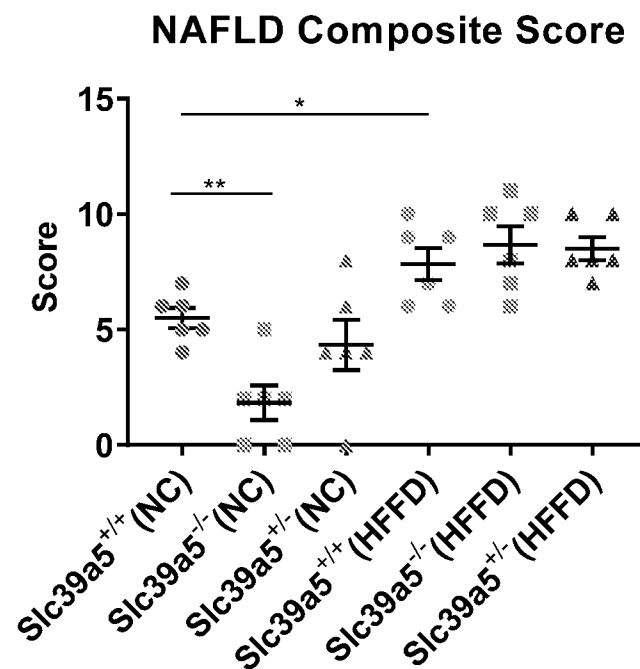
Liver histology – 29 weeks; NAFLD Composite Score: Macrovesicular Steatosis, Microvesicular Steatosis, Hepatocellular Hypertrophy, Inflammation, Fibrosis; *p<0.05, **p<0.01; Error bars: SEM

Figure 23 (cont.)



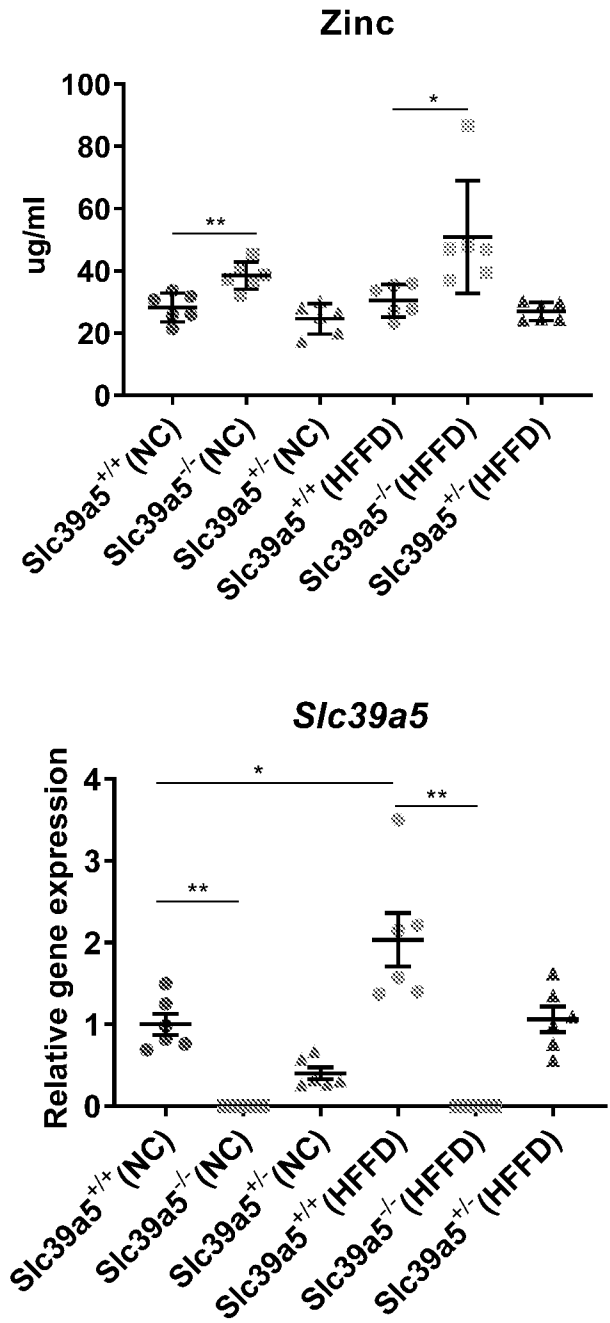
Liver histology – 29 weeks; NAFLD Composite Score: Macrovesicular Steatosis, Microvesicular Steatosis, Hepatocellular Hypertrophy, Inflammation, Fibrosis; *p<0.05, **p<0.01; Error bars: SEM

Figure 23 (cont.)



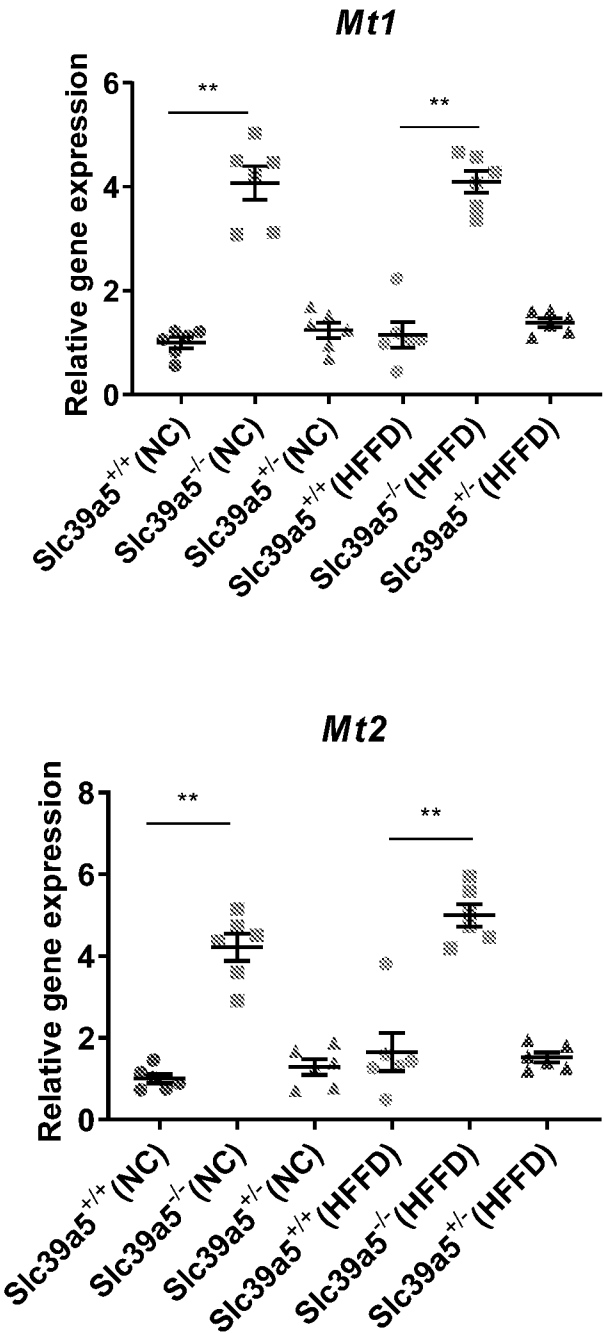
Liver histology – 29 weeks; NAFLD Composite Score: Macrovesicular Steatosis, Microvesicular Steatosis, Hepatocellular Hypertrophy, Inflammation, Fibrosis; * $p < 0.05$, ** $p < 0.01$; Error bars: SEM

Figure 23 (cont.)



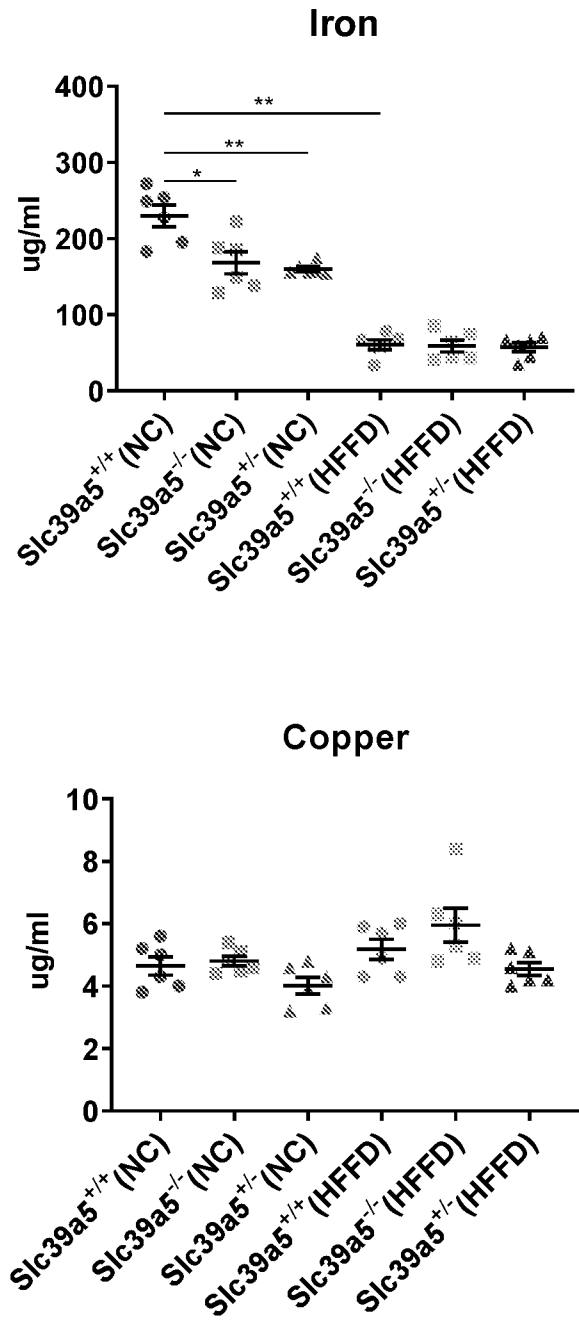
Hepatic ion quantification and Taqman analysis – 29 weeks; *p<0.05, **p<0.01;
Error bars: SEM

Figure 24A



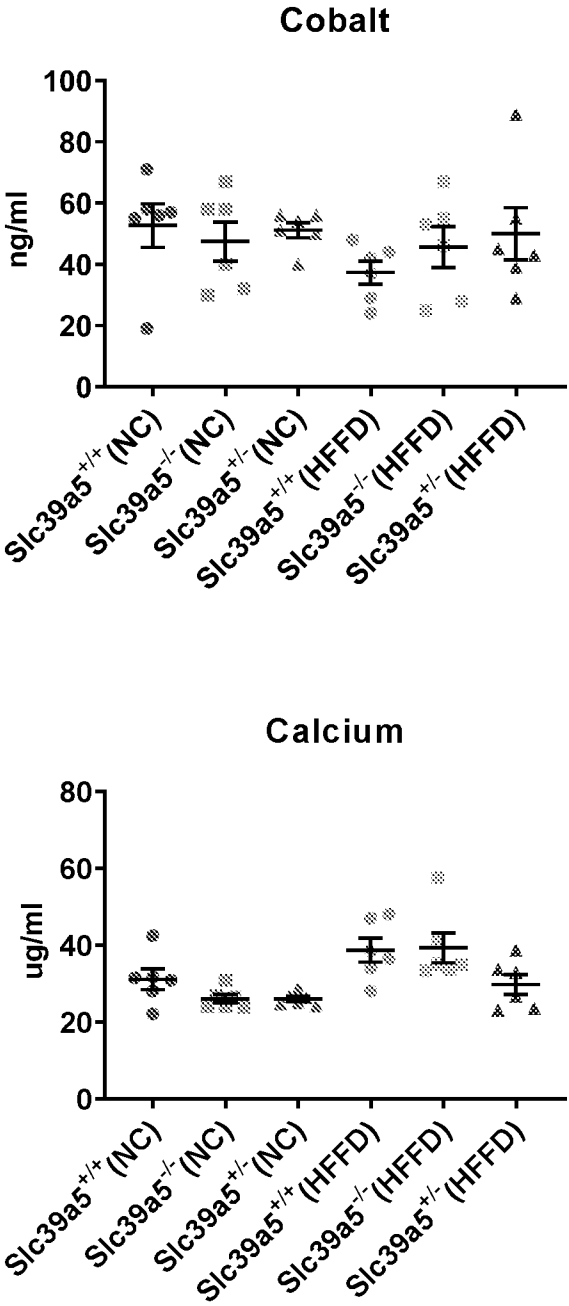
Hepatic ion quantification and Taqman analysis – 29 weeks; * $p < 0.05$, ** $p < 0.01$;
Error bars: SEM

Figure 24A (cont.)



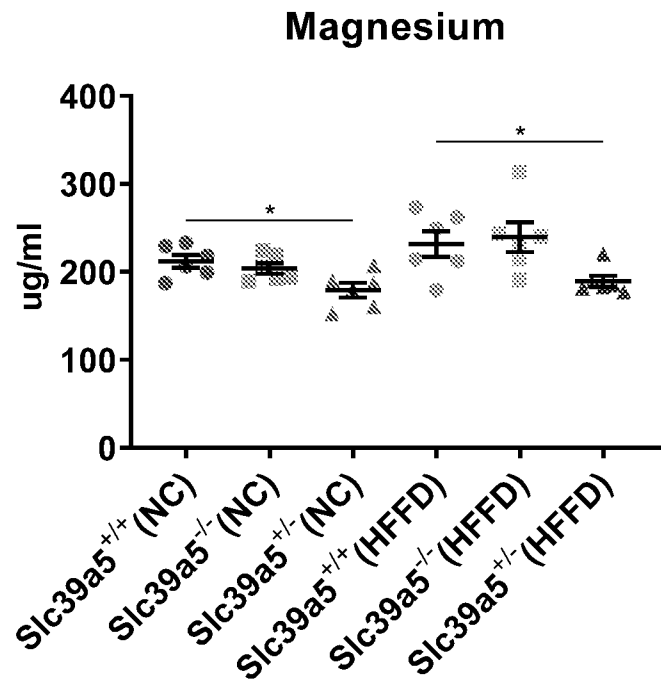
Hepatic ion quantification and Taqman analysis – 29 weeks; *p<0.05, **p<0.01;
Error bars: SEM

Figure 24A (cont.)



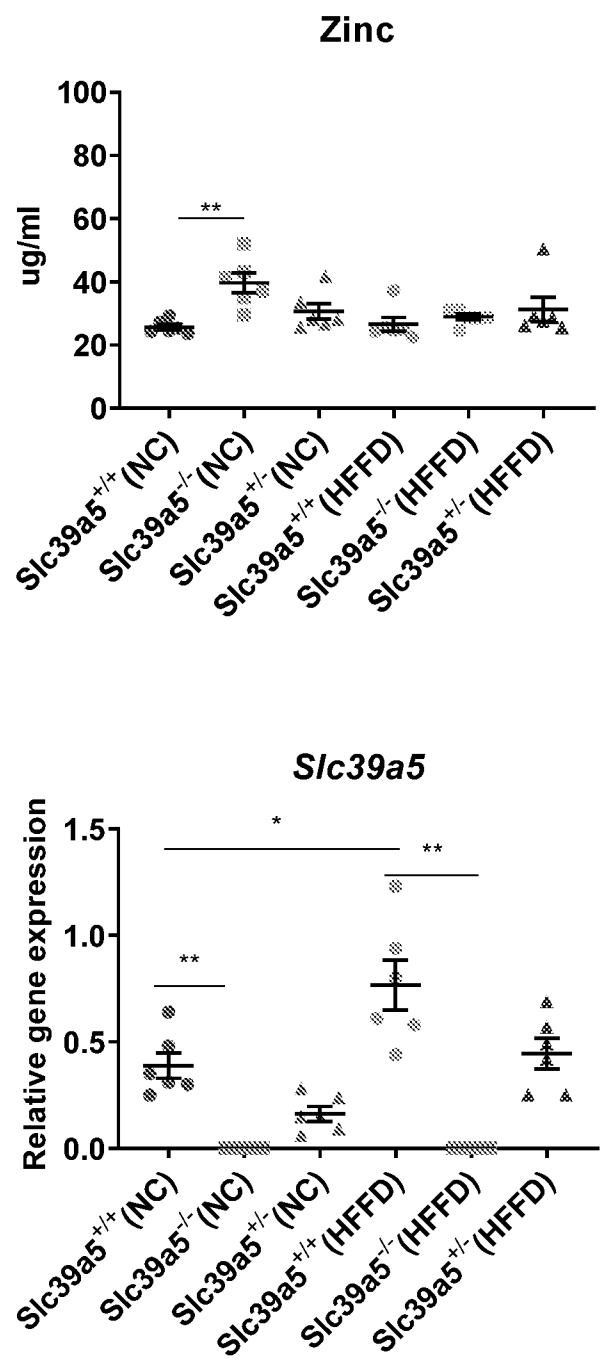
Hepatic ion quantification and Taqman analysis – 29 weeks; *p<0.05, **p<0.01;
Error bars: SEM

Figure 24A (cont.)



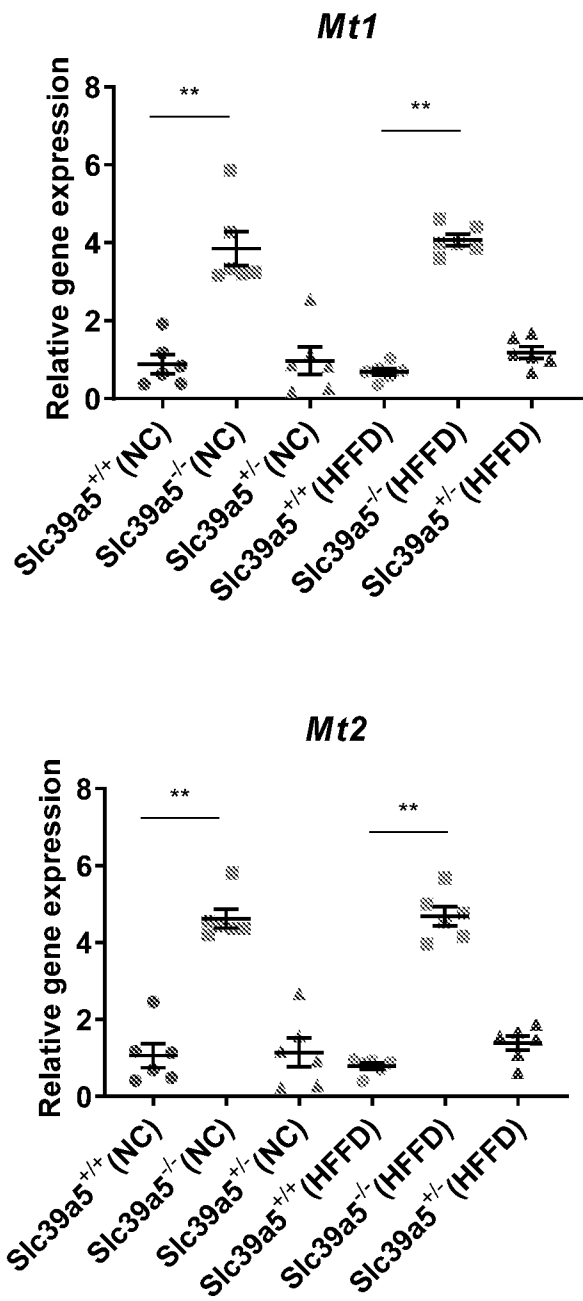
Hepatic ion quantification and Taqman analysis – 29 weeks; *p<0.05, **p<0.01;
Error bars: SEM

Figure 24A (cont.)



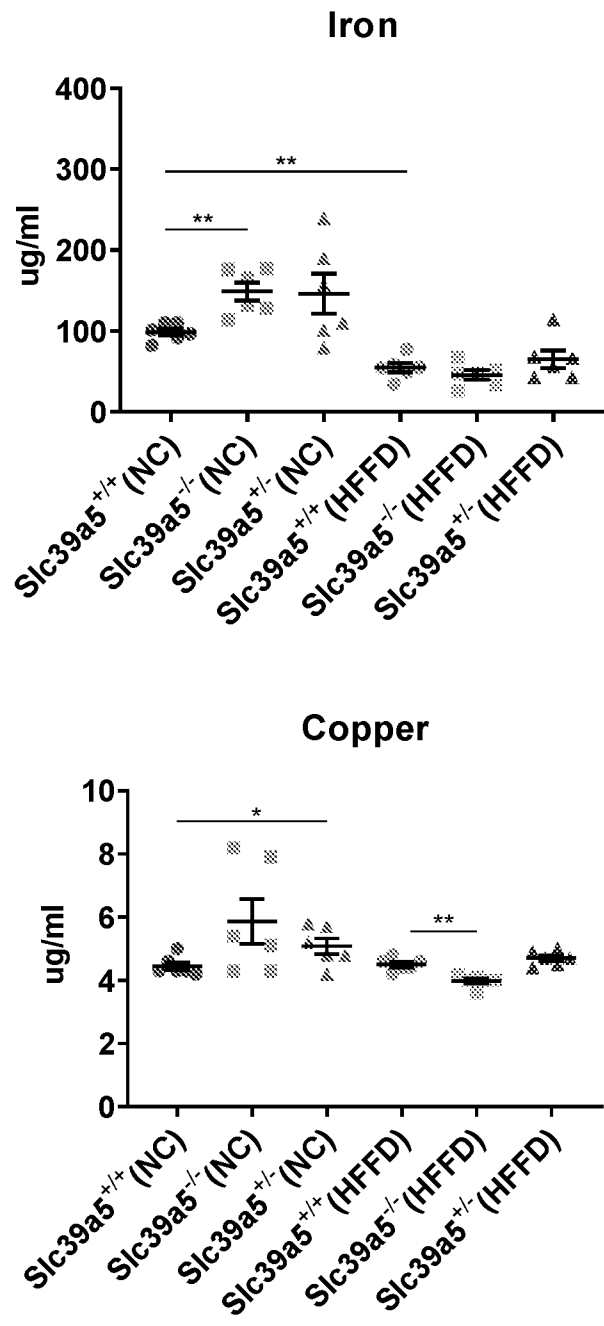
Hepatic ion quantification and Taqman analysis – 29 weeks; *p<0.05, **p<0.01;
Error bars: SEM

Figure 24B



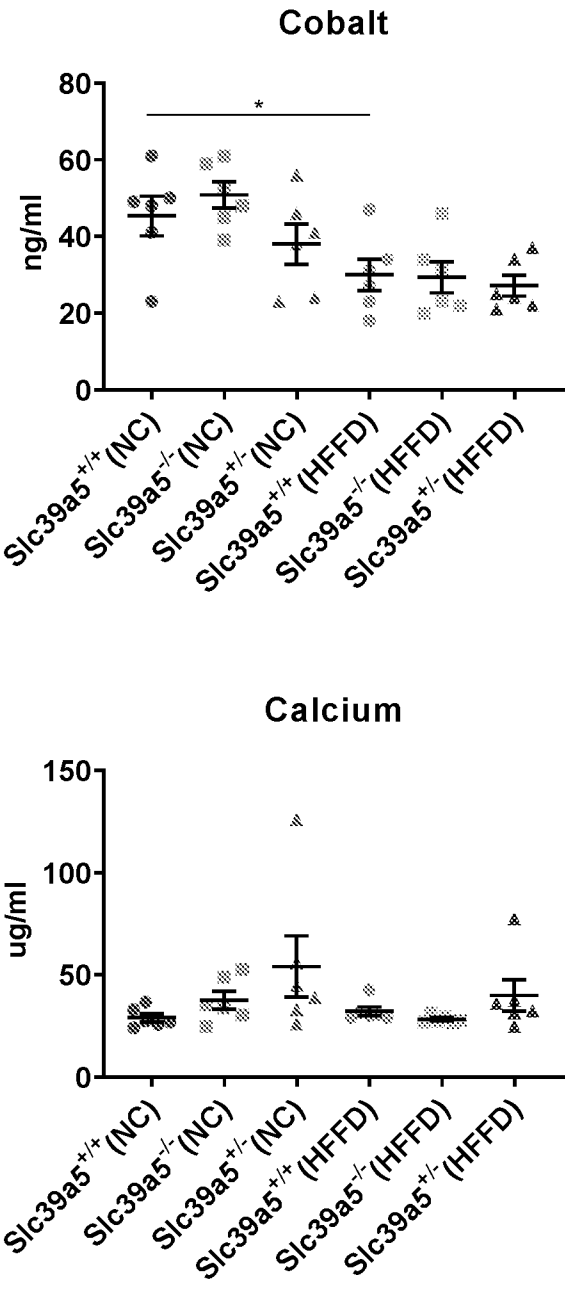
Hepatic iron quantification and Taqman analysis – 29 weeks; *p<0.05, **p<0.01;
Error bars: SEM

Figure 24B (cont.)



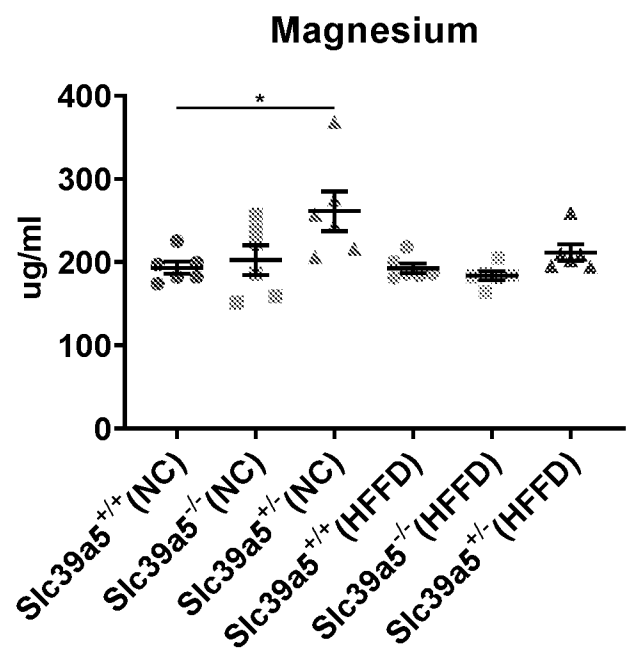
Hepatic ion quantification and Taqman analysis – 29 weeks; *p<0.05, **p<0.01;
Error bars: SEM

Figure 24B (cont.)



Hepatic ion quantification and Taqman analysis – 29 weeks; *p<0.05, **p<0.01;
Error bars: SEM

Figure 24B (cont.)



Hepatic ion quantification and Taqman analysis – 29 weeks; *p<0.05, **p<0.01;
Error bars: SEM

Figure 24B (cont.)

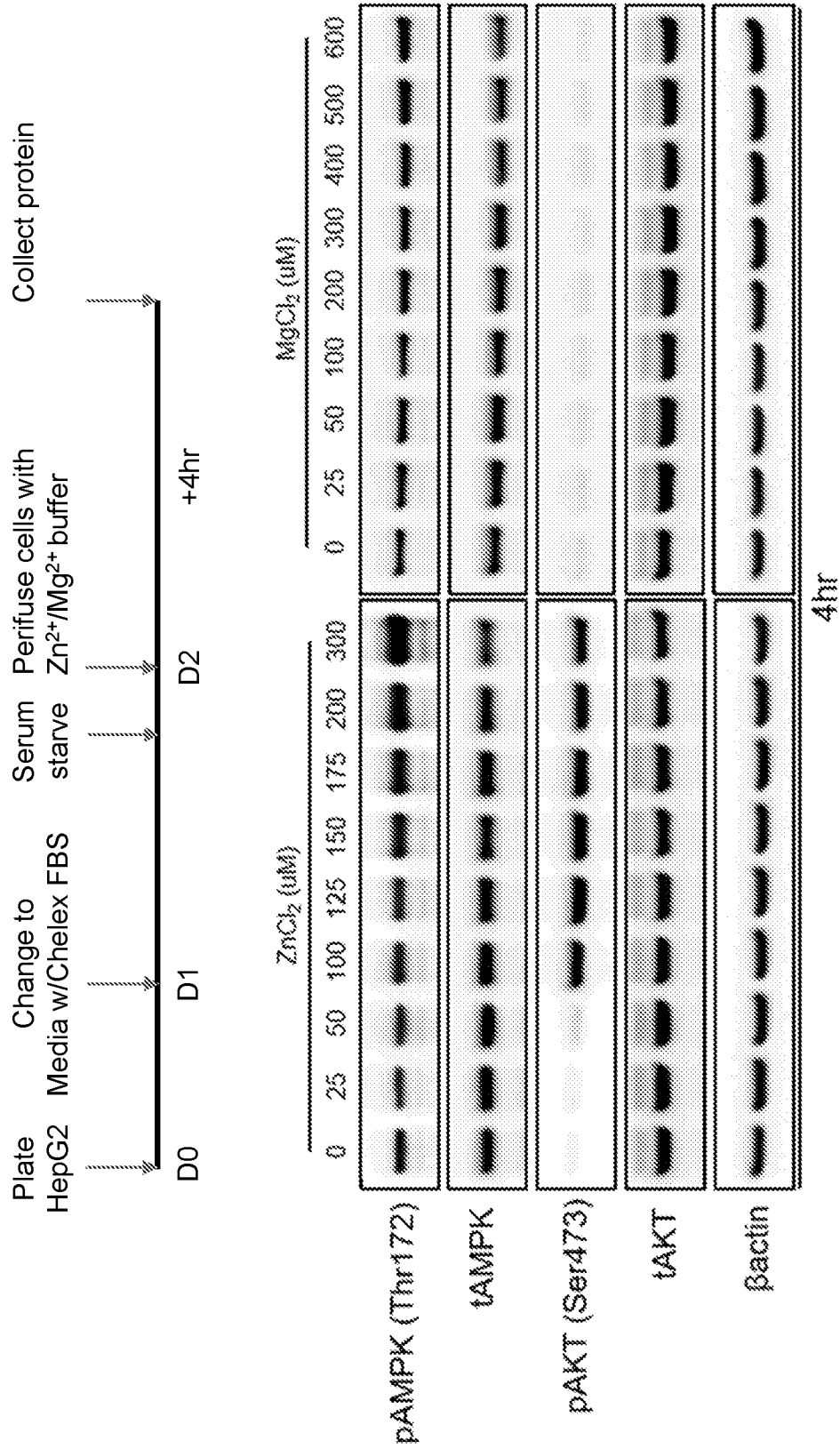


Figure 25A

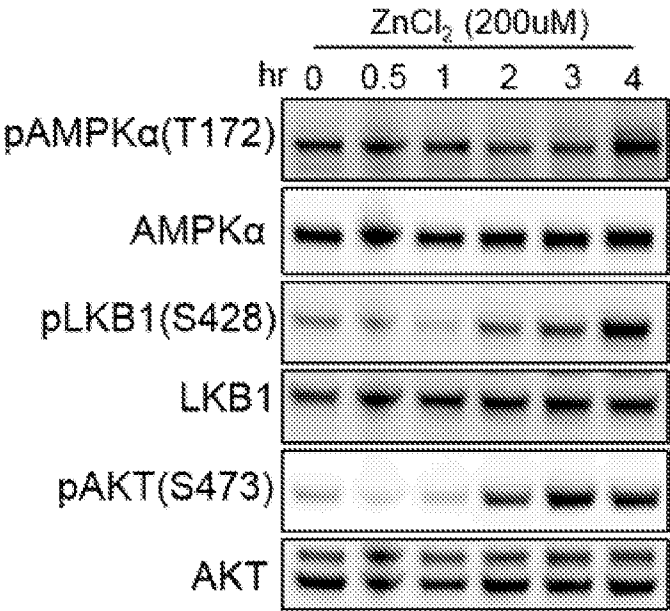


Figure 25A (cont.)

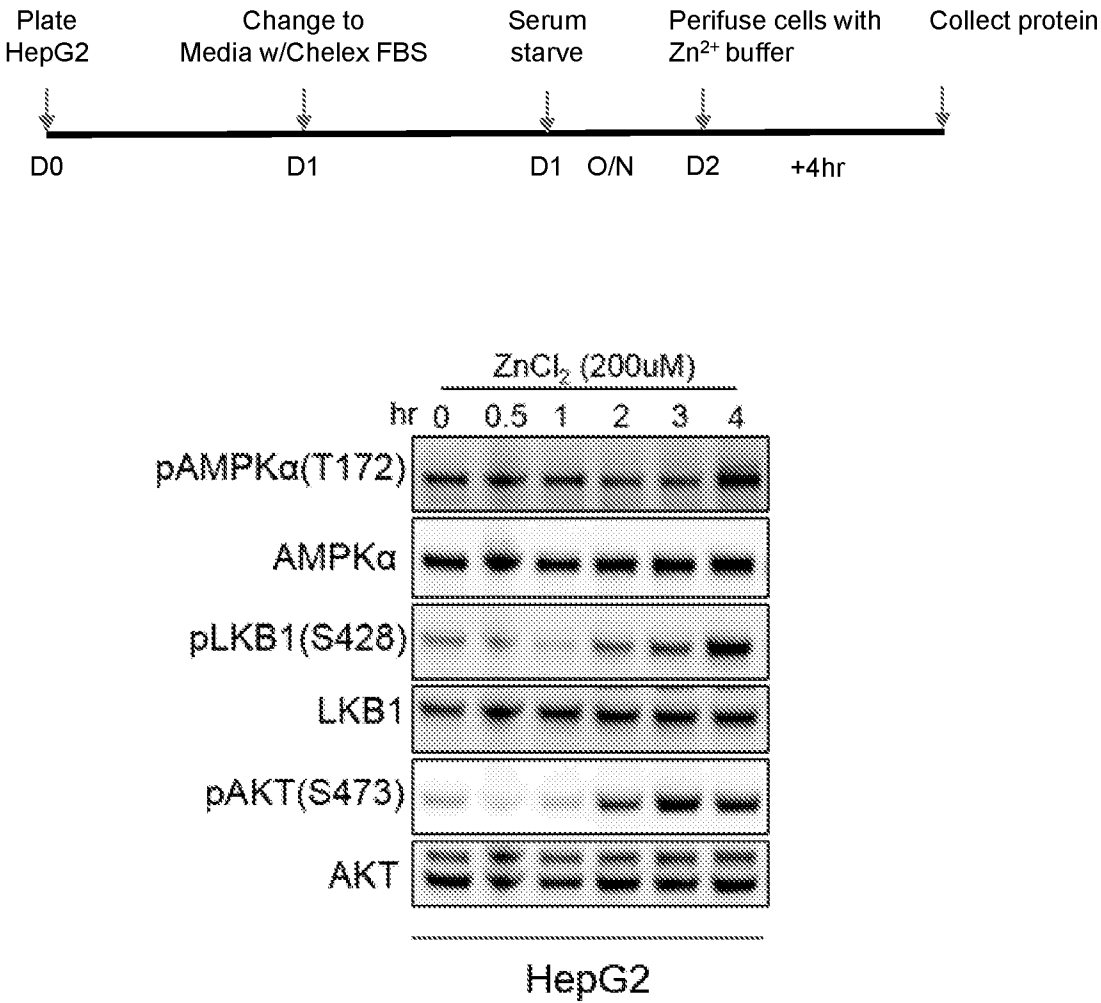
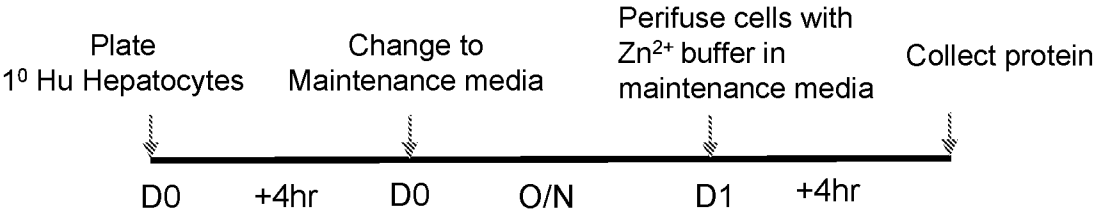
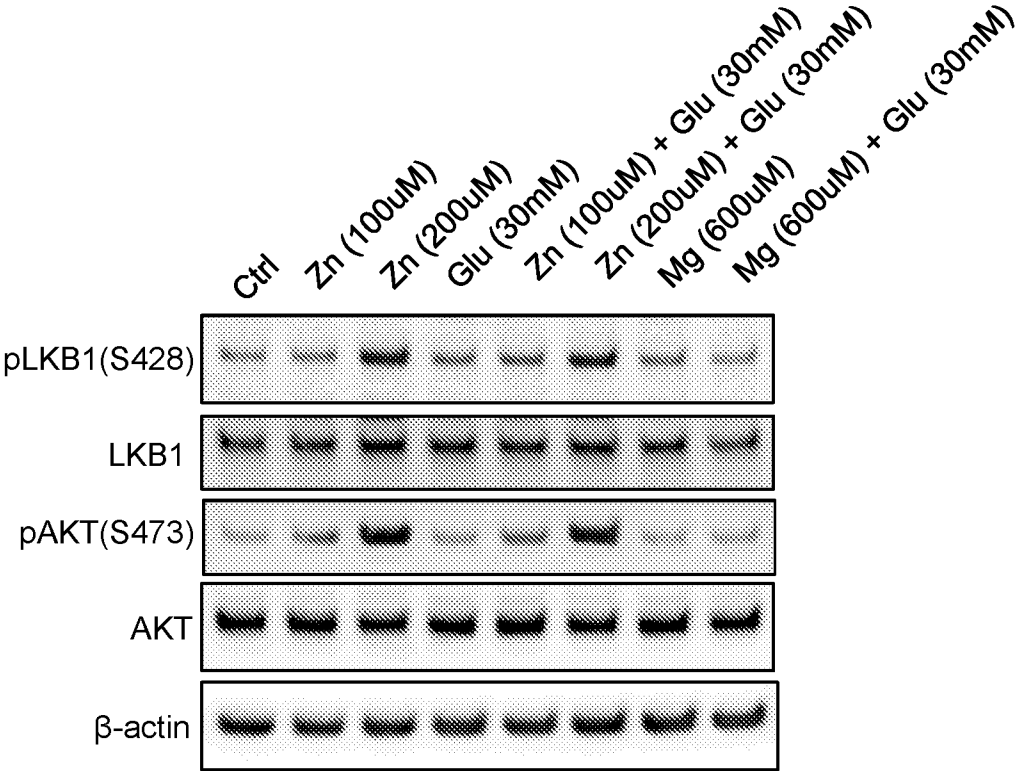


Figure 25B



10 Hu Hepatocytes* (5-donor pool);
4hr
 1^0 Hu Hepatocytes* (5-donor pool); HM CPP5, Thermofisher

Figure 25B (cont.)

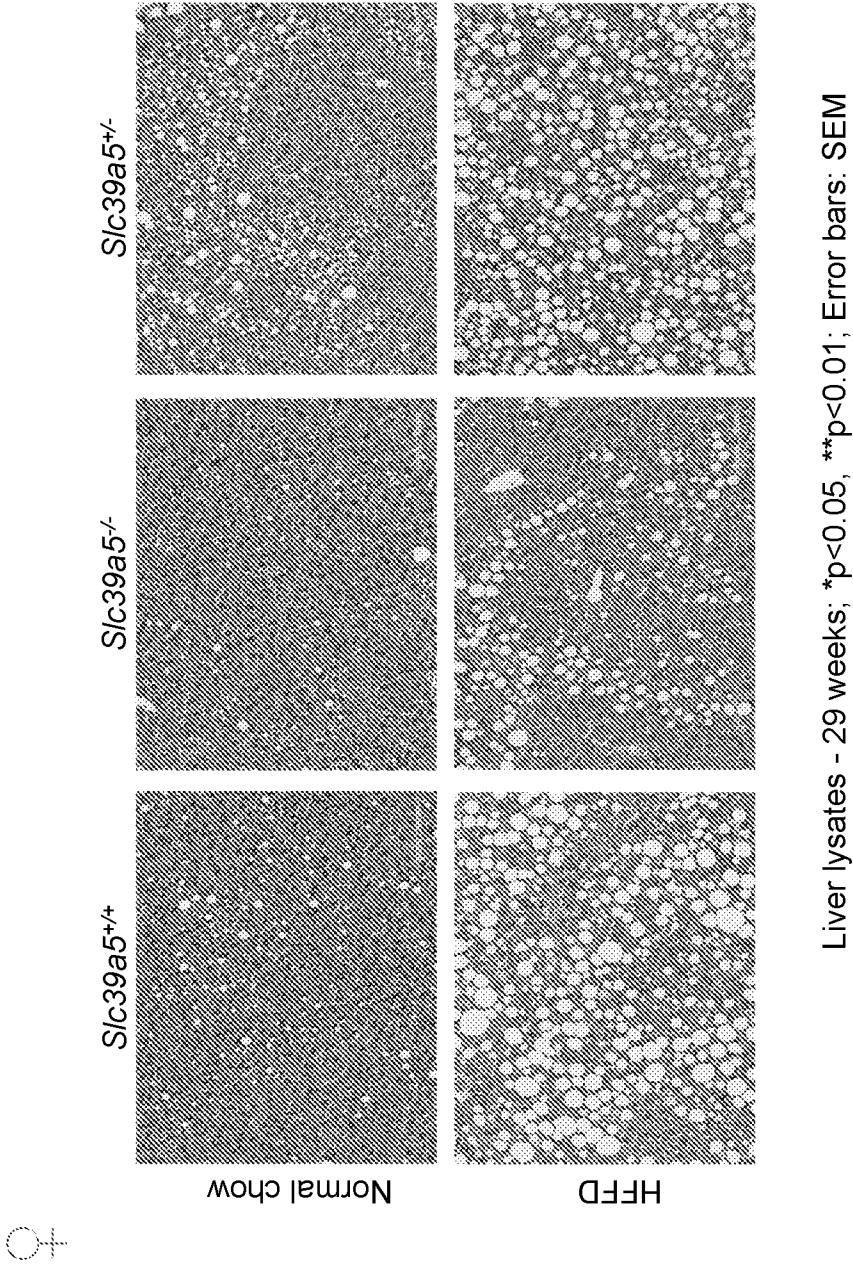
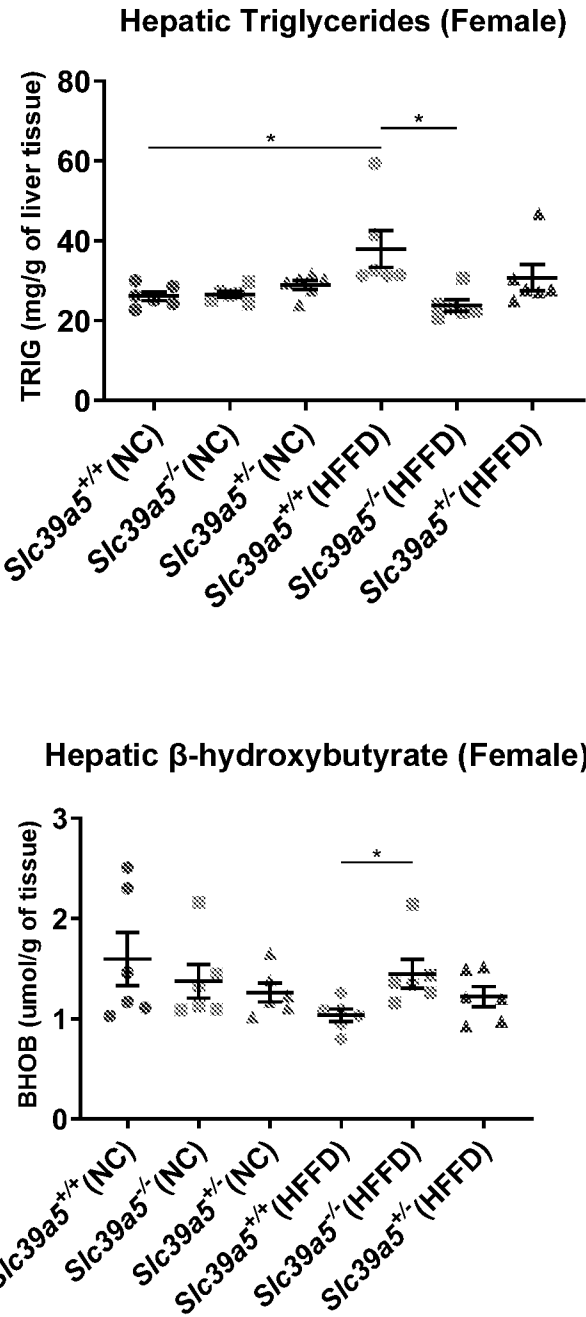
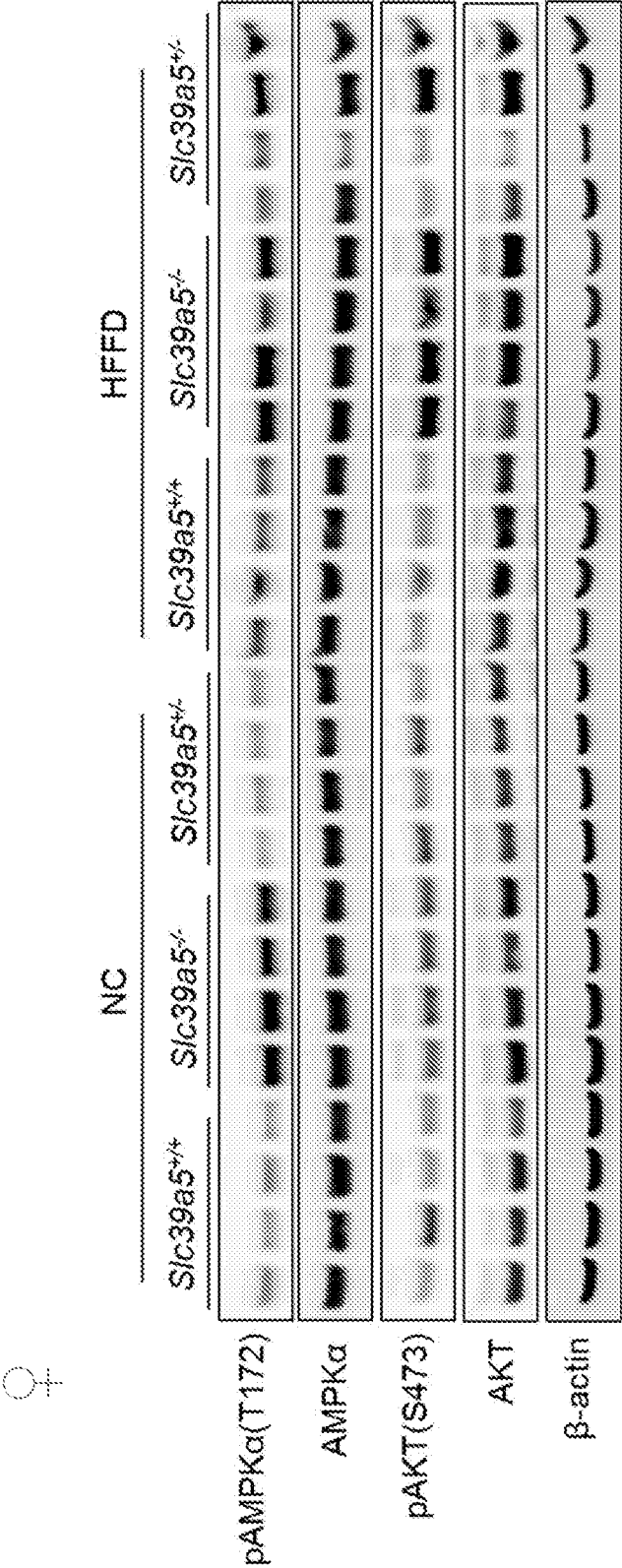


Figure 26A



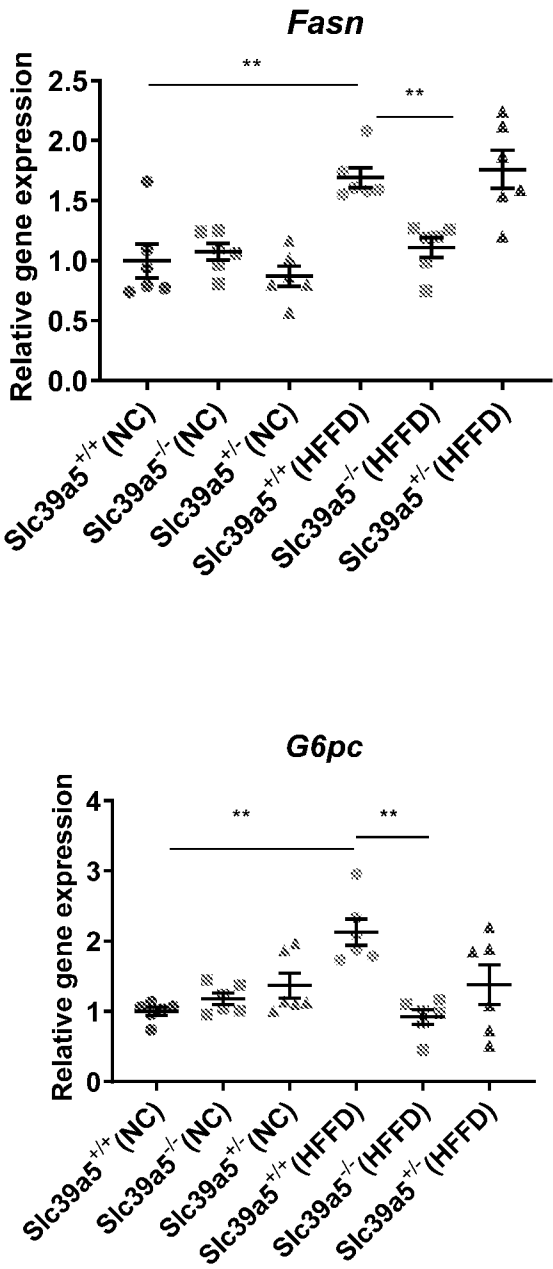
Liver lysates - 29 weeks; *p<0.05, **p<0.01; Error bars: SEM

Figure 26A (cont.)



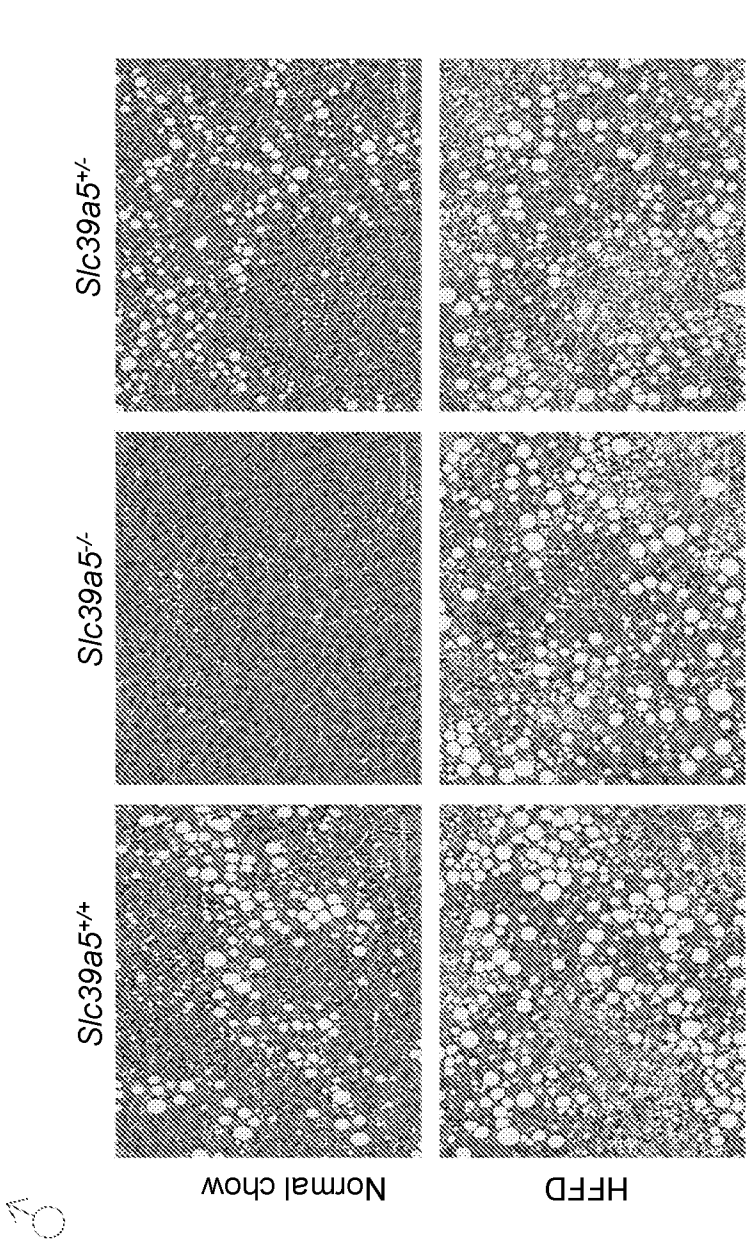
Liver lysates - 29 weeks; *p<0.05, **p<0.01; Error bars: SEM

Figure 26A (cont.)



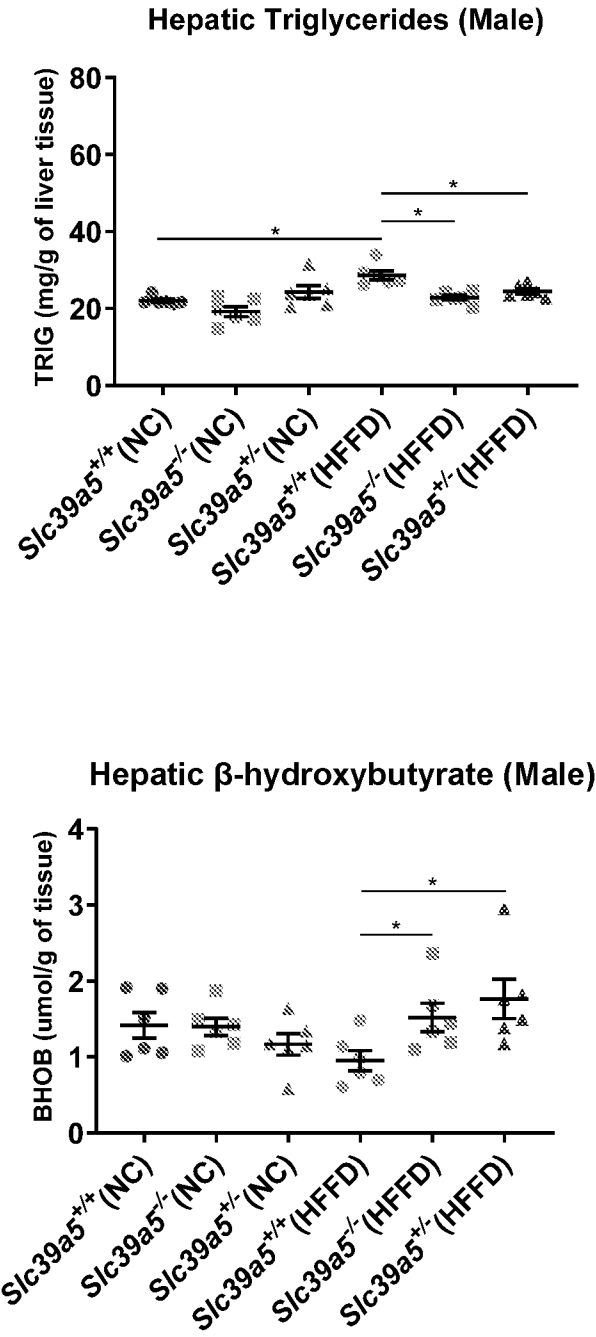
Liver lysates - 29 weeks; *p<0.05, **p<0.01; Error bars: SEM

Figure 26A (cont.)



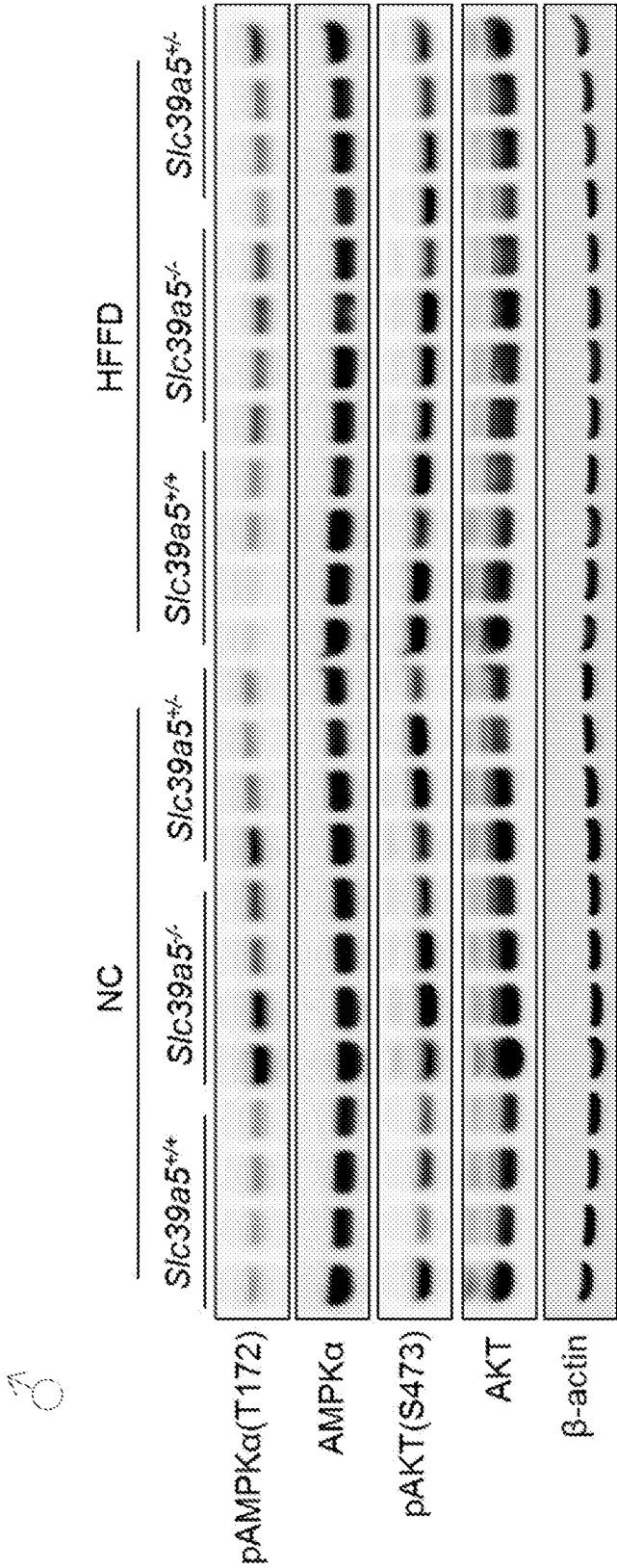
Liver lysates - 29 weeks; *p<0.05, **p<0.01; Error bars: SEM

Figure 26B



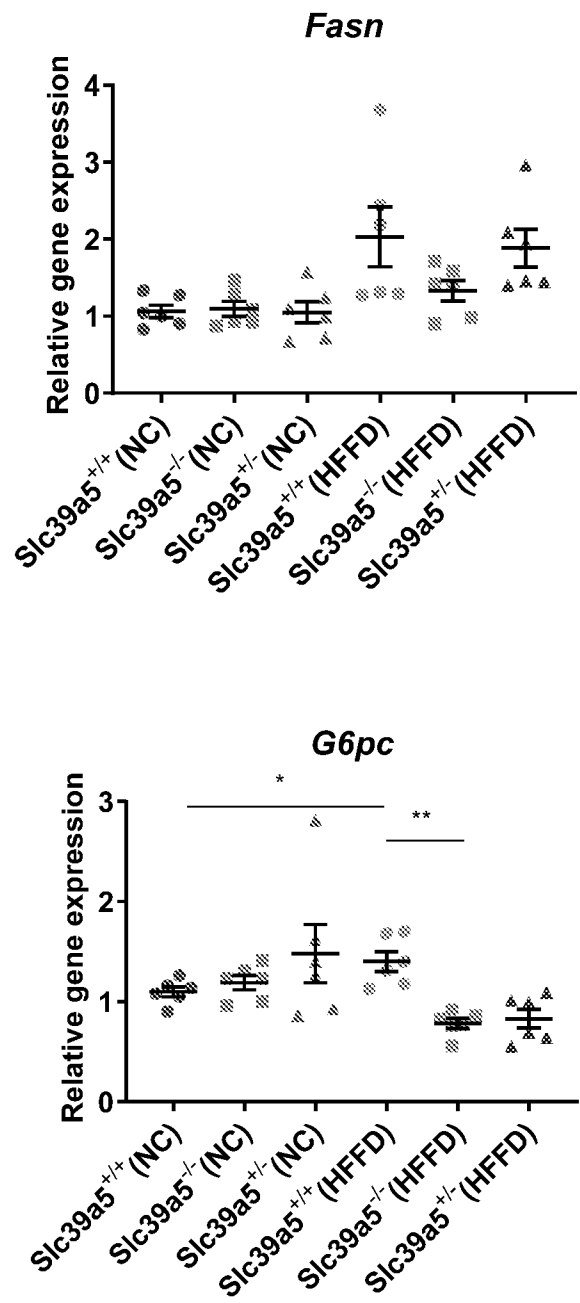
Liver lysates - 29 weeks; *p<0.05, **p<0.01; Error bars: SEM

Figure 26B (cont.)



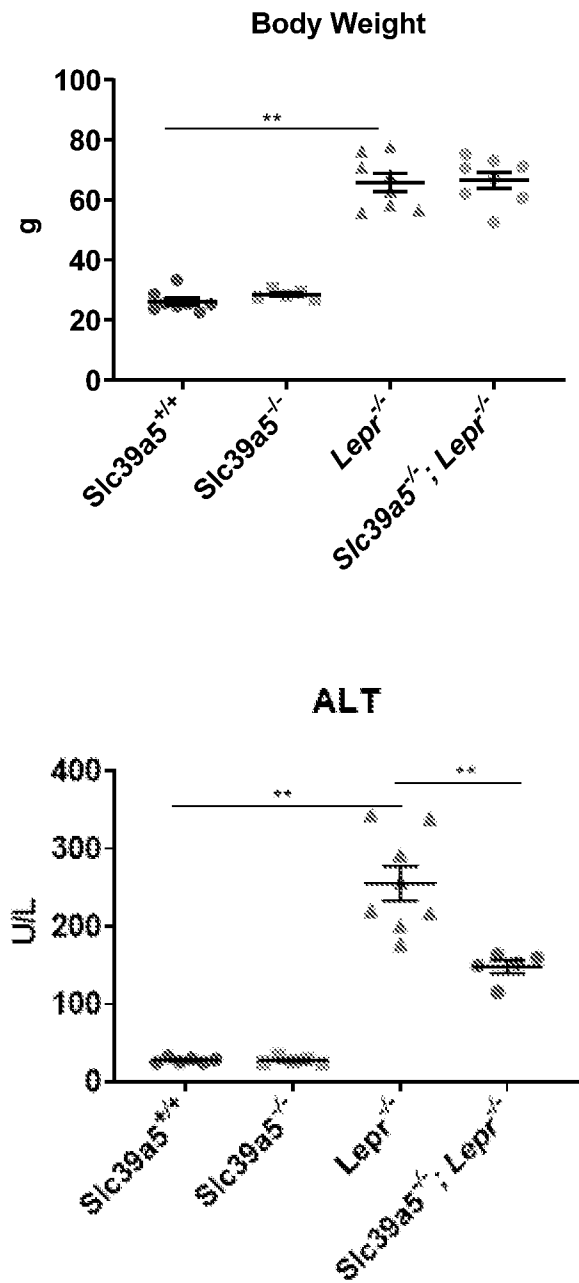
Liver lysates - 29 weeks; *p<0.05, **p<0.01; Error bars: SEM

Figure 26B (cont.)



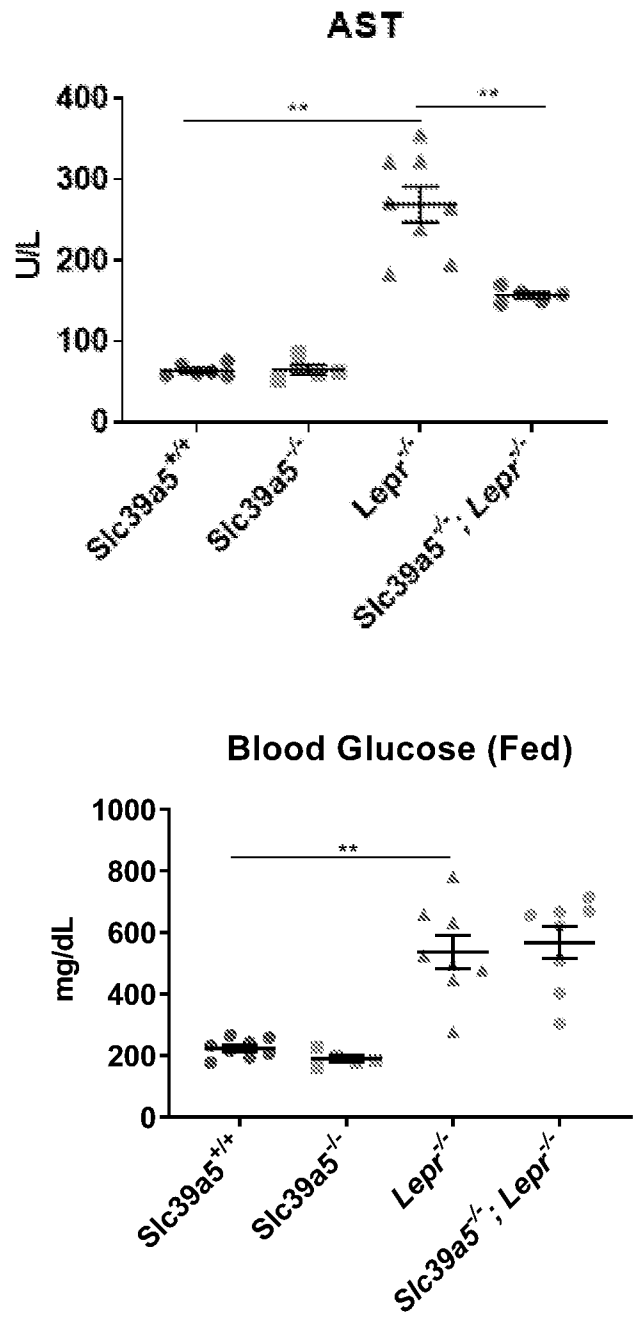
Liver lysates - 29 weeks; *p<0.05, **p<0.01; Error bars: SEM

Figure 26B (cont.)



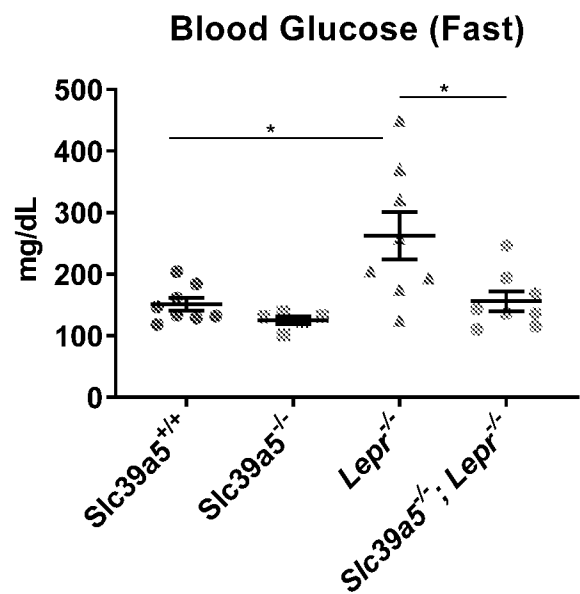
Normal Chow (Zinc 87ppm); Fasting blood glucose: **32weeks (Fed) and 34weeks (16hr/Fast)**;
*p<0.05, **p<0.01; Error bars: SEM

Figure 27



Normal Chow (Zinc 87ppm); Fasting blood glucose: **32weeks (Fed) and 34weeks (16hr/Fast)**;
*p<0.05, **p<0.01; Error bars: SEM

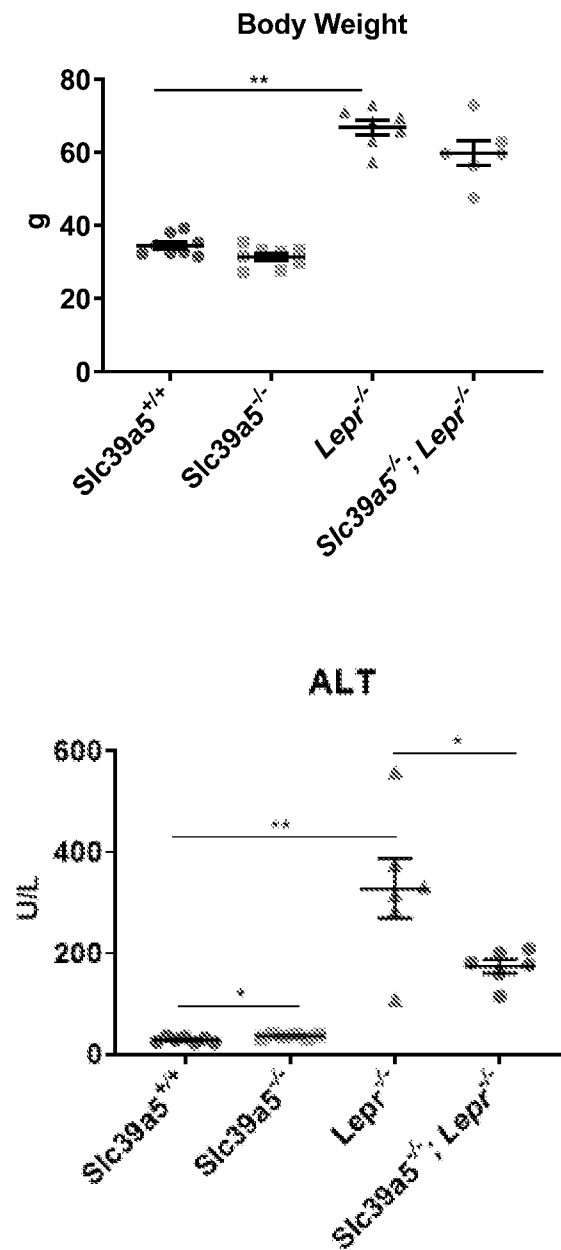
Figure 27 (cont.)



Normal Chow (Zinc 87ppm); Fasting blood glucose: **32weeks (Fed) and 34weeks (16hr/Fast)**;
*p<0.05, **p<0.01; Error bars: SEM

Figure 27 (cont.)

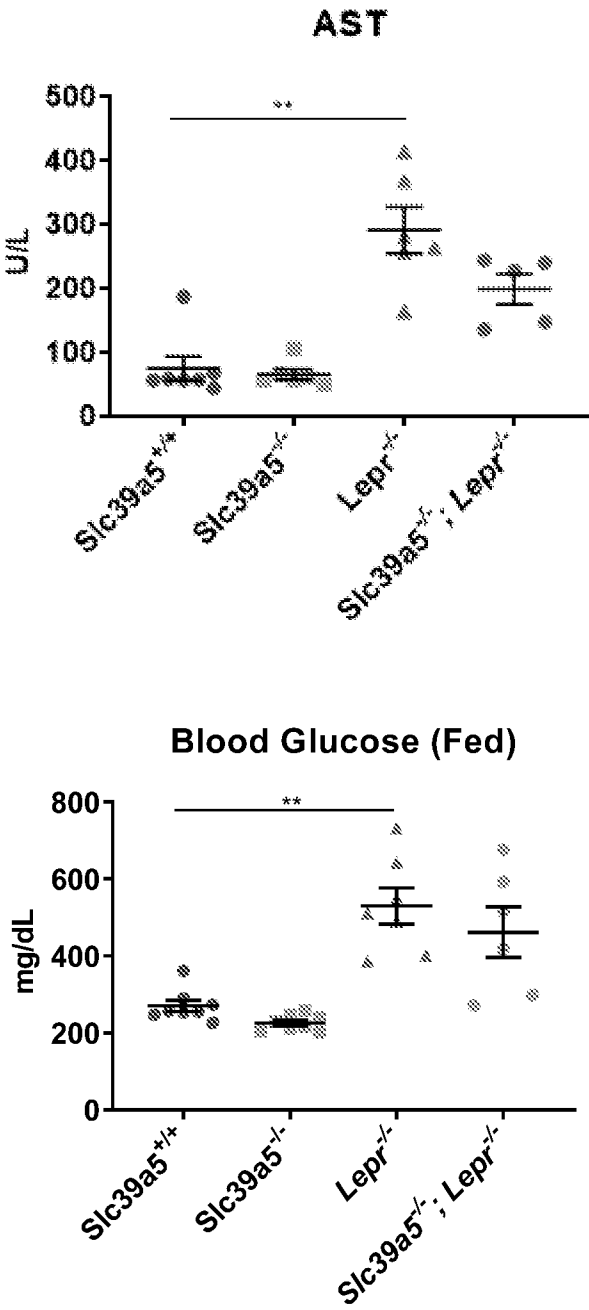
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Normal Chow (Zinc 87ppm); Fasting blood glucose: **32weeks (Fed) and 34weeks (16hr/Fast)**;

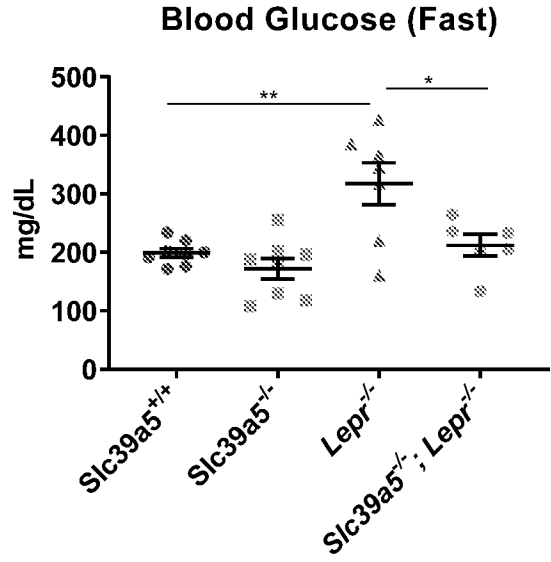
*p<0.05, **p<0.01; Error bars: SEM

Figure 27 (cont.)



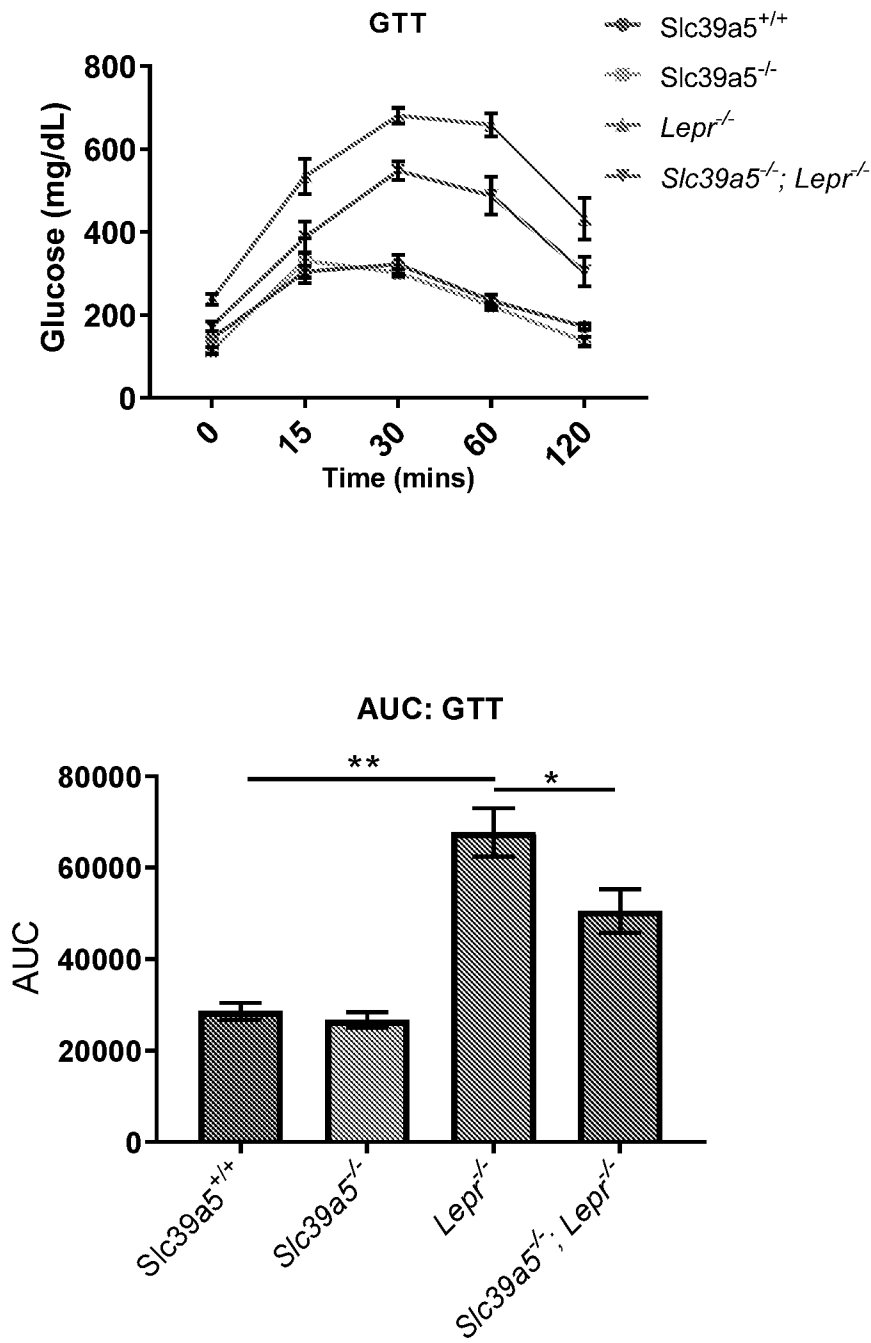
Normal Chow (Zinc 87ppm); Fasting blood glucose: **32weeks (Fed) and 34weeks (16hr/Fast)**;
*p<0.05, **p<0.01; Error bars: SEM

Figure 27 (cont.)



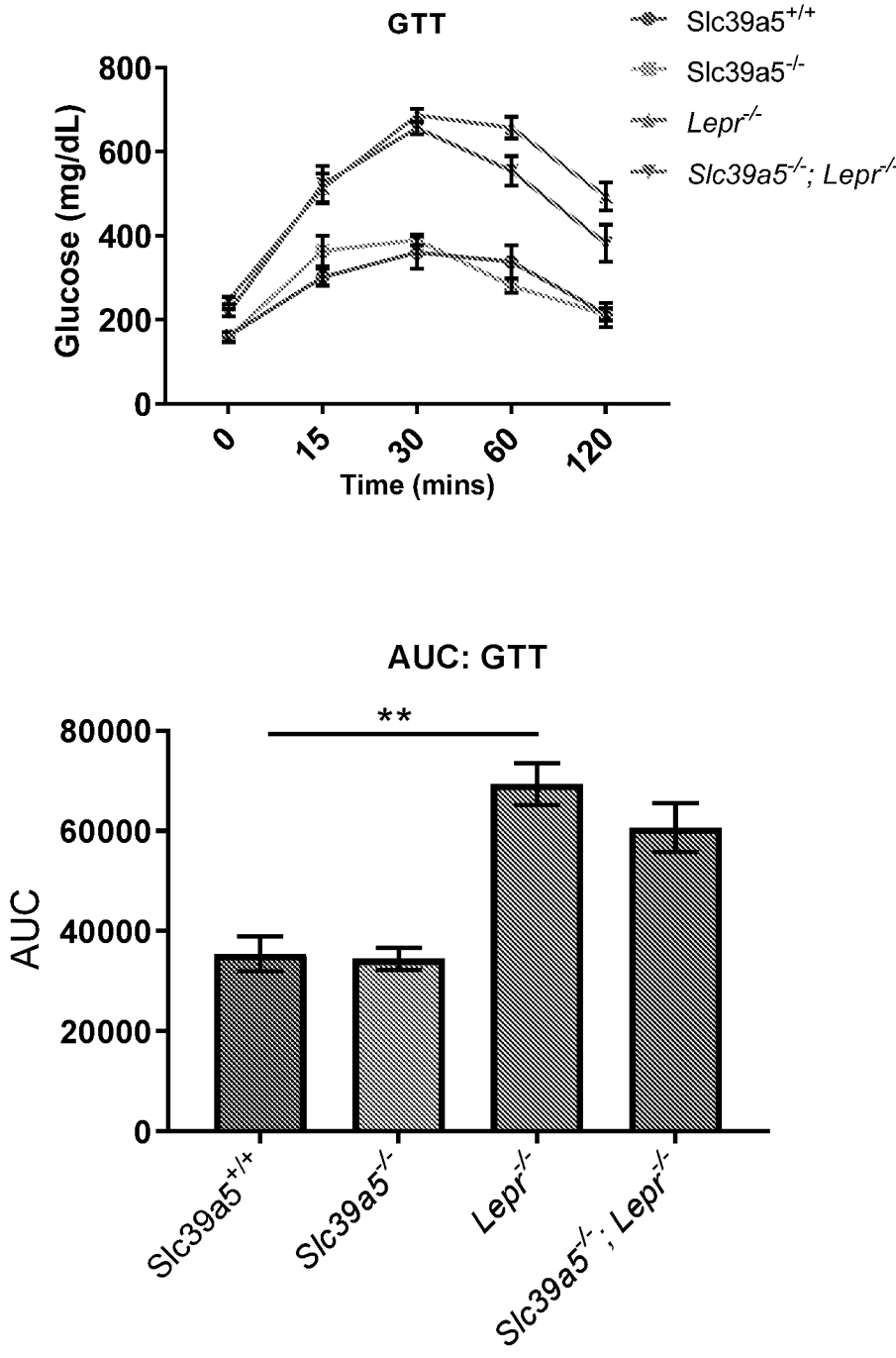
Normal Chow (Zinc 87ppm); Fasting blood glucose: **32weeks (Fed) and 34weeks (16hr/Fast)**;
*p<0.05, **p<0.01; Error bars: SEM

Figure 27 (cont.)



Normal chow; Zinc 87ppm; oGTT (20wk) after 16hr fast – 2mg/g body weight;
*p<0.05, **p<0.01; Error bars: SEM

Figure 28



Normal chow; Zinc 87ppm; oGTT (20wk) after 16hr fast – 2mg/g body weight;
*p<0.05, **p<0.01; Error bars: SEM

Figure 28 (cont.)

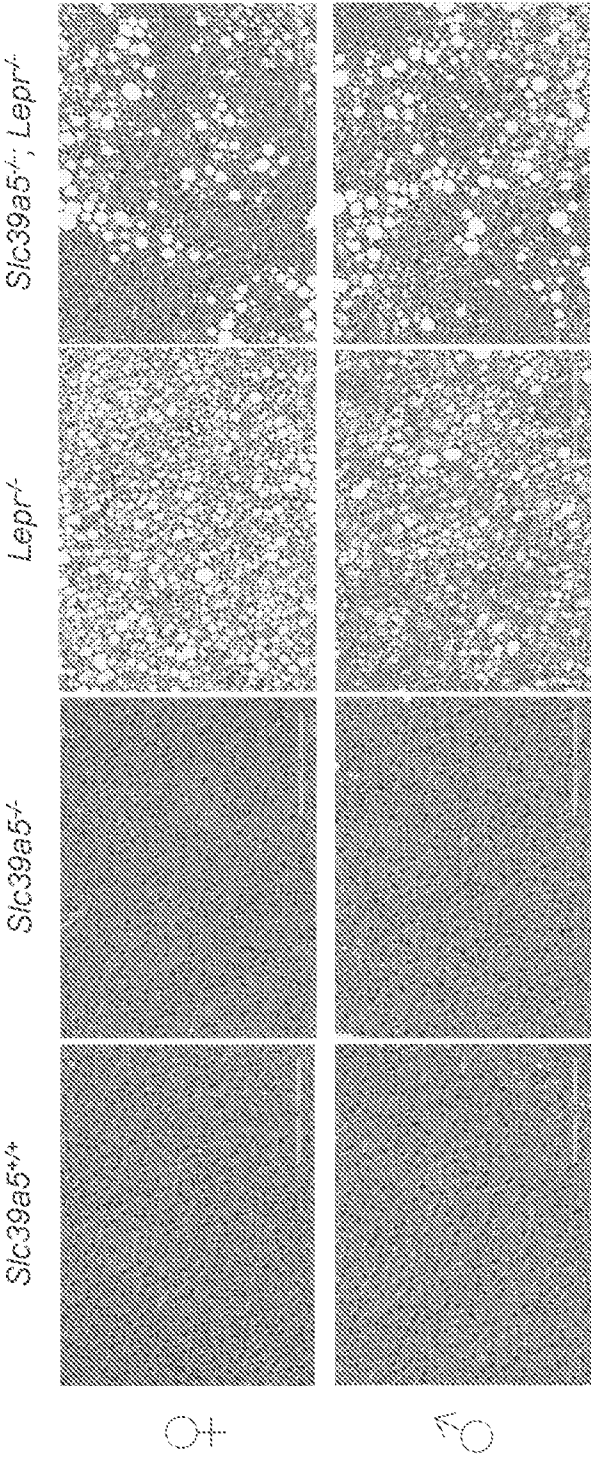
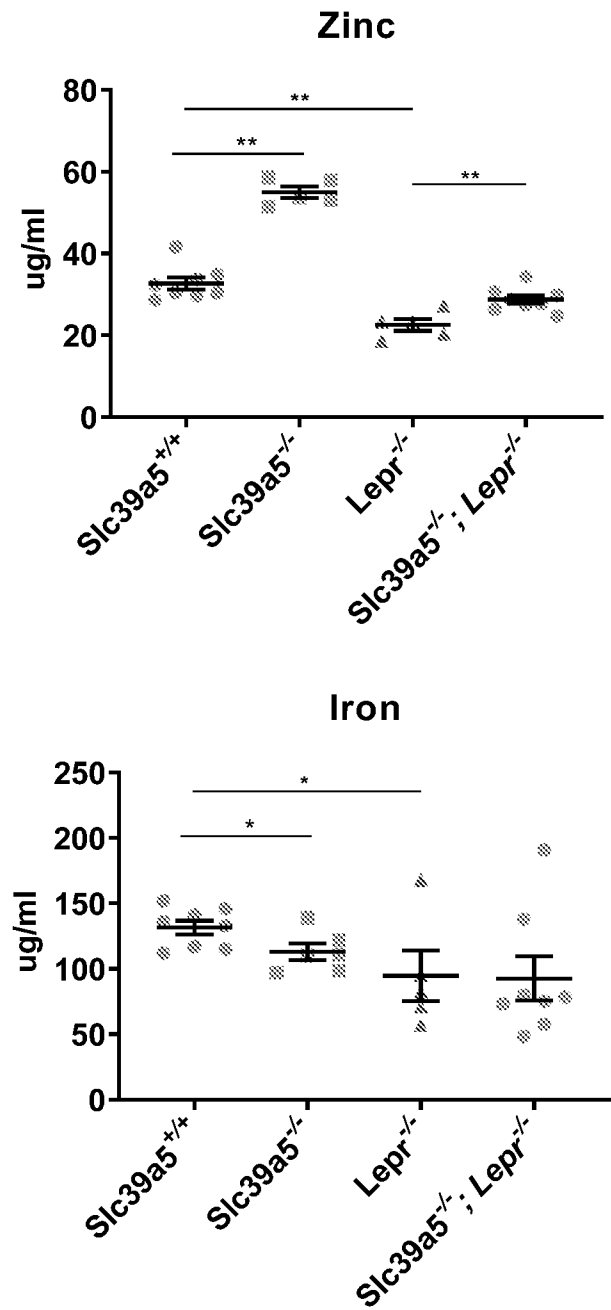


Figure 29

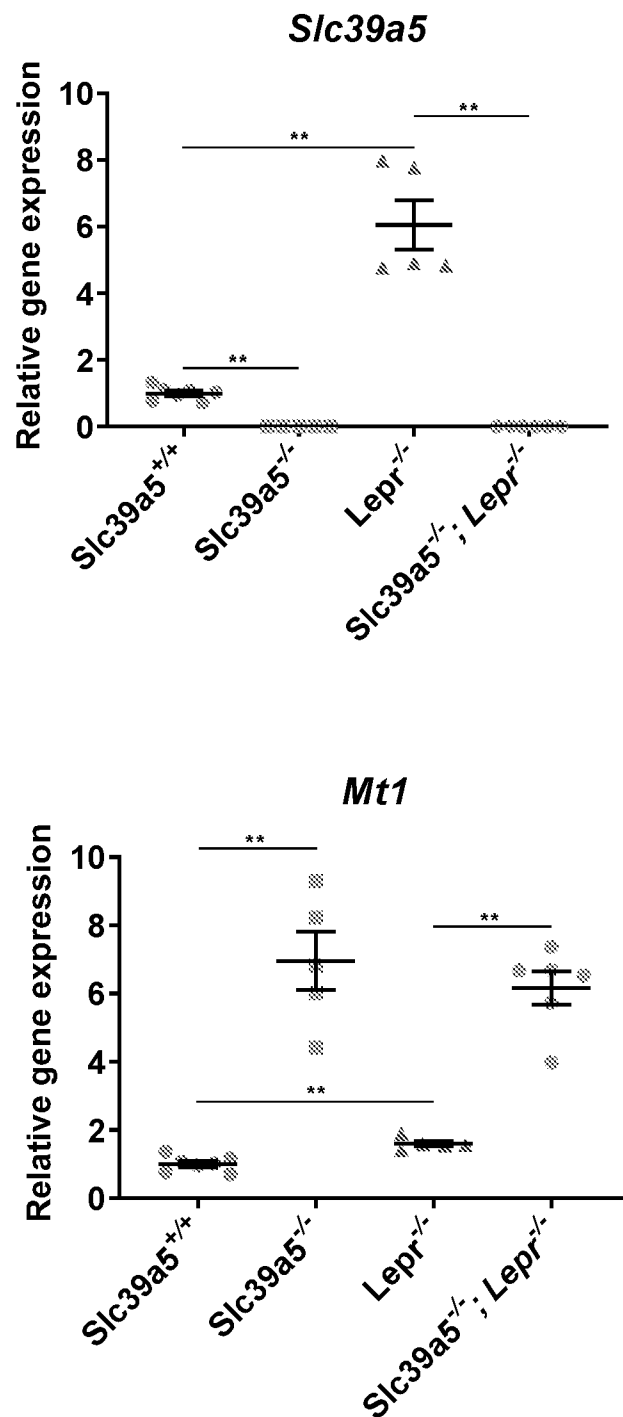


Hepatic ion quantification and Taqman analysis - 29 weeks; *p<0.05, **p<0.01; Error bars: SEM

Figure 30

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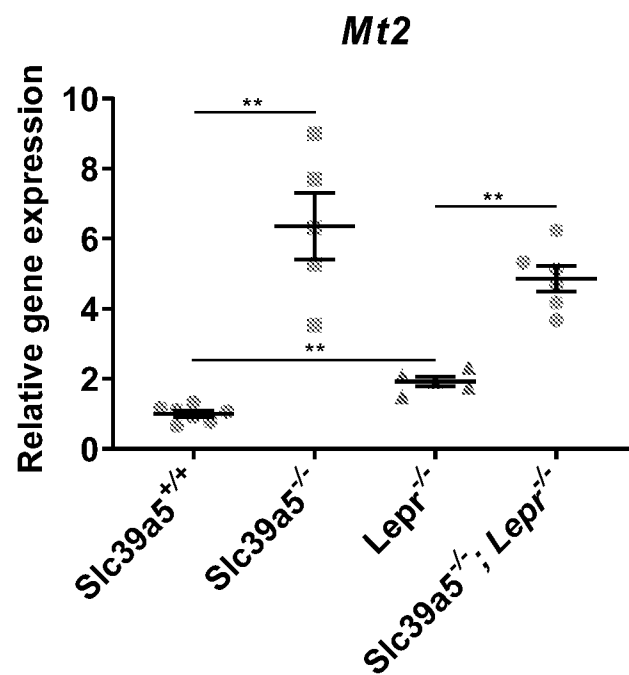
♀



Hepatic ion quantification and Taqman analysis - 29 weeks; * $p < 0.05$,
** $p < 0.01$; Error bars: SEM

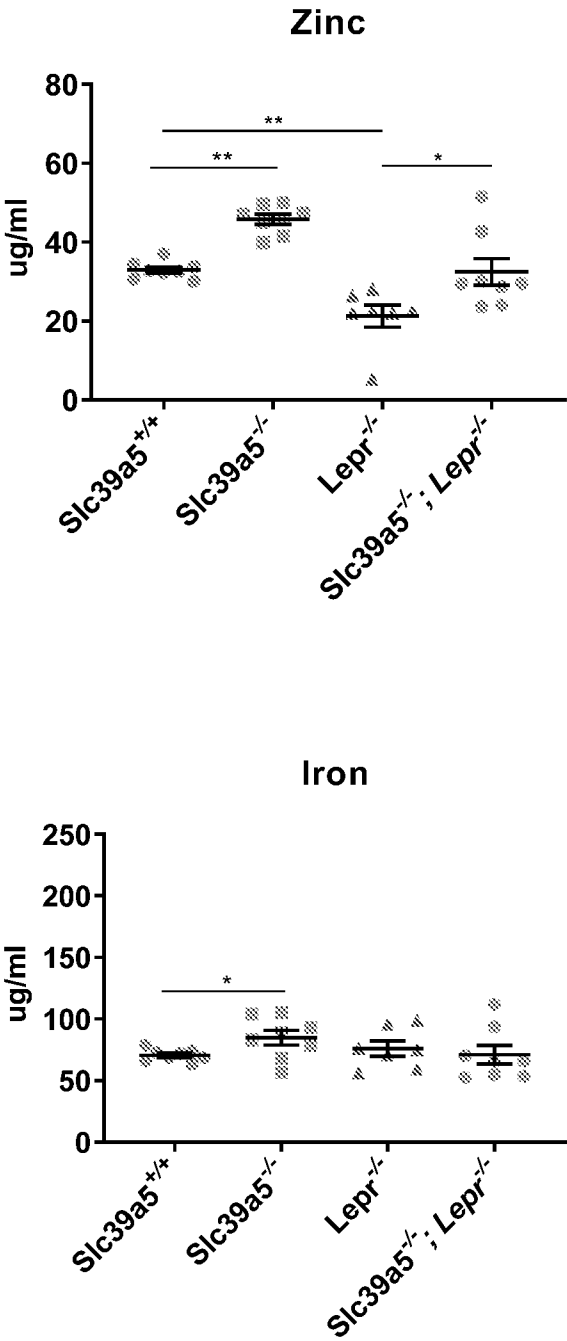
Figure 30 (cont.)

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Hepatic ion quantification and Taqman analysis - 29 weeks; *p<0.05,
**p<0.01; Error bars: SEM

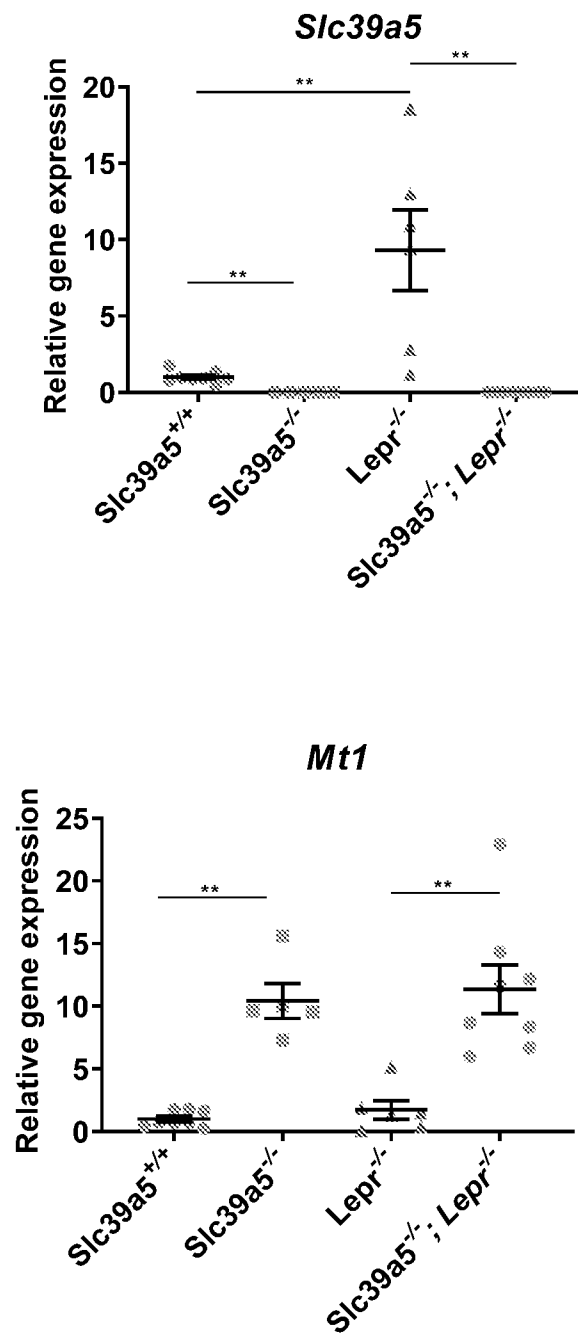
Figure 30 (cont.)



Hepatic ion quantification and Taqman analysis - 29 weeks; *p<0.05, **p<0.01; Error bars: SEM

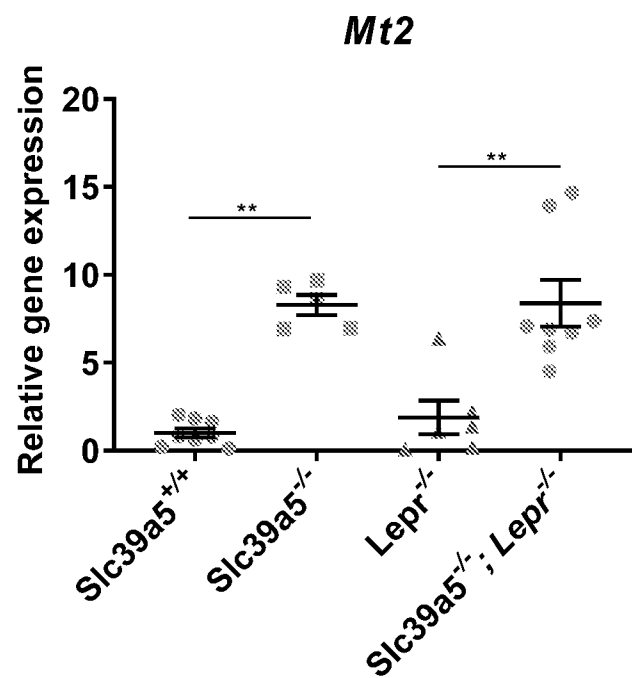
Figure 30 (cont.)

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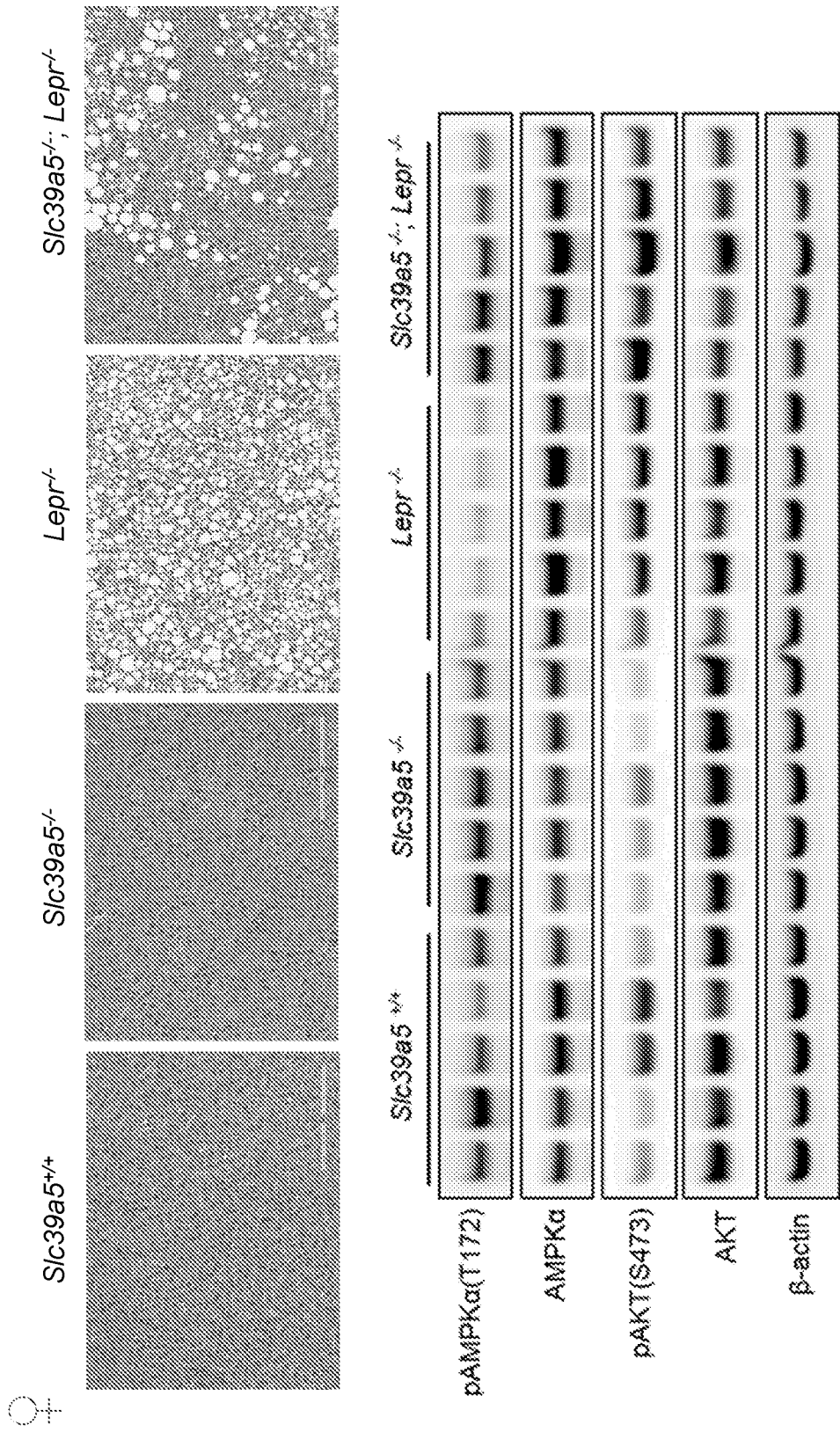
Hepatic iron quantification and Taqman analysis - 29 weeks; *p<0.05, **p<0.01; Error bars: SEM

Figure 30 (cont.)



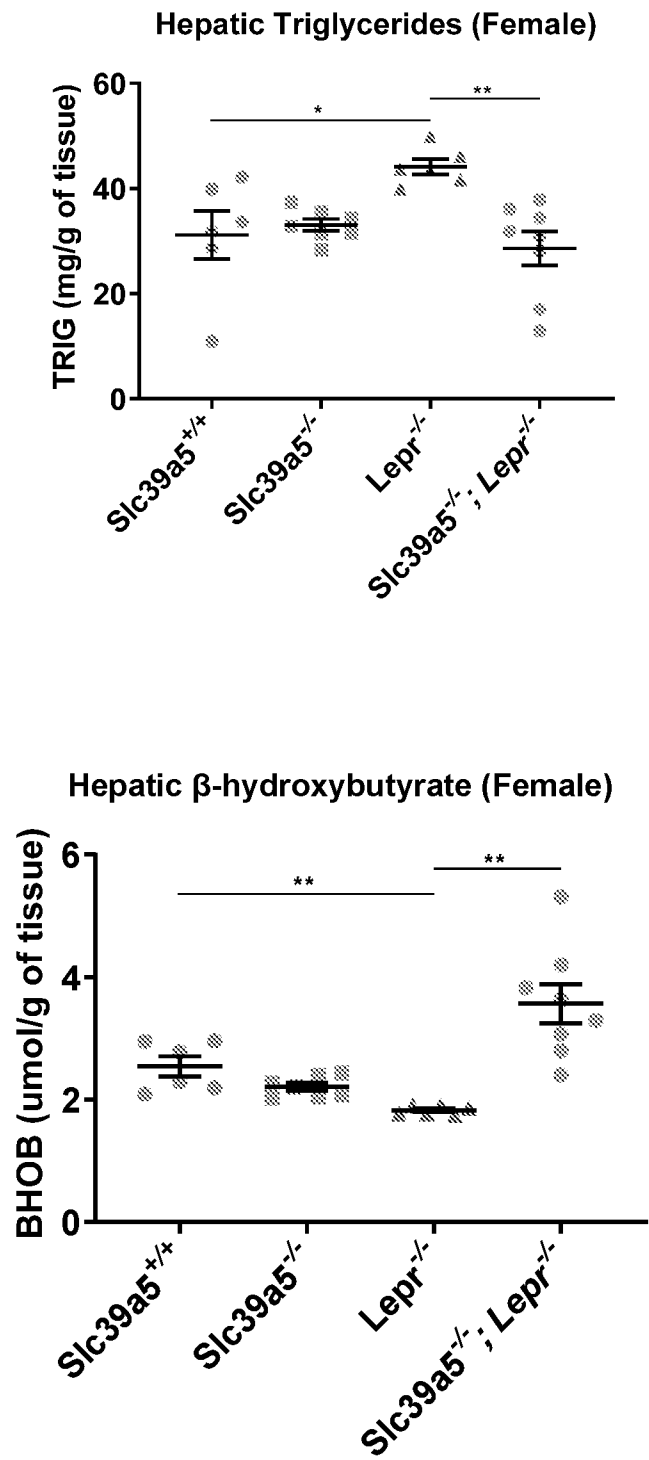
Hepatic ion quantification and Taqman analysis - 29 weeks; * $p < 0.05$,
** $p < 0.01$; Error bars: SEM

Figure 30 (cont.)



Liver lysates - 29 weeks; *p<0.05, **p<0.01; Error bars: SEM

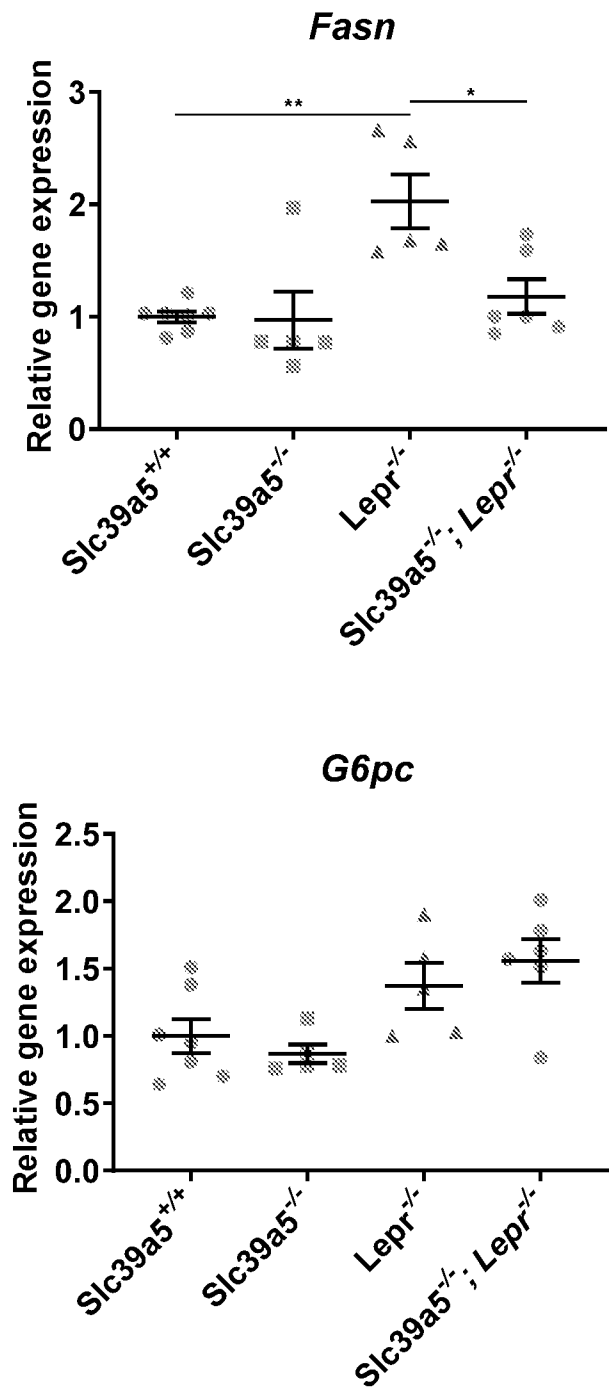
Figure 31A



Liver lysates - 29 weeks; *p<0.05, **p<0.01; Error bars: SEM

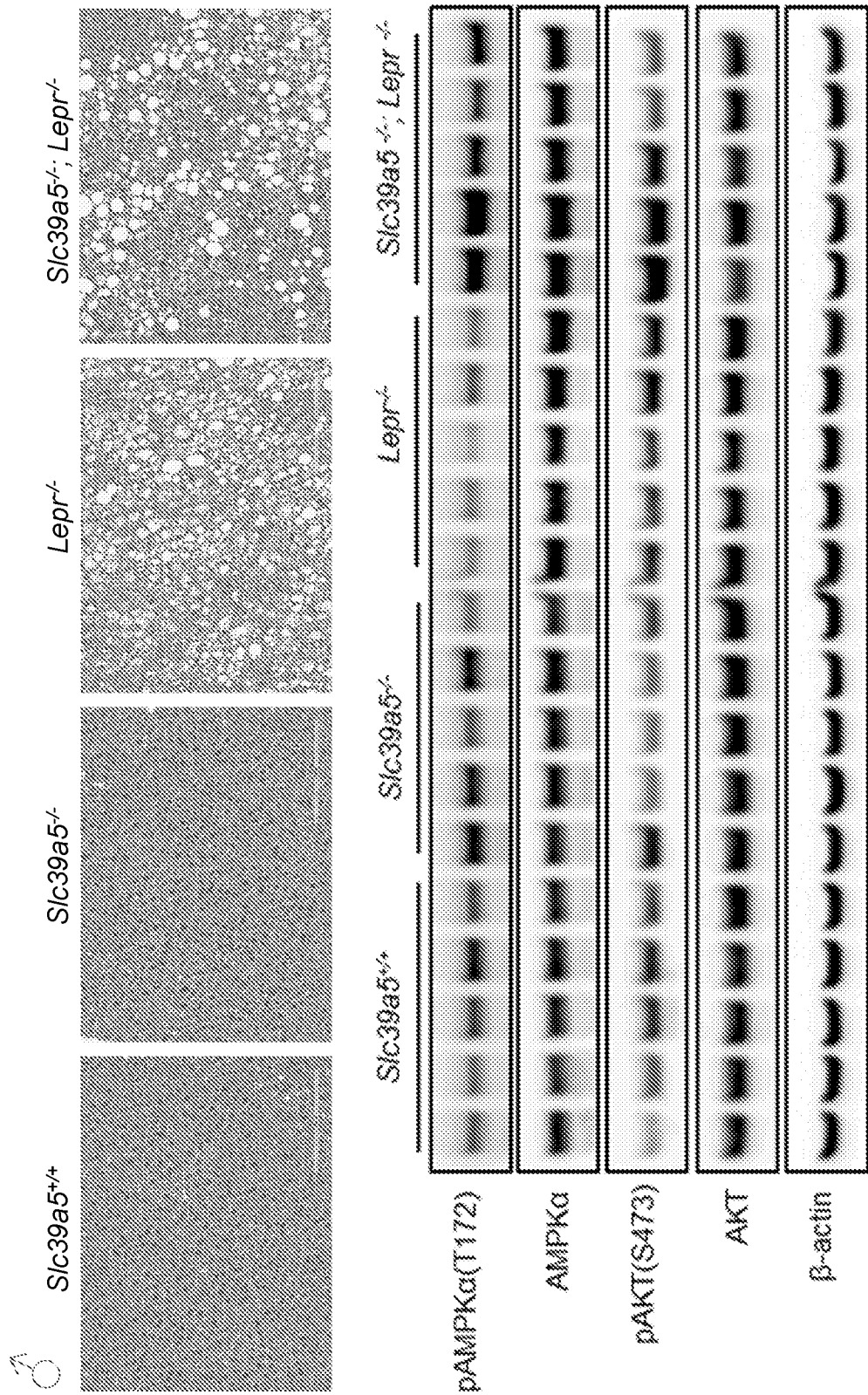
Figure 31A (cont.)

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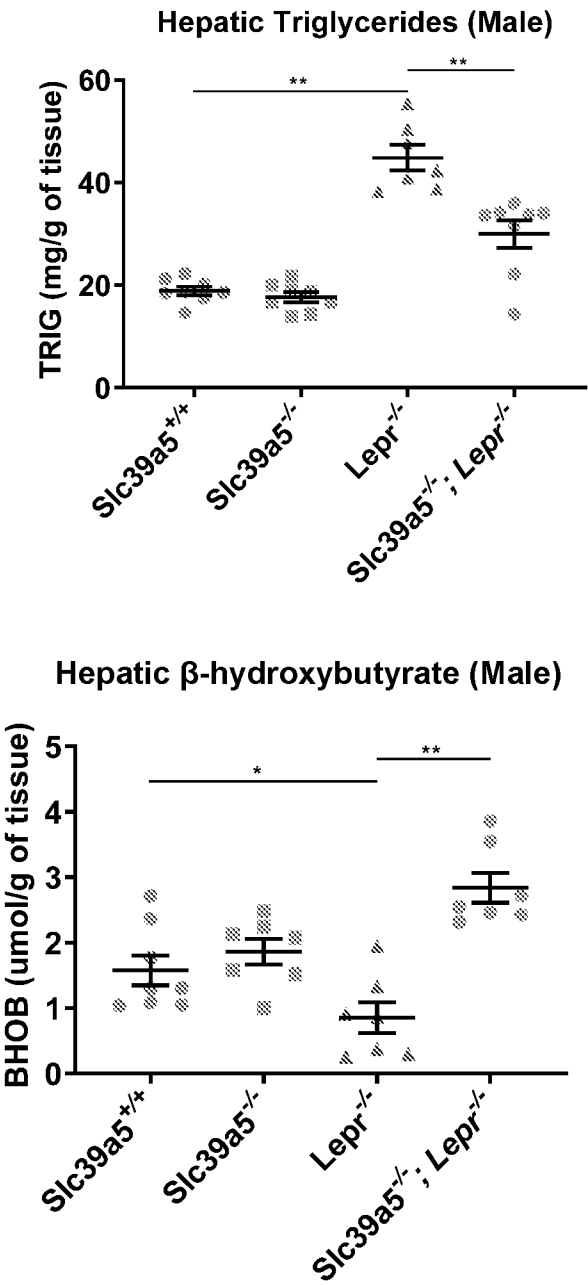
Liver lysates - 29 weeks; * $p < 0.05$, ** $p < 0.01$; Error bars: SEM

Figure 31A (cont.)



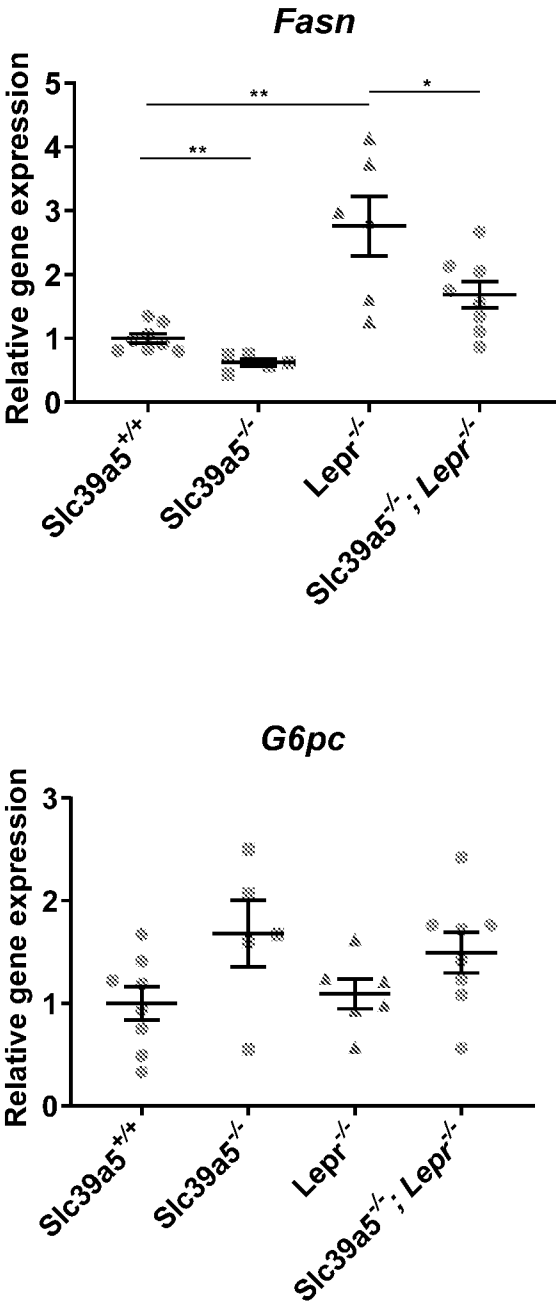
Liver lysates - 29 weeks; *p<0.05, **p<0.01; Error bars: SEM

Figure 3 1B



Liver lysates - 29 weeks; *p<0.05, **p<0.01; Error bars: SEM

Figure 31B (cont.)



Liver lysates - 29 weeks; *p<0.05, **p<0.01; Error bars: SEM

Figure 31B (cont.)

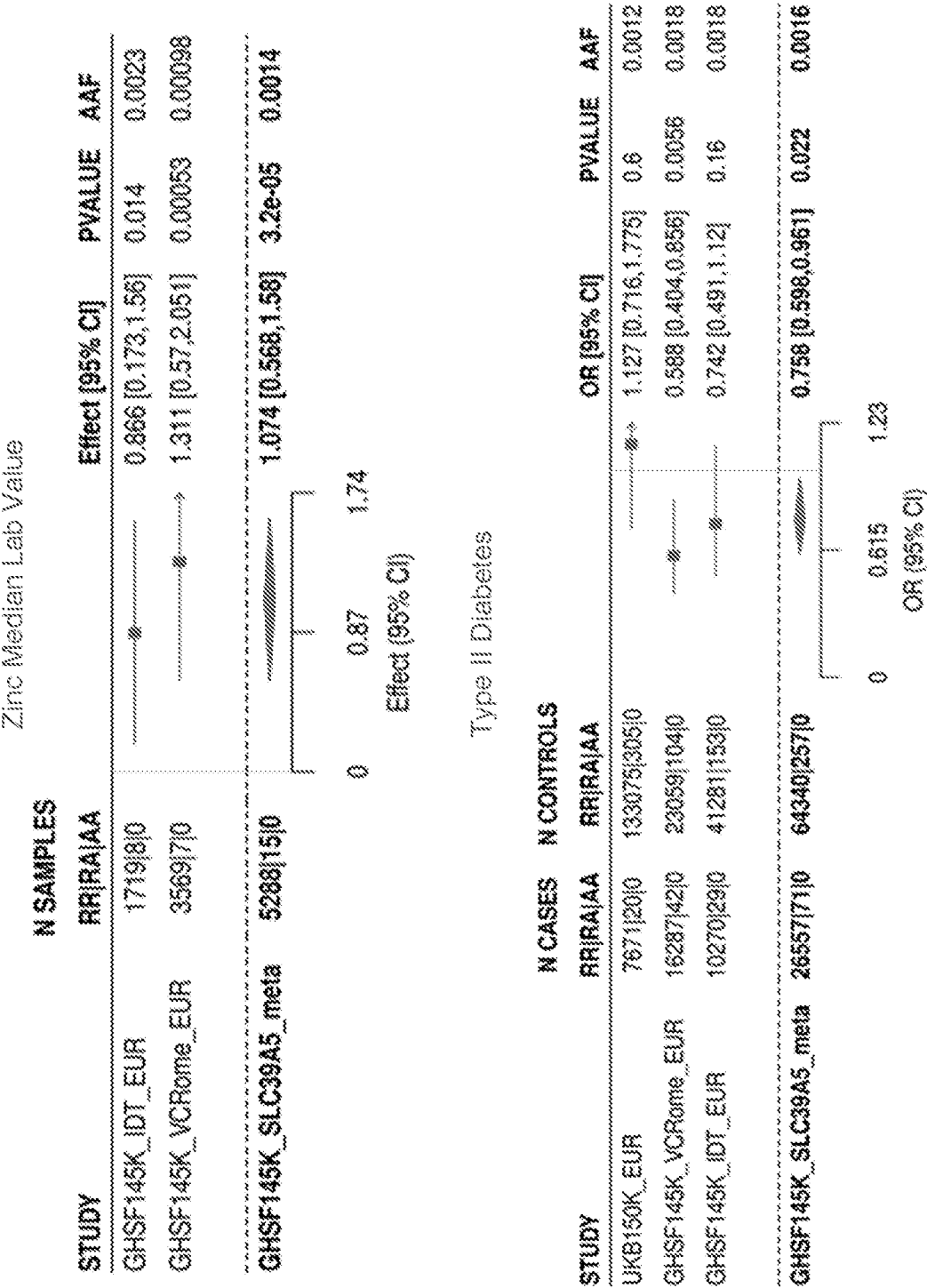


Figure 32

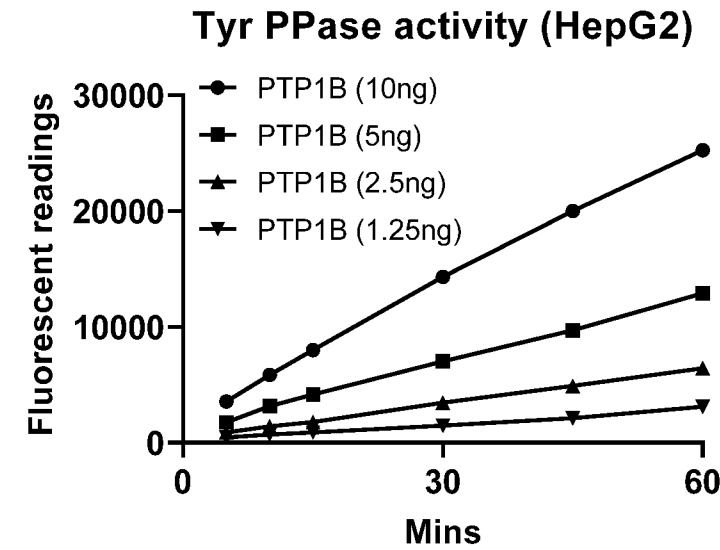
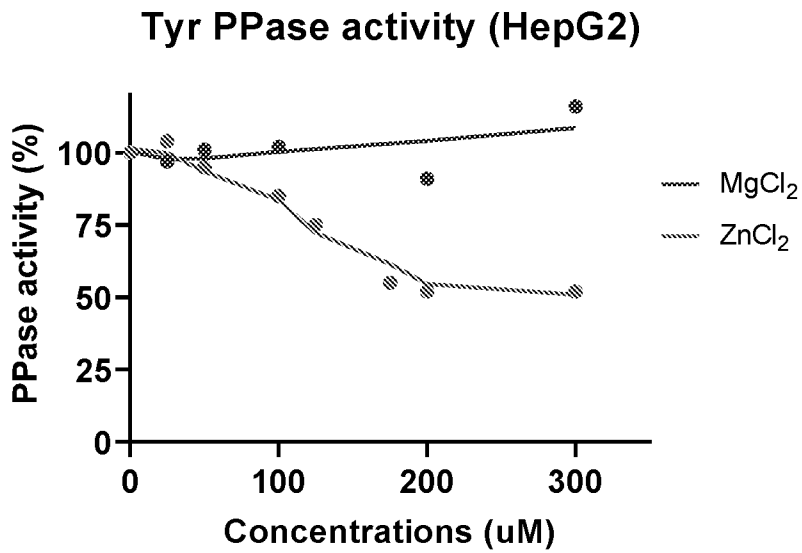


Figure 33A

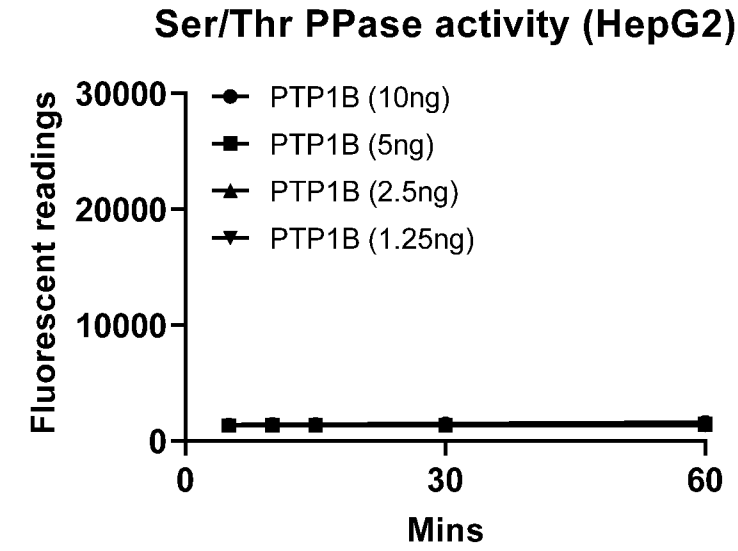
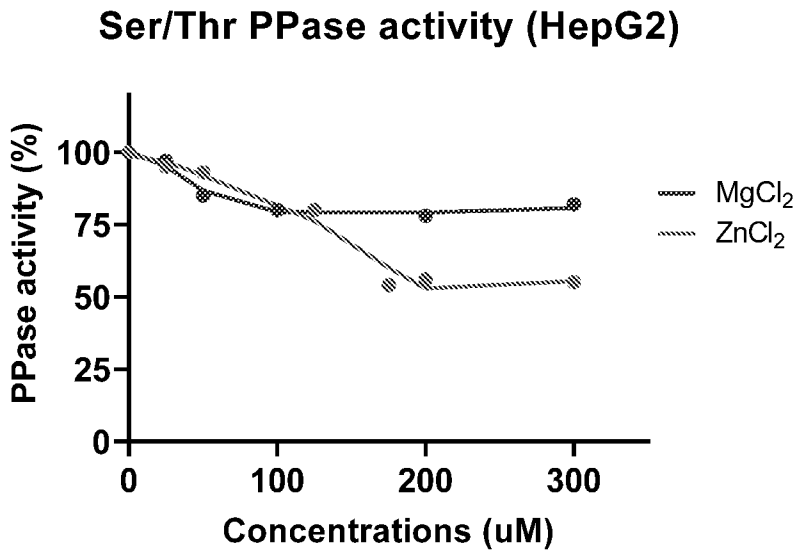


Figure 33B

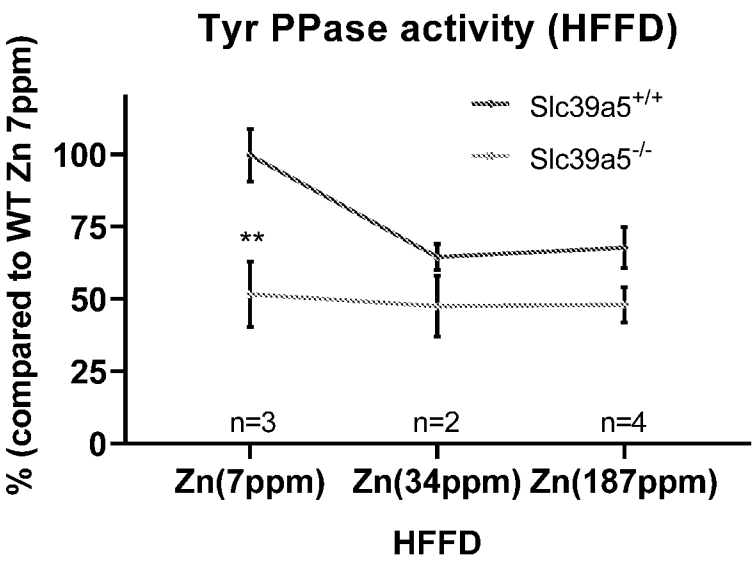
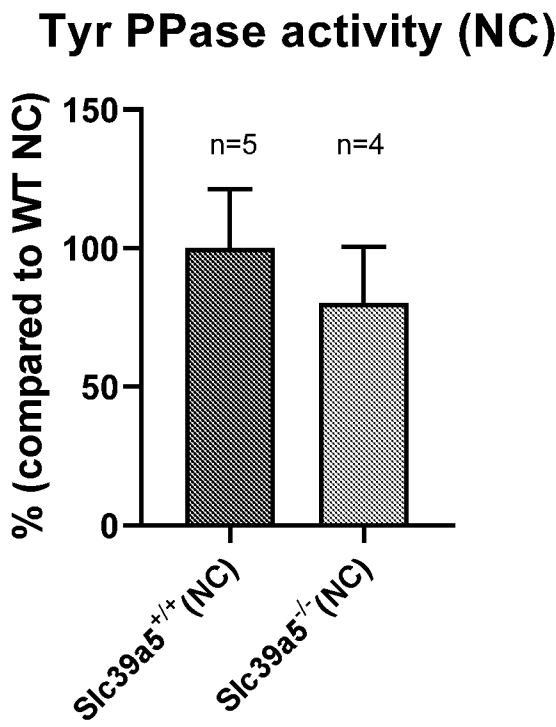
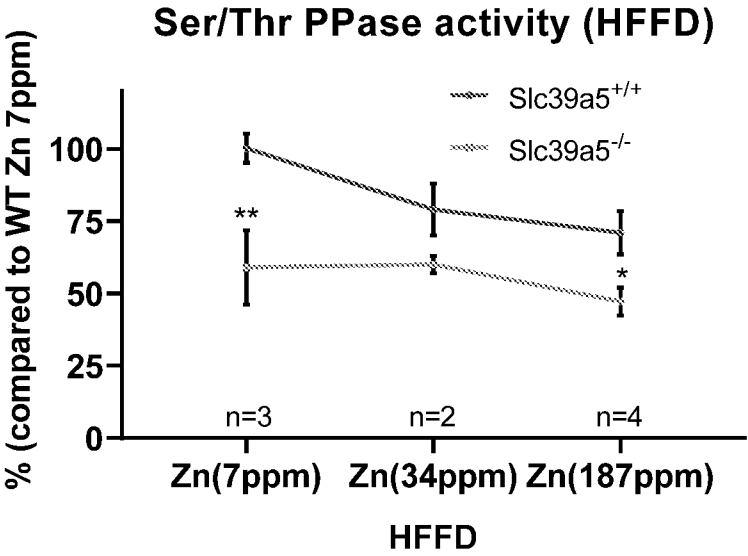


Figure 34A



Ser/Thr PPase activity (NC)

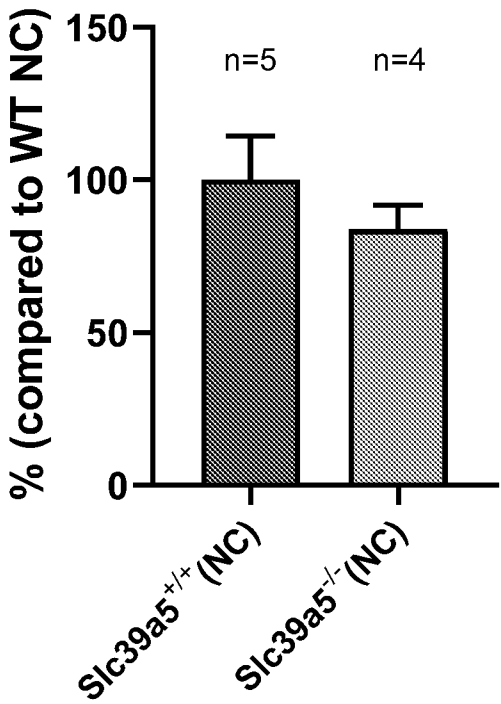


Figure 34B

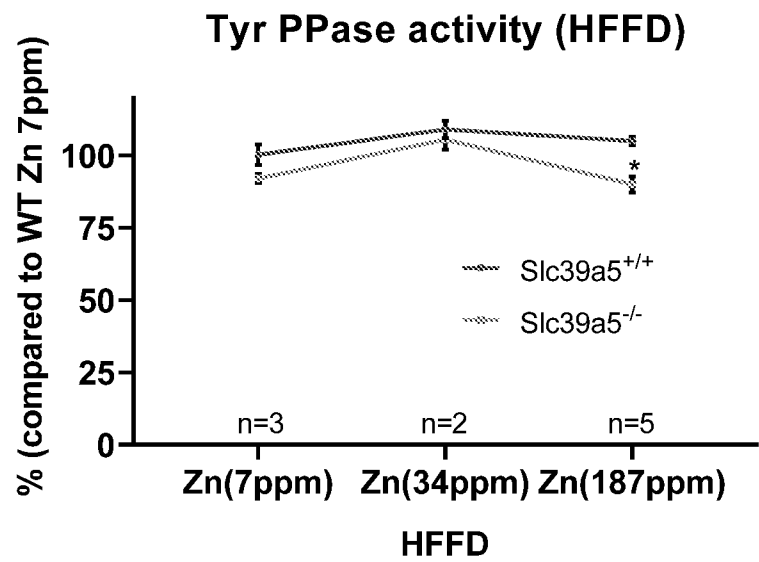
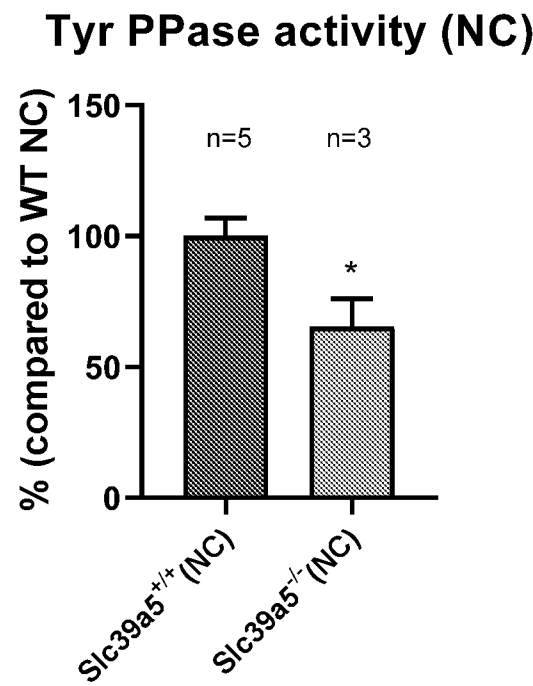


Figure 34C

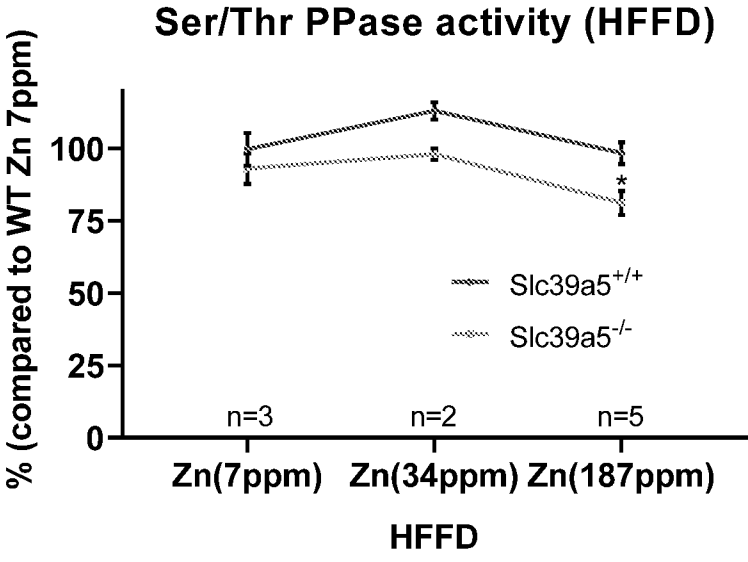
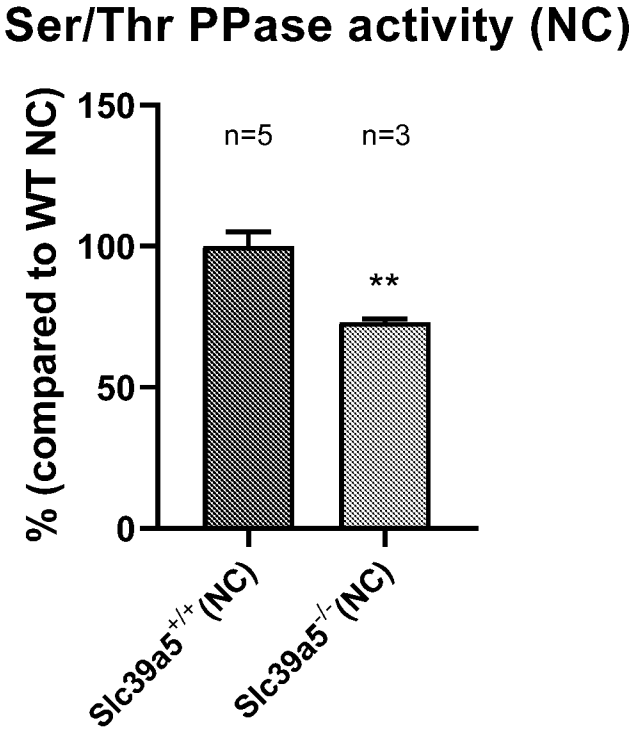


Figure 34D