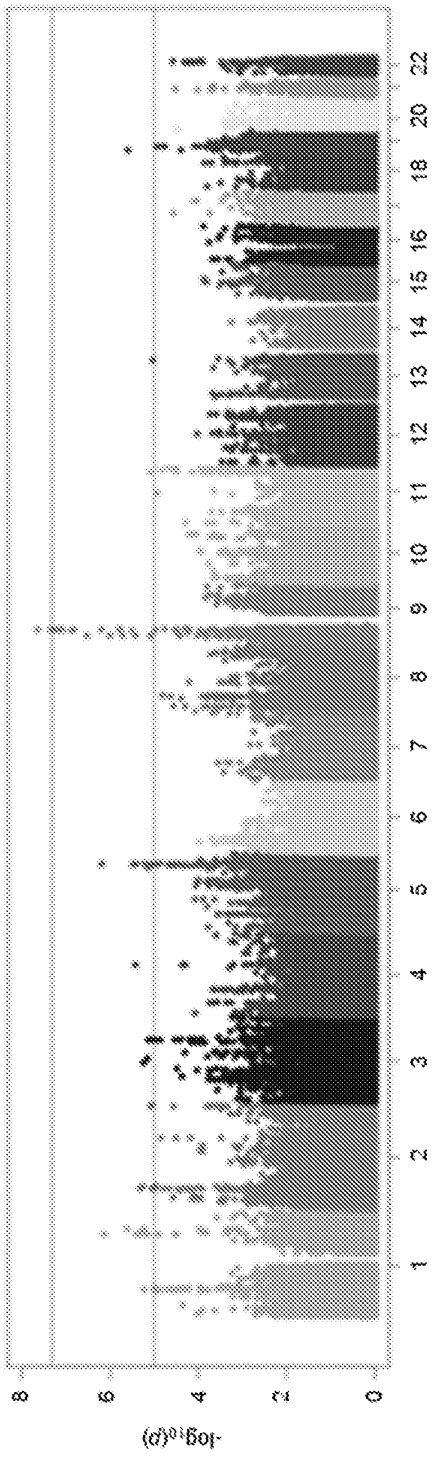


Figure 1

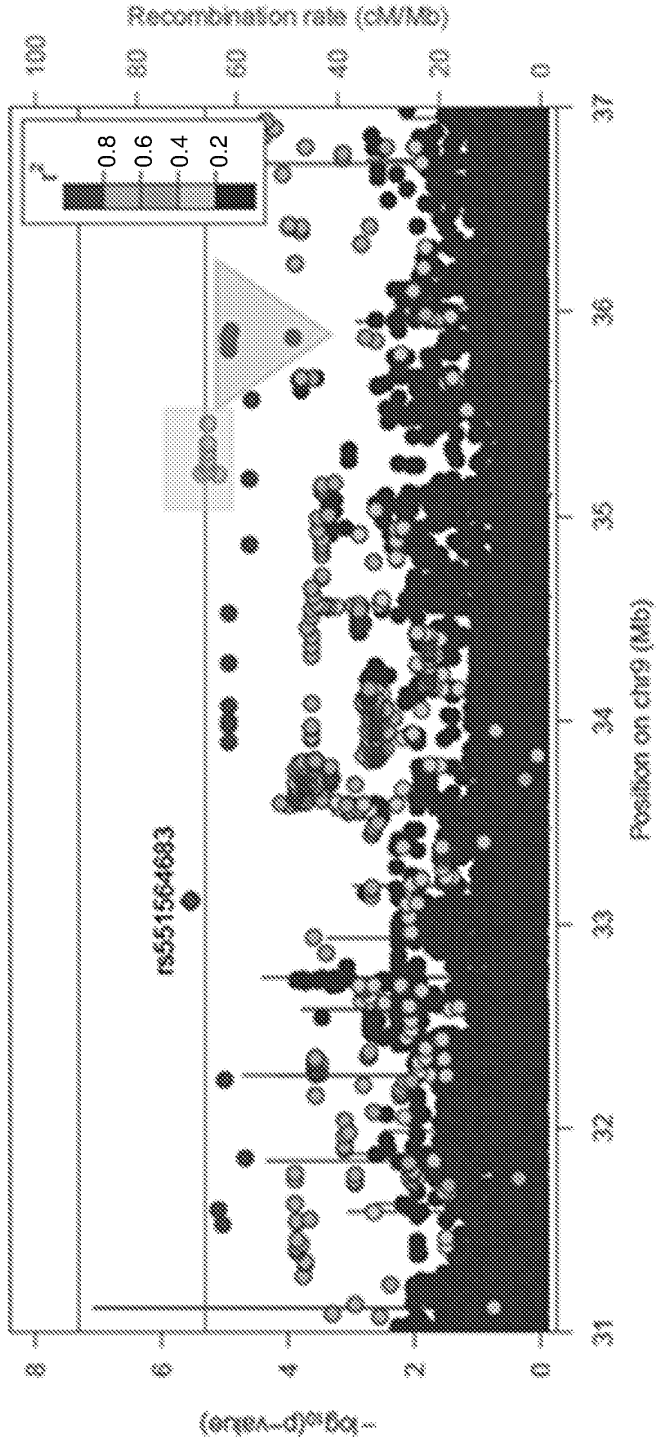

Recombination rate (cM/Mb)
100
80
60
40
20
0
r²
0.8
0.6
0.4
0.2
rs55156683
37
36
35
34
33
32
31
Position on chr9 (Mb)
8
6
4
2
0
−log10(p-value)

Figure 2

Haplotype	Copies	9:31523876	9:31599161	9:31863663	9:32231857	rs551564663	9:33892787	9:33971380
A	115	1	1	1	1	1	1	1
B	7	1	1	1	1	1	0	0
C	6	0	0	0	0	1	1	1
Haplotype	Copies	9:33991394	9:34066623	9:34277757	9:34520551	9:34860994	9:35176756	9:35570095
A	115	1	1	1	1	1	1	1
B	7	0	0	0	0	0	0	0
C	6	1	1	1	1	1	1	1

Figure 3

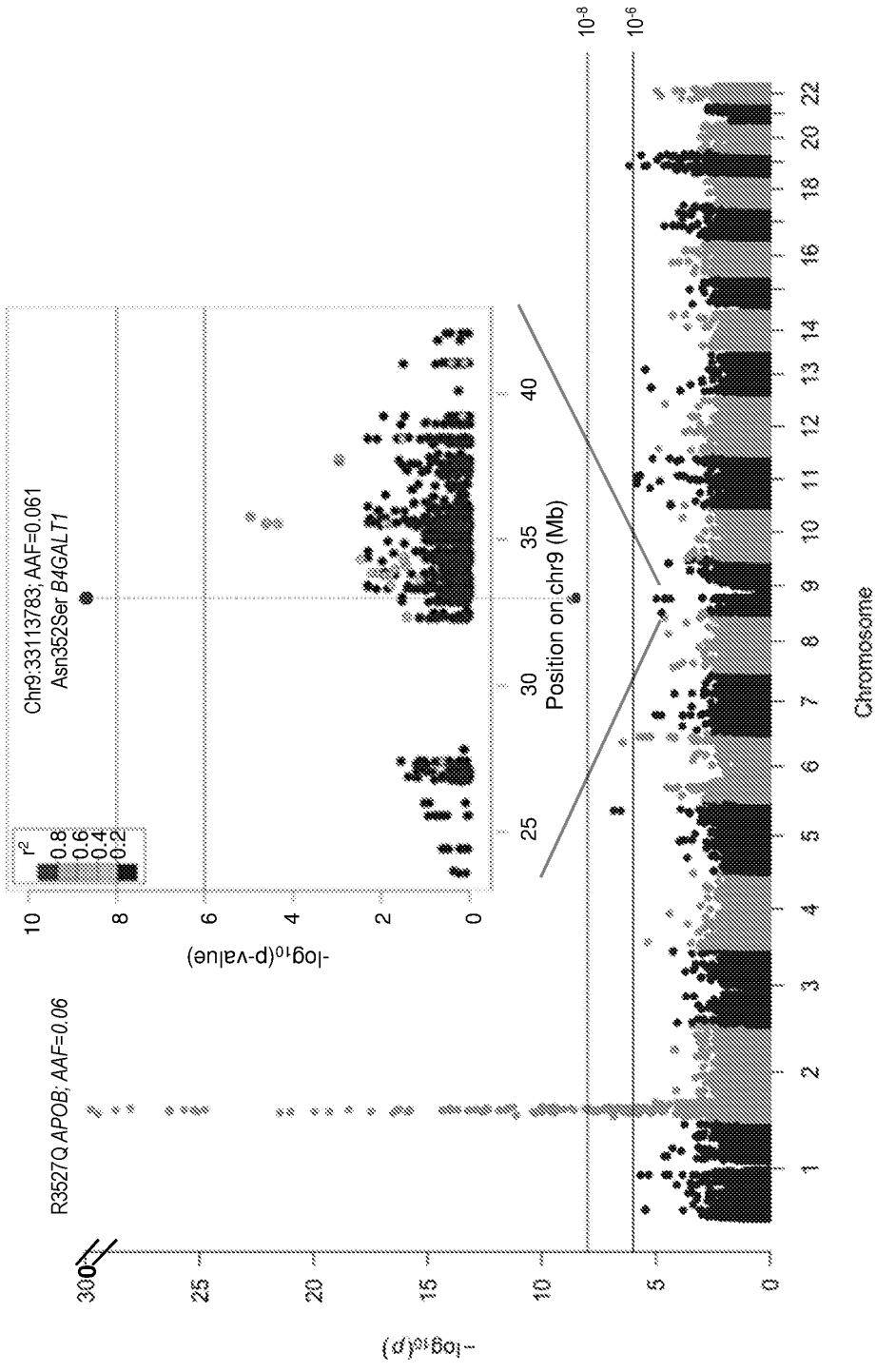
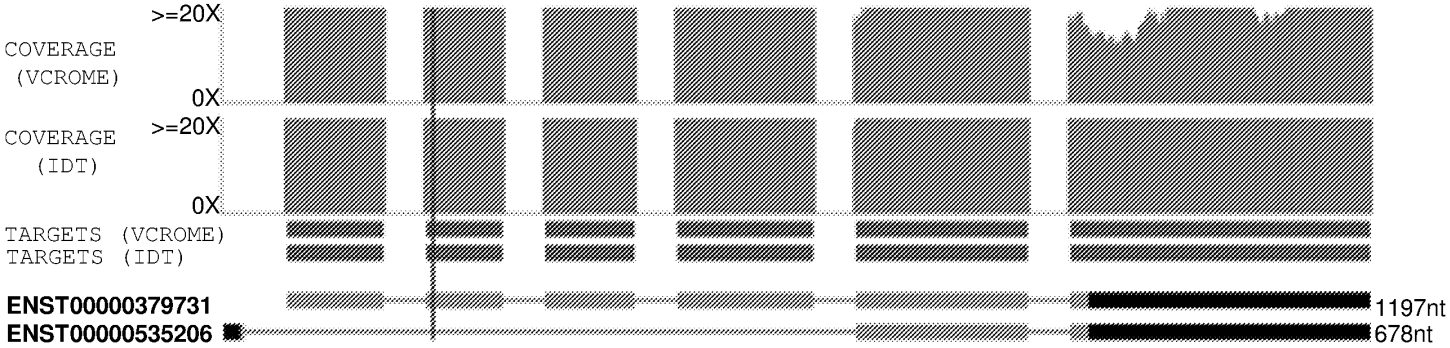

R3527Q APOB; AAF=0.06
Chr9:33113783; AAF=0.061
Asn352Ser B4GALT1
r²
0.8
0.6
0.4
0.2
-log10(p-value)
Position on chr9 (Mb)
-log10(p)
Chromosome
10⁻⁸
10⁻⁶

Figure 4

Variant coordinates: 9:33113783:T:C
rsID: rs551564683
Internal links: [EVE-QT] [EVE carriers]



Genomic coordinates for 'B4GALT1' ('-' strand): 9:33104751-33167169

Population	AAF
UMD Amish Research Clinic (Amish, 5k)	0.061
Clinic for Special Children (Amish and Mennonite, 2k)	0.018
National Institute of Mental Illness (Amish, 460)	0.003
Geisinger Health Center (66k)	0.000053
All RGC (130k)	0.0025
ExAC (60k)	0
deCode (Iceland, 2.5 k WGS)	<0.005

Figure 5

Population	Population size	# HET carriers	# HOM carriers	AAF
BCH	580	0	0	0.000000
CNCD	96	0	0	0.000000
COL-CHUNG	4064	0	0	0.000000
COL-CHUNG_FBC	1193	0	0	0.000000
CSC	2084	65	5	0.017994
DHS	4654	0	0	0.000000
DRIFT-NIMH	460	3	0	0.002081
DUKE	8783	2	0	0.000114
ECO	858	0	0	0.000000
GHS	66216	7	0	0.000053
IOWA	58	0	0	0.000000
MADGC	2393	1	0	0.000209
MARIO	127	0	0	0.000000
NIAID	95	0	0	0.000000
SIMONS	96	0	0	0.000000
SINAI	96	0	0	0.000000
TAICHI	13963	0	0	0.000000
TSK	3407	0	0	0.000000
UCHC	1039	0	0	0.000000
UMD	4725	548	13	0.060741
UPENN	11451	1	0	0.000044
UTAH	3688	0	0	0.000000
Total	130126	627	18	0.002548

Figure 5 (cont.)

Phenotype	Genotypic Means*	Genotypic Means Unadjusted	Counts (Ref/Het/Alt)	Effect (95% CI)	Pvalue
Serum lipids					
Cholesterol, mg/dL	210.6 / 190.9 / 172.7	210.4 / 192.3 / 176.2	3993/527/12	-17.18 (-22.4, -11.95)	1.3E-10
LDL, mg/dL	134.7 / 117.4 / 103.5	134.6 / 118.3 / 103.5	3991/526/12	-14.61 (-19.37, -9.86)	1.8E-09
HDL, mg/dL	61.4 / 59.4 / 58.6	61.3 / 59.6 / 61.6	3995/527/12	-2.14 (-3.88, -0.41)	0.0155
Triglycerides (log10), mg/dL	73.9 / 72.9 / 72.7	71.9 / 72.0 / 85.8	3995/527/12	-3.39 (-8.17,1.62) %	0.1760
Chol/HDL (log10)	3.39 / 3.15 / 2.94	3.39 / 3.16 / 2.87	3318/450/11	-6.67 (-8.68, -2.28) %	0.0003
NonHDL Cholesterol, mg/dL	161.5 / 144.5 / 91.1	161.0 / 149.0 / 99.0	727/87/1	-14.33 (-23.57, -5.08)	0.0025

0.0774* Genotypic means are on the clinical scale, removing the effects of Age, Age2, Sex, and Study
** Also adjusted for BMI
*** Result generated at UMD in a model with Age Sex, Study as covariates.

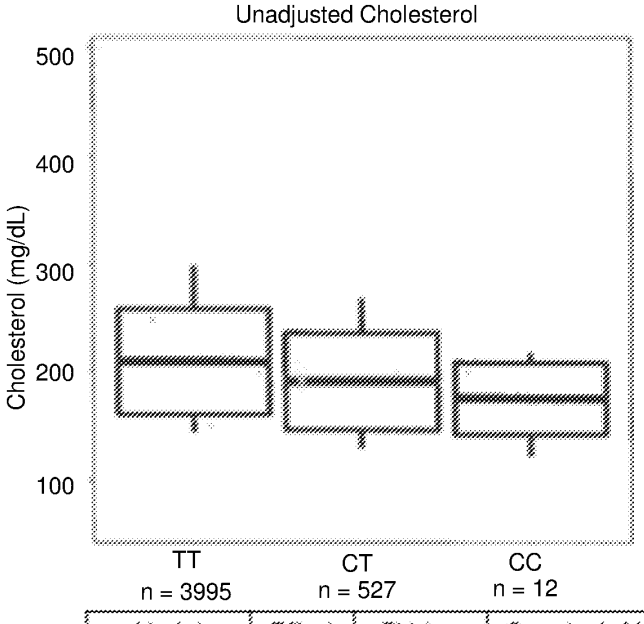
Figure 6

Phenotype	Genotypic Means*	Genotypic Means Unadjusted	Counts (Ref/Het/Alt)	Effect (95% CI)	Pvalue
CAD-related traits					
Coronary Calcification (log10)	0.301 / 0.301 / NA	0.299 / 0.220 / NA	202/42/0	-22.4 (-38.3, -0.92) %	0.0433
Coronary Calcification (log10)***	1.87 / 1.44 / 0	NA	346/94/1	-19 %	0.1349
Pericardial Fat**	69.5 / 82.7 / NA	71.3 / 73.4 / NA	148/27/0	12.76 (1.06, 24.46)	0.0339
Liver traits					
AST (log10), U/L	18.0 / 18.6 / 35.2	18.0 / 18.7 / 34.3	3910/317/12	7.15 (4.71, 12.20) %	6.0E-08
ALT (log10), U/L	17.2 / 16.8 / 20.3	17.2 / 16.9 / 19.7	3978/330/13	-0.23 (-4.50, 4.71) %	0.8920
AlkPhos (log10), U/L	53.8 / 52.9 / 62.9	53.6 / 53.1 / 61.8	3987/331/13	0.92 (-3.87, 2.09) %	0.5391
Liver fat (by EBCT)	1.27 / 1.33 / NA	1.27 / 1.32 / NA	166/38/0	0.05 (-0.005, 0.110)	

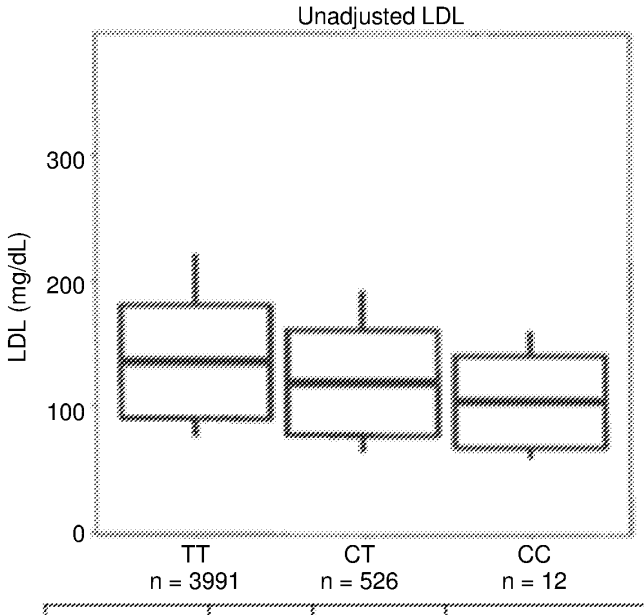
0.0774* Genotypic means are on the clinical scale, removing the effects of Age, Age2, Sex, and Study
** Also adjusted for BMI
*** Result generated at UMD in a model with Age Sex, Study as covariates.

Figure 6 (cont.)

B4GALT1 ASN352SER IS HIGHLY ASSOCIATED WITH SERUM LIPIDS AND AST



Model	Effect	PValue	Genotypic Means
Unadjusted	-17.0	1.01E-09	210.4/192.3/176.2
w/ Covars*	-17.2	1.30E-10	210.6/190.9/172.7



Model	Effect	PValue	Genotypic Means
Unadjusted	-14.5	9.35E-09	134.6/118.3/103.5
w/ Covars*	-14.6	1.84E-09	134.7/117.4/103.5

*Statistical models account for Age, Age^2, Sex, and Study; further adjustment for R3527Q *APOB* does not appreciably alter results; AST normal reference range = 10-35 U/L

Figure 7

B4GALT1 ASN352SER IS HIGHLY ASSOCIATED WITH SERUM LIPIDS AND AST

Model	Effect	PValue	Genotypic Means
Unadjusted	7.9%	2.10E-07	17.99/18.66/34.28
w/ Covars*	7.9%	6.02E-08	17.99/18.62/35.25

*Statistical models account for Age, Age^2, Sex, and Study; further adjustment for R3527Q *APOB* does not appreciably alter results; AST normal reference range = 10-35 U/L

Figure 7 (cont.)

B4GALT1 ASN352SER IS ASSOCIATED WITH DECREASES IN ALL LIPID SUBFRACTIONS
(AMISH HAPI HEART STUDY)

Phenotype	Genotypic Means*	Genotypic Means Unadjusted	Counts(Ref/Het/Alt)	Effect	Pvalue
HDL2, mg/dL	15.9 / 13.5 / 19.6	15.9 / 13.7 / 21.0	660/74/1	-2.07 (-3.68, -0.46)	0.012
HDL2a, mg/dL	11.2 / 9.7 / 15.3	11.2 / 9.8 / 16.4	660/74/1	-1.23 (-2.38, -0.09)	0.036
HDL2b, mg/dL	3.2 / 2.9 / 3.6	3.2 / 2.9 / 3.9	660/74/1	-0.33 (-0.73, 0.08)	0.113
HDL2c, mg/dL	1.5 / 1.1 / 0.1	1.5 / 1.1 / 0.2	660/74/1	-0.47 (-0.87, -0.07)	0.023
HDL3, mg/dL	39.5 / 36.8 / 39.3	39.4 / 37.1 / 41.0	660/74/1	-2.48 (-4.23, -0.72)	0.006
HDL3a, mg/dL	14.8 / 12.8 / 17.1	14.8 / 12.9 / 18.3	660/74/1	-1.73 (-3, -0.47)	0.007
HDL3b, mg/dL	6.2 / 6.4 / 5.8	6.2 / 6.4 / 5.9	660/74/1	0.09 (-0.3, 0.49)	0.640
HDL3c, mg/dL	9.5 / 9 / 9.3	9.5 / 9.0 / 9.7	660/74/1	-0.49 (-0.96, -0.03)	0.037
HDL3d, mg/dL	9 / 8.7 / 7.5	8.9 / 8.7 / 7.5	660/74/1	-0.34 (-0.7, 0.03)	0.070
LDL1, mg/dL	22.8 / 20.2 / 15.2	22.7 / 20.9 / 17.4	660/74/1	-3.17 (-5.89, -0.45)	0.023
LDL2, mg/dL	48.3 / 39.4 / 32.1	48.2 / 39.7 / 34.4	660/74/1	-8.43 (-14.47, -2.38)	0.006
LDL3, mg/dL	45.7 / 43.2 / 18.2	45.4 / 44.4 / 18.3	660/74/1	-1.69 (-6.77, 3.38)	0.513
LipoproteinA, mg/dL	7.7 / 6.6 / 11.6	7.7 / 6.7 / 12.0	660/74/1	-0.66 (-1.56, 0.24)	0.150
Lpa1 (log10), mg/dL	3.79 / 3.39 / 5.13	3.78 / 3.50 / 5.50	220/10/1	-4.50 (-33.9, 34.9) %	0.764
Lpa2 (log10), mg/dL	1.91 / 1.66 / NA	1.91 / 1.66 / NA	206/29/0	-14.9 (-41.1, 23.0) %	0.395
Lpa3 (log10), mg/dL	4.58 / 3.72 / NA	4.58 / 3.72 / NA	323/47/0	-18.7 (-30.8, -4.50) %	0.009
Lpa4 (log10), mg/dL	3.78 / 3.65 / NA	3.76 / 3.85 / NA	204/23/0	-4.50 (-27.6, 28.8) %	0.784
Lpa5 (log10), mg/dL	3.37 / 2.89 / 5.74	3.36 / 2.95 / 6.10	252/25/1	-8.80 (-24.1, 9.65) %	0.339

*Statistical models account for Age, Age^2, Sex, and Study

Figure 8

B4GALT1 ASN352SER IS ASSOCIATED WITH DECREASED FIBRINOGEN LEVELS (AMISH PAPI STUDY) + OTHER TRAITS OF POTENTIAL INTEREST

Phenotype	Genotypic Means*	Genotypic Means Unadjusted	GenoCounts (Ref/Het/Alt)	Effect	Pvalue
Fibrinogen, drug naïve, mg/dL	280.8 / 255 / 253.8	280.5 / 257.1 / 273.3	564/54/3	-23.97 (-38.35, -9.59)	1.15E-03
Fibrinogen, post-clopidogrel, mg/dL	276 / 247.7 / 182	275. / 249.7 / 197.0	549/54/3	-32.45 (-47.5, -17.41)	2.74E-05

Of 20+ platelet aggregation measures, pre/post-clopidogrel/post-aspirin, only 2 are nominally significant

Phenotype	Control Counts (Ref/Het/Alt)	Case Counts (Ref/Het/Alt)	Control Freq	Case Freq	OR (95% CI)	OR Het (95% CI)	OR Hom	Pvalue
CAD (logistic)	3535/473/11	101/13/0	0.061	0.057	0.78 (0.45, 1.48)	0.96 (0.54, 1.72)	-	0.42

Phenotype	Genotypic Means*	Genotypic Means Unadjusted	Counts (Ref/Het/Alt)	Effect	Pvalue
Creatinine (log10), mg/dL	0.747 / 0.767 / 0.789	0.748 / 0.763 / 0.756	3987/531/13	2.23 (0.46, 1.04) %	0.0095
eGFR, mL/min/1.73m^2	107.2 / 104.1 / 97.0	107.2 / 103.5 / 95.5	3910/517/12	-2.86 (-5.10, -0.63)	0.0121
Basophils (log10), %	0.402 / 0.376 / 0.369	0.402 / 0.378 / 0.370	3275/444/11	-6.67 (-10.87, 0.69) %	0.0259
Hematocrit, %	40.5 / 40.8 / 42.8	40.5 / 40.7 / 41.4	3897/514/12	0.34 (0.04, 0.63)	0.0271

*Statistical models account for Age, Age^2, Sex, and Study

Figure 9

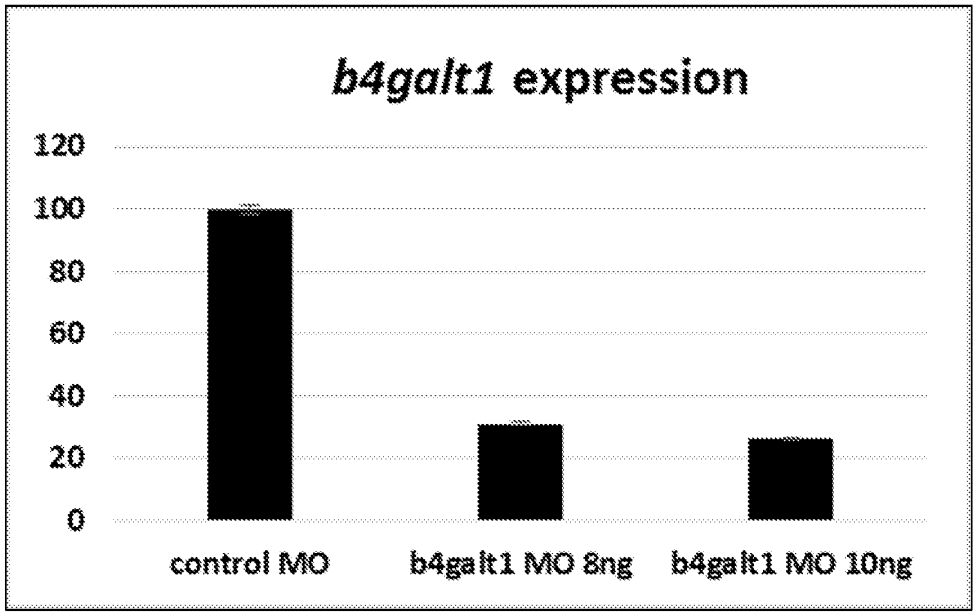

b4galt1 expression
120
100
80
60
40
20
0
control MO
b4galt1 MO 8ng
b4galt1 MO 10ng

Figure 10

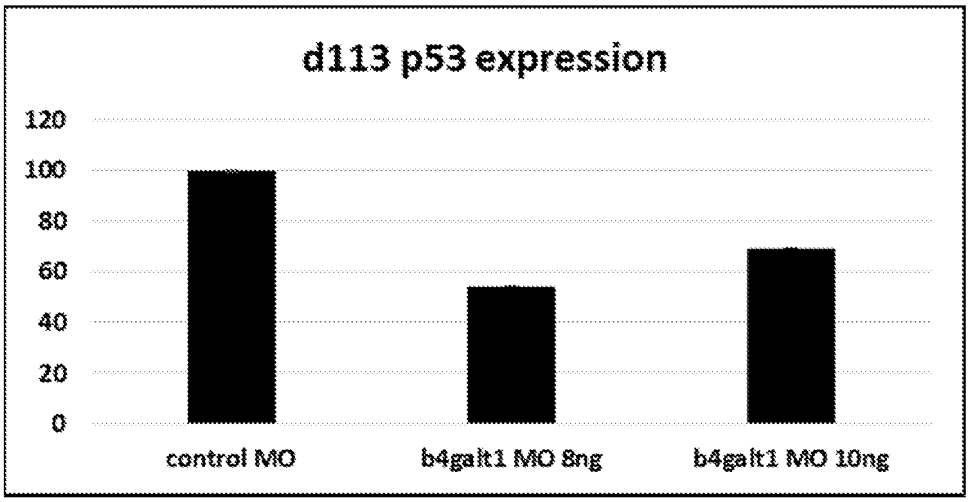

d113 p53 expression
120
100
80
60
40
20
0
control MO
b4galt1 MO 8ng
b4galt1 MO 10ng

Figure 11

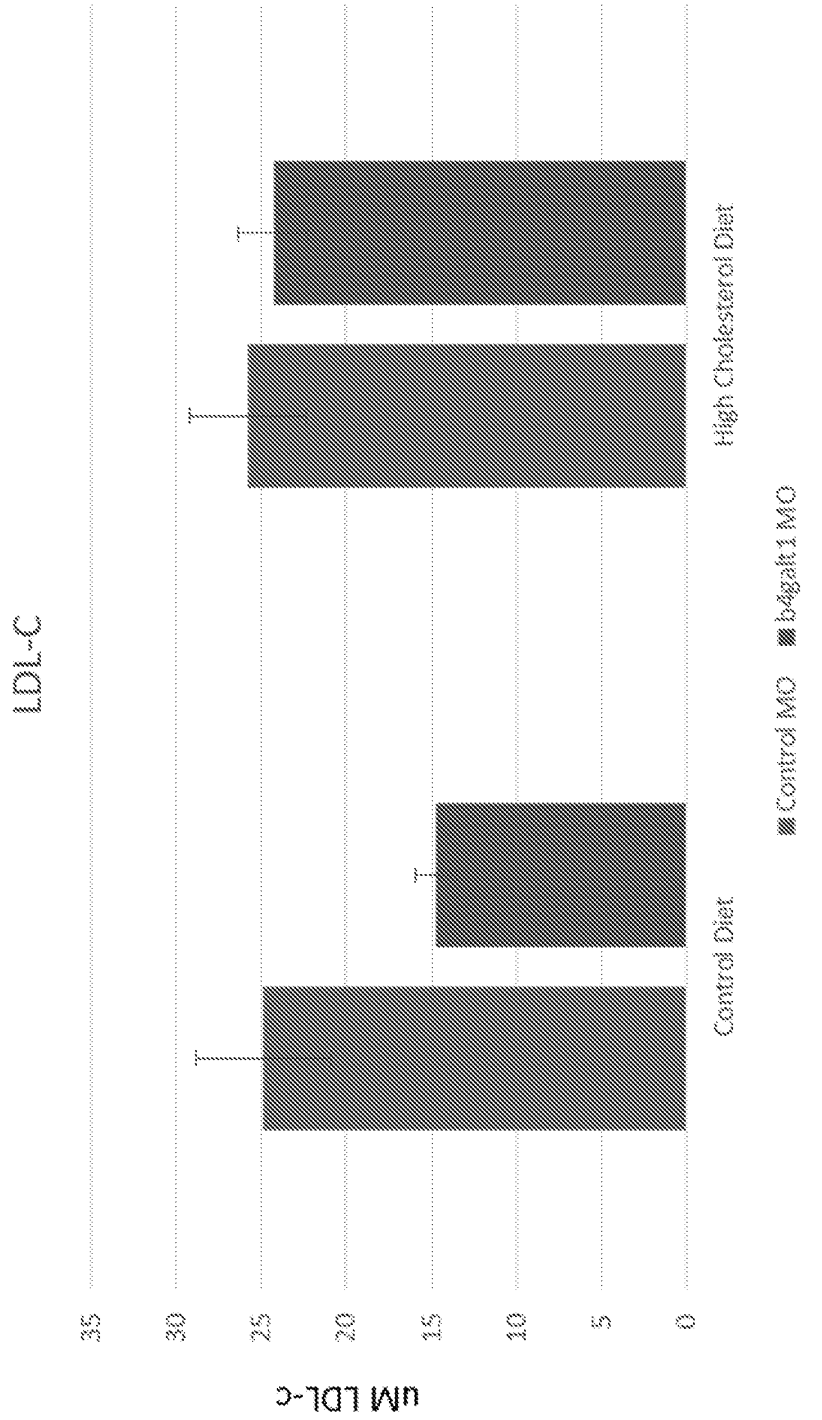

LDL-C
uM LDL-c
35
30
25
20
15
10
5
0
Control Diet
High Cholesterol Diet
Control MO
b4galt1 MO

Figure 12

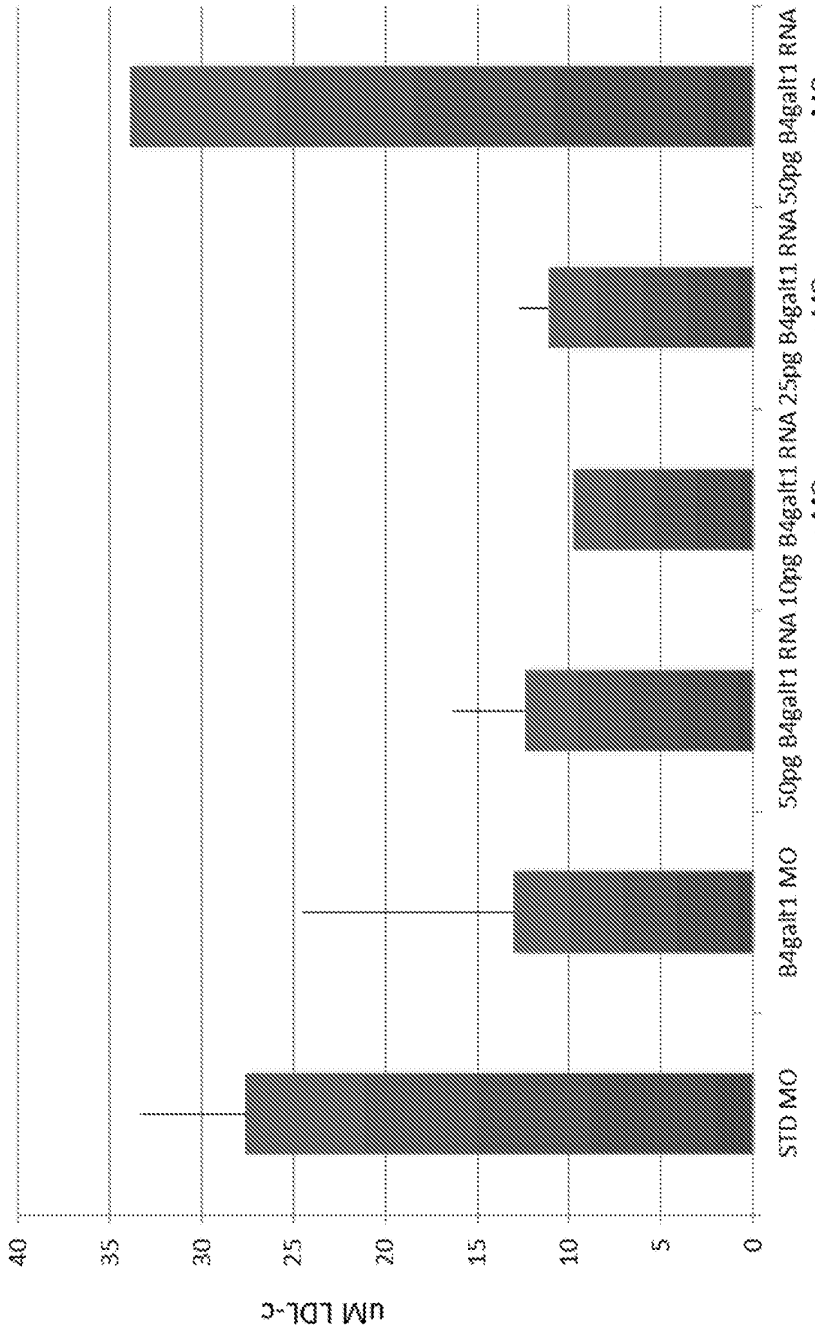

LDL-c in larvae on control diet
uM LDL-c
0
5
10
15
20
25
30
35
40
STD MO
B4galt1 MO
50pg B4galt1 RNA + MO
10pg B4galt1 RNA + MO
25pg B4galt1 RNA + MO
50pg B4galt1 RNA + MO

Figure 13

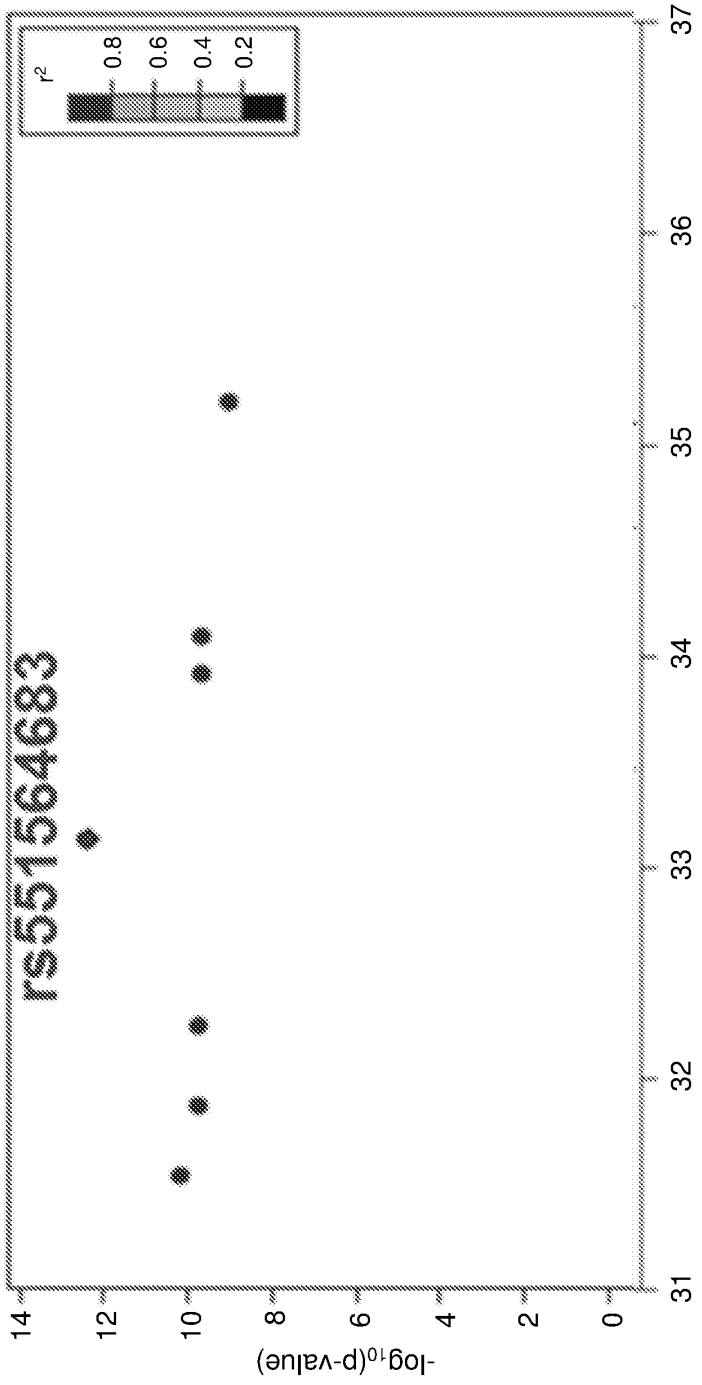

rs551564683
r²
0.8
0.6
0.4
0.2
-log10(p-value)
0
2
4
6
8
10
12
14
31
32
33
34
35
36
37
Position on chr9 (Mb)

Figure 14

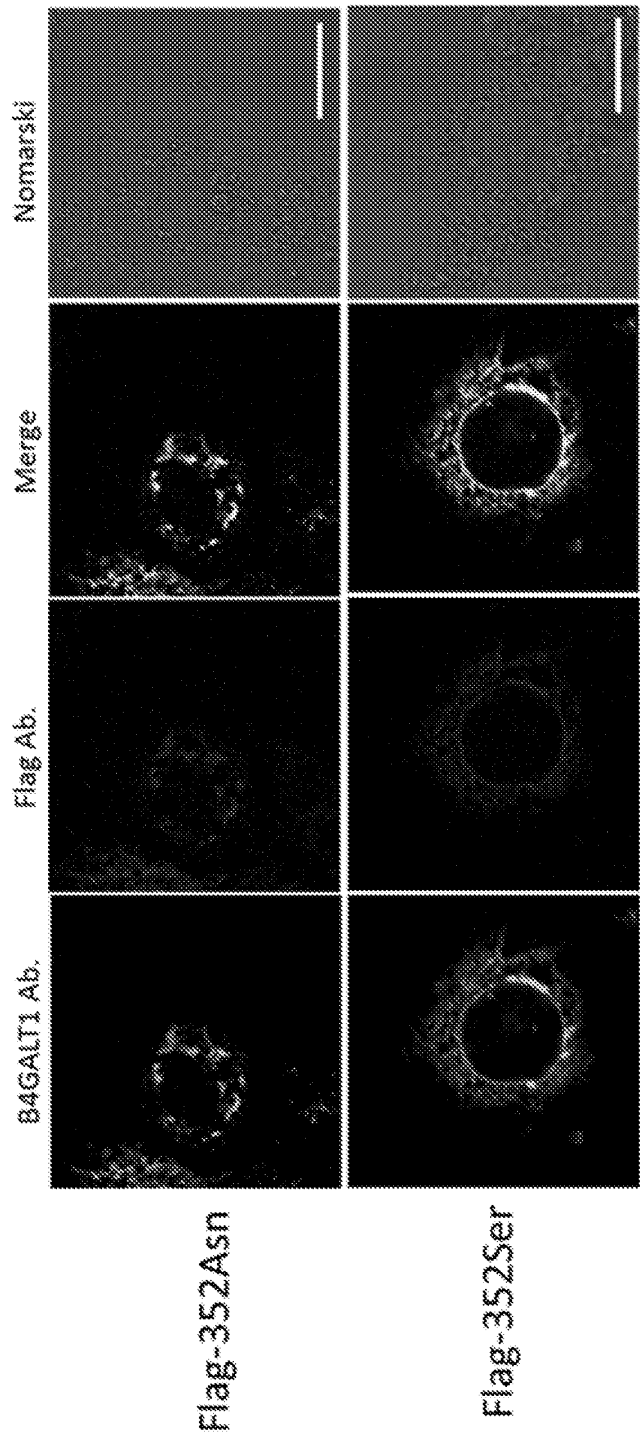


Figure 15

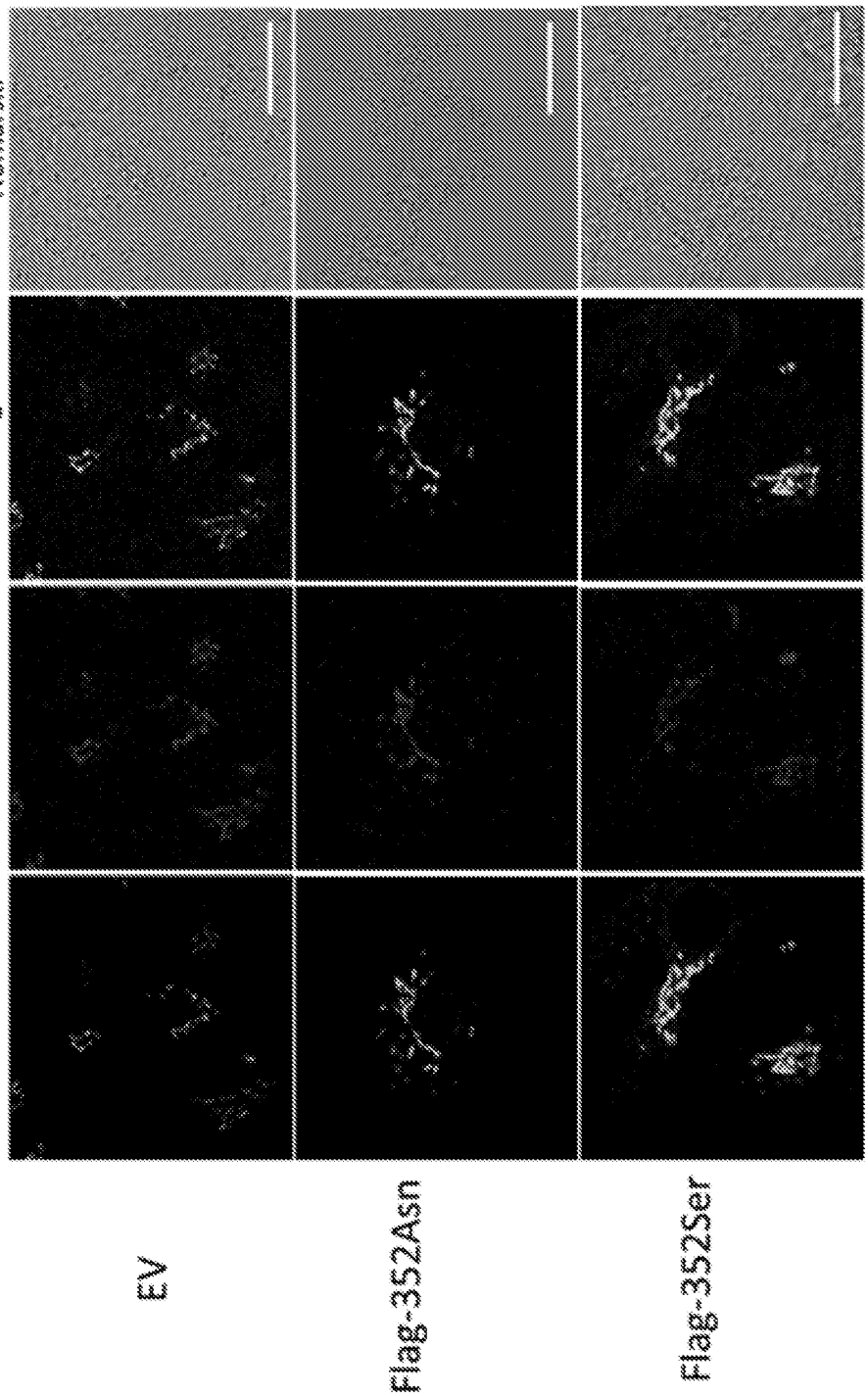

B4GALT1 Ab.
TGN46 Ab.
Merge
Nomarski
EV
Flag-352Asn
Flag-352Ser

Figure 16

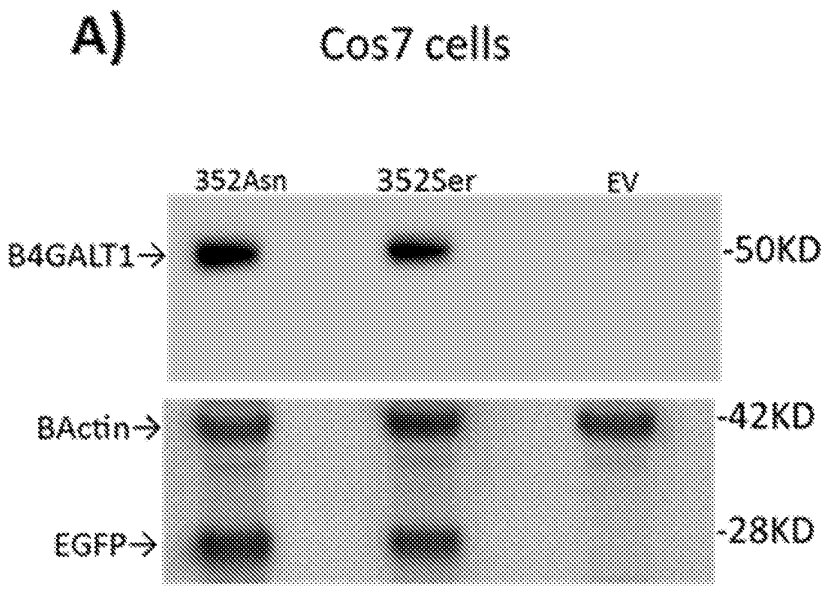

A)
Cos7 cells
352Asn
352Ser
EV
B4GALT1→
-50KD
BActin→
-42KD
EGFP→
-28KD

Figure 17

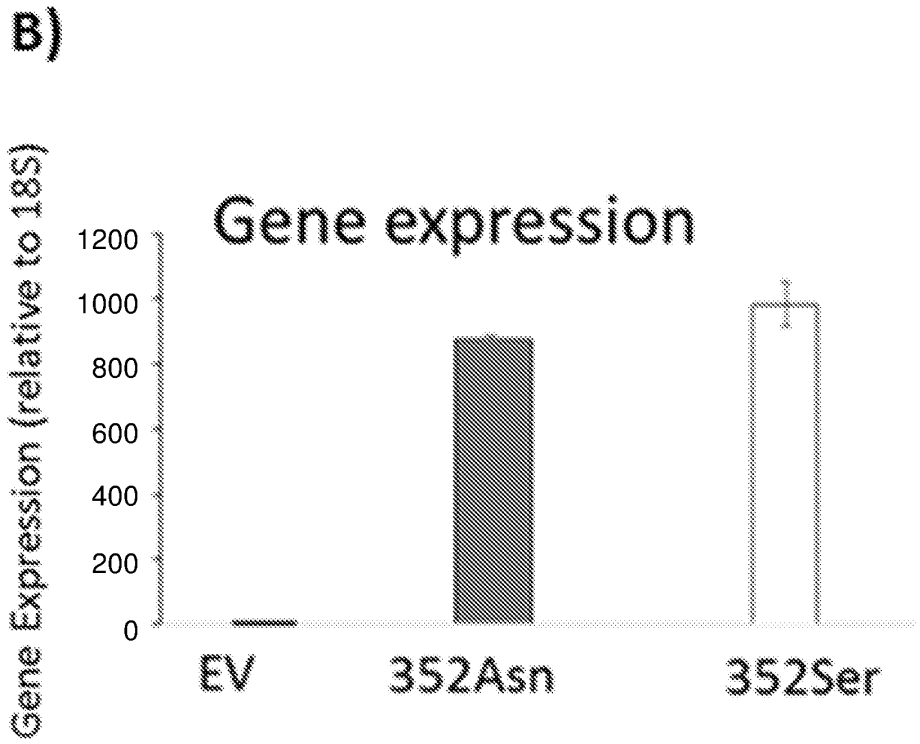


Figure 17 (cont.)

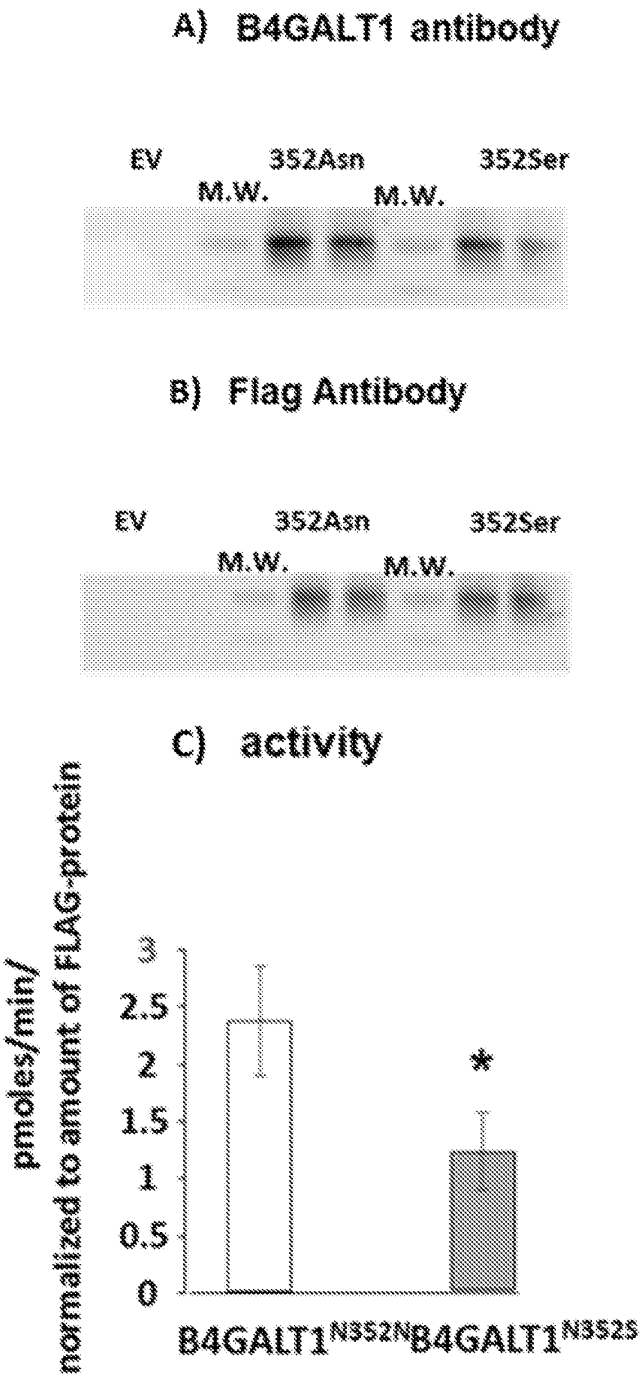

A) B4GALT1 antibody
EV
352Asn
352Ser
M.W.
M.W.
B) Flag Antibody
EV
352Asn
352Ser
M.W.
M.W.
C) activity
pmoles/min/
normalized to amount of FLAG-protein
3
2.5
2
1.5
1
0.5
0
*
B4GALT1N352N
B4GALT1N352S

Figure 18

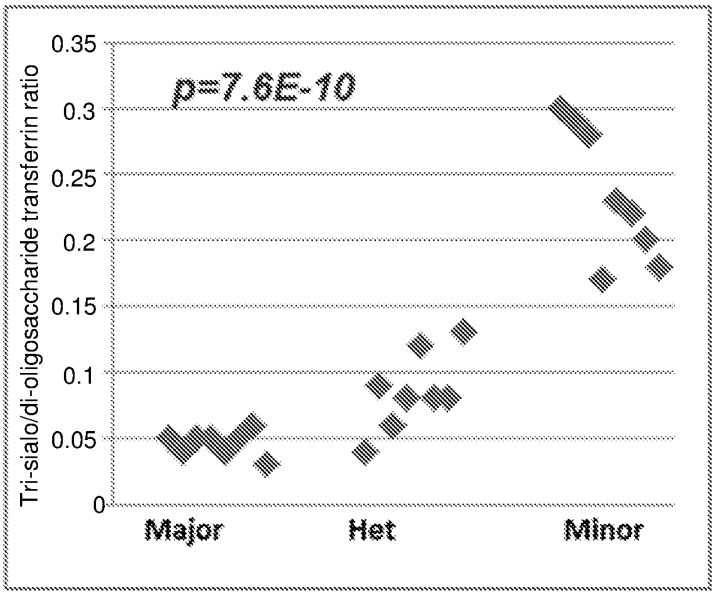

p=7.6E-10
Tri-sialo/di-oligosaccharide transferrin ratio
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
Major
Het
Minor

Figure 19

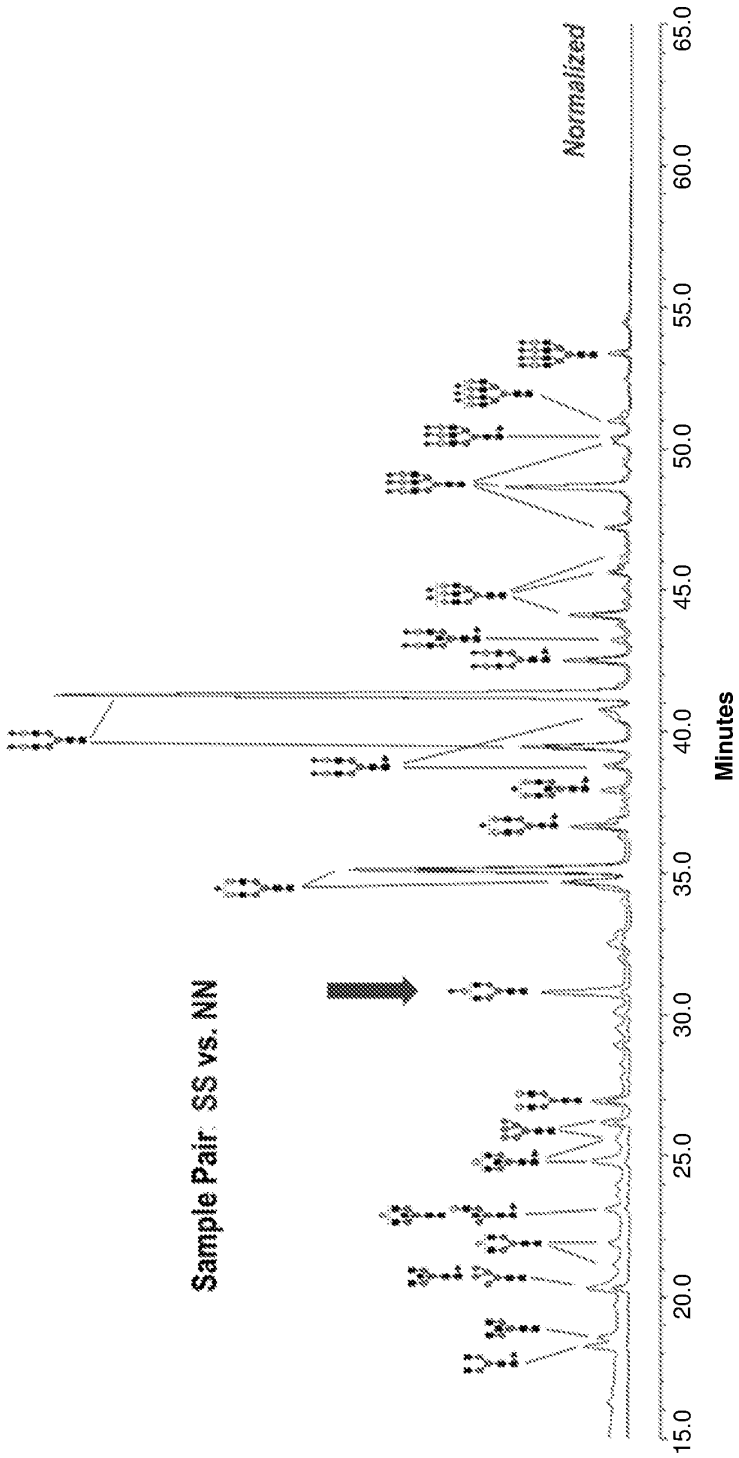

Sample Pair: SS vs. NN
Normalized
Minutes
15.0
20.0
25.0
30.0
35.0
40.0
45.0
50.0
55.0
60.0
65.0

Figure 20

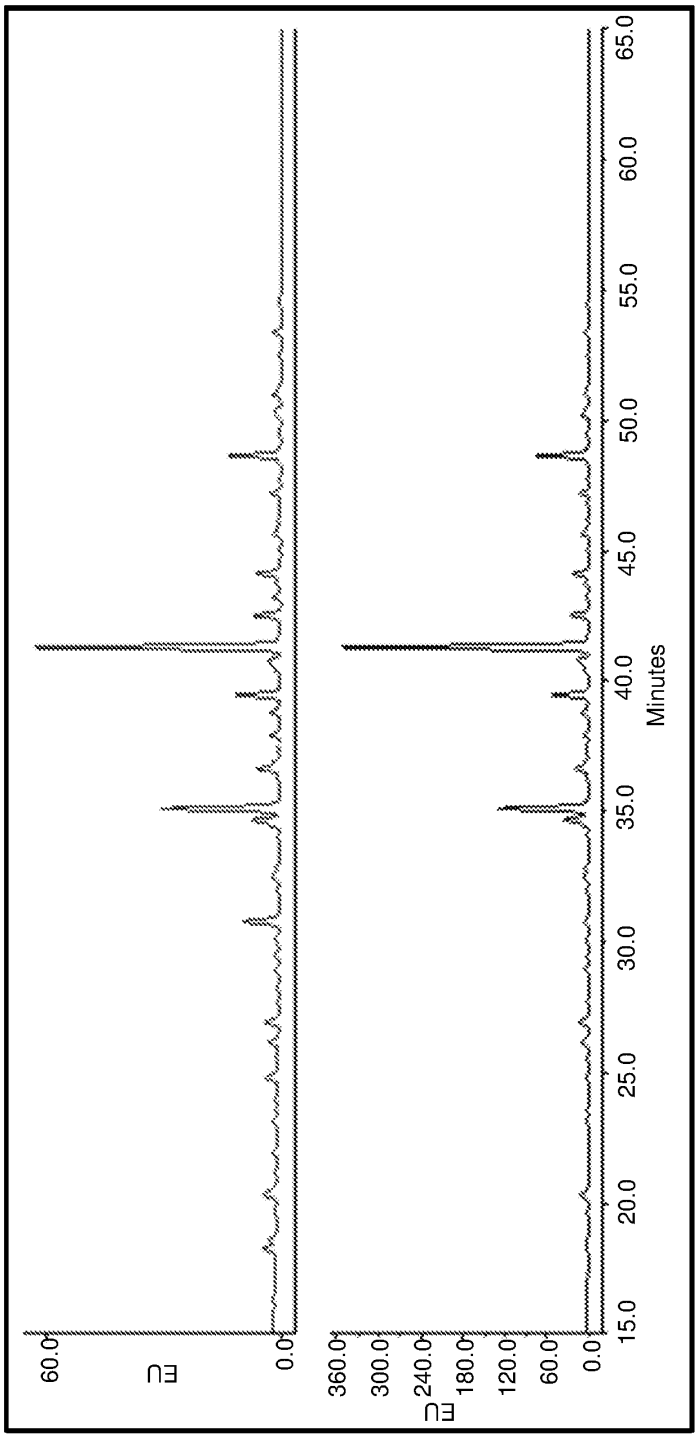


Figure 20 (cont.)