Natriuretic Peptide Receptor 2 Locus Contributes to Carotid Remodeling

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BACKGROUND: Carotid artery intima/media thickness (IMT) is a hallmark trait associated with future cardiovascular events. The goal of this study was to map new genes that regulate carotid IMT by genome-wide association.

METHODS AND RESULTS: We induced IMT by ligation procedure of the left carotid artery in 30 inbred mouse strains. Histologic reconstruction revealed significant variation in left carotid artery intima, media, adventitia, external elastic lamina volumes, intima-to-media ratio, and (intima+media)/external elastic lamina percent ratio in inbred mice. The carotid remodeling trait was regulated by distinct genomic signatures with a dozen common single-nucleotide polymorphisms associated with left carotid artery intima volume, intima-to-media ratio, and (intima+media)/external elastic lamina percent ratio. Among genetic loci on mouse chromosomes 1, 4, and 12, there was natriuretic peptide receptor 2 (Npr2), a strong candidate gene. We observed that only male, not female, mice heterozygous for a targeted Npr2 deletion (Npr2+/−) exhibited defective carotid artery remodeling compared with Npr2 wild-type (Npr2+/+) littermates. Fibrosis in carotid IMT was significantly increased in Npr2+/− males compared with Npr2+/− females or Npr2+/+ mice. We also detected decreased Npr2 expression in human atherosclerotic plaques, similar to that seen in studies in Npr2+/− mice.

CONCLUSIONS: We found that components of carotid IMT were regulated by distinct genetic factors. We also showed a critical role for Npr2 in genetic regulation of vascular fibrosis associated with defective carotid remodeling.

Key Words: carotid artery ■ genome-wide association ■ inbred mice ■ Npr2 ■ vascular remodeling

Atherosclerosis is a complex disorder regulated by multiple genetic and environmental factors. Recently, many candidate genetic mechanisms have been proposed but most do not have major effects on development of human atherosclerosis. A reliable clinical measure of atherosclerosis progression is carotid intima/media thickness (IMT), which predicts cardiovascular complications. Genetic linkage studies in Framingham Heart and Dominican Family cohorts identified significant quantitative traits loci (QTLs) on human chromosome (chr)7q, chr12q, and chr14q that control carotid IMT. Genome-wide association (GWA) studies mapped a number of single-nucleotide polymorphisms (SNPs) associated with variation in carotid IMT. Despite such advances, those studies were underpowered and there are technical limitations to assessing specific mechanisms of carotid IMT and atherosclerotic plaque progression and regression in humans.

We developed a robust mouse model of carotid IMT and showed significant genetic effects in 5 inbred strains of mice. A forward genetic approach followed by congenic mapping was effective in uncovering 3 carotid intima modifier QTLs on mouse chr2, chr11, and chr18. Additional QTLs were identified on mouse chr5, chr9, chr12, and chr13, that contribute...
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CLINICAL PERSPECTIVE

What Is New?
• Genetic variation in natriuretic peptide receptor 2 (Npr2) associated with defective carotid artery remodeling in a panel of mice that represent a human population.
• Male but not female mice with a targeted Npr2 deletion exhibited defective carotid artery remodeling with increased fibrosis.
• Expression of the Npr2 was reduced in human atherosclerotic plaques.

What Are the Clinical Implications?
• Npr2 is a plausible target for new diagnostic and therapeutic approaches to treat vascular disease.

METHODS

The authors declare that all supporting data are available within the article and its online supplementary material.

Animals
We studied flow-induced carotid remodeling in 9- to 12-week-old male mice from 30 inbred strains (Table S1). We purchased 10 mice per strain, 4 sham and 6 ligated, from the Jackson Laboratory (Bar Harbor, Maine). However, some of the inbred mouse strains exhibited poor survival and required additional mice, as we recently reported for 129X1 in a comparison with C57BL/6J. We also used male and female Npr2 wild-type (Npr2+/+) and Npr2 heterozygous (Npr2+/-) littermate mice from our recently established colony. Presence of Npr2 alleles was determined by genotyping, as described previously. We were unable to use Npr2 knockout (Npr2−/−) mice for surgery because of low body weights. Experimental mice were housed individually under a 12-hour light/12-hour dark cycle with free access to water and chow. All animal procedures were approved by the animal care committee of the University of Rochester and were in accordance with the Guide for the Care and Use of Laboratory Animals.

Tail-Cuff Plethysmography
Systolic blood pressure (BP) and heart rate were collected with a BP-2000 (Visitech Systems, Apex, North Carolina) system in Npr2 mice. We performed our experiments according to a method described previously. Briefly, animals were anesthetized with a cocktail of ketamine and xylazine (130 and 9 mg/kg, respectively, intraperitoneally). The neck area was opened by a midline incision and the bifurcation of the left carotid artery (LCA) was isolated. The internal and external LCA branches were ligated with 6-0 silk, leaving the occipital artery intact. The neck opening was closed with a 6-0 coated Vicryl suture. An analgesic flunixin meglumine (120 mg/kg, intraperitoneally) was given immediately after and once per day for 3 days after the surgery. A plastic box with additional bedding material was given to mice housed individually after the surgery.

Carotid Artery Ligation
We studied flow-induced carotid remodeling 2 weeks after the ligation procedure in all mice, as described previously. Briefly, animals were anesthetized with a cocktail of ketamine and xylazine (130 and 9 mg/kg, respectively, intraperitoneally). The neck area was opened by a midline incision and the bifurcation of the left carotid artery (LCA) was isolated. The internal and external LCA branches were ligated with 6-0 silk, leaving the occipital artery intact. The neck opening was closed with a 6-0 coated Vicryl suture. An analgesic flunixin meglumine (120 mg/kg, intraperitoneally) was given immediately after and once per day for 3 days after the surgery. A plastic box with additional bedding material was given to mice housed individually after the surgery.

Vascular Ultrasound
We measured blood flow in the LCA in inbred mouse strains with a ultrasonic transit-time volume flowmeter (Transonic Systems, Ithaca, New York) before termination, as described elsewhere. Carotid artery imaging in anesthetized Npr2 mice was done with a Vevo2100 machine (FUJIFILM VisualSonics, Toronto, Ontario, Canada) as described in our previous work.

Nonstandard Abbreviations and Acronyms

3D 3-dimensional
BP systolic blood pressure
chr human chromosome
EEL external elastic lamina
eNOS endothelial nitric oxide synthase
IMT intima/media thickness
LCA left carotid artery
Npr2−/− Npr2 knockout
Npr2 natriuretic peptide receptor 2
Npr2+/- Npr2 heterozygous
Npr2+/- Npr2 wild-type
QTLs quantitative traits loci
SNP single-nucleotide polymorphism

to carotid atherosclerosis. A plausible approach to identification of atherosclerosis traits includes GWA studies in a panel of mouse inbred strains. In an earlier study, we utilized this approach and identified several causative genes that control the elevated heart rate trait. The primary goal of this study was to use GWA to identify new genes that regulate carotid remodeling. By studying 30 strains of mice, we characterized a genetic locus that houses a novel gene candidate—natriuretic peptide receptor 2 (Npr2)—that regulates carotid artery remodeling.
Histology and Morphometry
Two weeks after ligation, mice were perfusion fixed under anesthesia; carotids were collected, processed, and stained with hematoxylin and eosin; followed by morphometry analyses (MCID image software), as described elsewhere.11 We evaluated 10 area divisions of the LCA from the bifurcation every 200 μm through the 2-mm length. Averaged area measurements of the LCA for each group were used to produce 3-dimensional (3D) images with MATLAB programming (The Mathworks, Natick, Massachusetts), as described elsewhere.26 Unstained LCA sections of ligated Npr2 mice were processed with an Alcin Blue kit (ScienCell Research Laboratories, Carlsbad, California) or PicroSirius Red kit (Abcam, Cambridge, Massachusetts). We also stained consecutive cross-sections of human endarterectomy with rabbit anti-NPR2 (1:100; overnight at +4°C; Abcam), mouse sections of human endarterectomy with rabbit anti-Massachusetts). We also stained consecutive cross-sections of human endarterectomy with rabbit anti-

Genome-Wide Association of Carotid Remodeling in 30 Inbred Strains of Mice
GWA mapping for carotid remodeling traits was done using an efficient mixed-model association method with a significance for P-value thresholds (4.1×10−6) on the basis of power calculations in a similar number of mouse strains.28 The GWA results on variation for LCA intima, media, adventitia, and external elastic lamina (EEL) volumes, intima/media ratio, and (intima+media)/EEL×100% are listed in Tables S2 through S7. We observed greater variation in LCA media, EEL, and adventitia volumes (Figures S3 through S6). There was disparity in the relationship between LCA intima volume and (intima+media)/EEL×100%. For example, below 40% LCA (intima+media)/EEL×100% was observed in mouse strains without (eg, BTBR) or with (eg, C3H) intima (Figure 1D). In contrast, mouse strains with a greater percentage of LCA (intima+media)/EEL×100% had small (SM) vs large (SJL) LCA intima volume (Figure 1E). Thus, we characterized a significant variation in response to vascular injury across 30 inbred mouse strains permitting GWA studies for carotid remodeling traits.

Human Samples
Cross-sections of de-identified human endarterectomy samples from 3 patients undergoing surgery on a carotid artery were collected with the approval from the subjects review board of the University of Rochester School of Medicine and Dentistry Research (RSRB00069961).

Statistical Analysis
Results are presented as mean±SEM. Statistical significance was determined using JMP version 13.0.0 software (SAS). Initial analyses of data sets across experiments showed a normal distribution. Two groups were compared using Student’s t test. One-way ANOVA was evaluated for each parameter with post-hoc comparisons of means using the Tukey–Kramer honestly significant difference test. We performed multivariate and linear regression analyses between LCA intima volumes and LCA (intima-media)/EEL×100% to determine pairwise correlations in the experimental groups. P<0.05 was considered significant.

RESULTS
Variation of the Remodeling Traits Across 30 Inbred Mouse Strains
A forward genetic approach followed by congenic mapping was effective in revealing the causes of increased LCA intima.13–15 To map the carotid intima trait, we investigated variation in the most common inbred strains (Figure 1A). We found that relative changes in LCA blood flow were similar among the studied strains compared with RCA blood flow after ligation (Table S1). However, the same reduction in blood flow resulted in significant variation in carotid arteries on the basis of 3D reconstruction of histologic measurements across the strains (Figures S1 through S3). There were 5 inbred strains that significantly differed in LCA intima volume from controls or other strains, whereas no intima was detected in controls (Figure 1A). Similar results were observed for intima/media ratio and (intima+media)/EEL×100% across 30 mouse strains (Figure 1B and 1C). We observed greater variation in LCA media, EEL, and adventitia volumes (Figures S3 through S6). There was disparity in the relationship between LCA intima volume and (intima+media)/EEL×100%. For example, below 40% LCA (intima+media)/EEL×100% was observed in mouse strains without (eg, BTBR) or with (eg, C3H) intima (Figure 1D). In contrast, mouse strains with a greater percentage of LCA (intima+media)/EEL×100% had small (SM) vs large (SJL) LCA intima volume (Figure 1E). Thus, we characterized a significant variation in response to vascular injury across 30 inbred mouse strains permitting GWA studies for carotid remodeling traits.

GWA Analysis of Carotid Remodeling Traits in 30 Inbred Strains of Mice
Most SNPs were associated with LCA intima/media ratio after ligation (Figure 2B and Table S6). Importantly, there were common SNPs regulating LCA intima volume, intima/media ratio, and
Among 12 common SNPs, we discovered 6 candidate genes (Slc24a4, solute carrier family 24 sodium/potassium/calcium exchanger, member 4; Tln1, talin 1; Npr2, natriuretic peptide receptor 2; Fam221b, family with sequence similarity 221, member B; Tmem8b, transmembrane protein 8B; Spaar, small regulatory polypeptide of amino acid response) known to regulate carotid intima and remodeling (Table). Our findings are supported by another mouse genetic study that proposed Npr2...

**Figure 1.** Variation in carotid remodeling in 30 mouse strains. 

A, Left carotid artery (LCA) intima volume, \( \times 10^{-6} \) \( \mu m^3 \). B, LCA intima/media ratio. C, LCA (intima+media)/EEL\( \times 100\% \). Open circles indicate controls. Black circles indicate ligated mice. Values are mean\( \pm \)SEM; *P<0.05 vs control or other mouse strains. n=4 to 6 per group. D, Representative 3-dimensional (3D) reconstructions of the 2 mm-length from the bifurcation of the ligated LCA in mice with low values of LCA (intima+media)/EEL\( \times 100\% \). E, Representative 3D reconstructions of mouse strains with a greater percentage of LCA (intima+media)/EEL\( \times 100\% \). Black color shows lumen, yellow indicates intima, red indicates media, and green indicates adventitia volume. EEL indicates external elastic lamina.
Figure 2. GWA of carotid remodeling traits in 30 mouse strains. 
A, GWA of LCA intima volume, $x10^{-6}$ $\mu$m$^3$. B, GWA of LCA intima/media ratio. C, GWA of LCA (intima+media)/EEL$\times$100%. Each circle represents an SNP. Mouse chromosomes are presented on the X-axis. Blue lines show significance threshold. Black rhombi point to common regions of significant SNPs associated with LCA intima, intima/media ratio, and (intima+media)/EEL$\times$100% traits in 30 inbred mouse strains. EEL indicates external elastic lamina; GWA, genome-wide association; LCA, left carotid artery; and SNP, single-nucleotide polymorphism.
with its ligand, C-type natriuretic peptide, as candidate genes in high blood pressure.\textsuperscript{30,31} Thus, we found that Npr2 is a plausible candidate for regulation of carotid remodeling traits in response to injury.

### Carotid Remodeling in Npr2-Npr2\textsuperscript{+/-} Mice

We confirmed earlier genetic studies in mice on a causal role for the Npr2 gene in salt-induced kidney injury.\textsuperscript{12} As we reported for direct BP measurements, tail-cuff systolic BP (114–117 mm Hg) and heart rate (574–618 beats/min) profiles were similar between Npr2\textsuperscript{+/-} and Npr2\textsuperscript{+/-} males and females (not shown). We found that a carotid ligation procedure resulted in a similar reduction of blood flow (Table S8) or estimated shear stress (not shown) between Npr2\textsuperscript{+/-} and Npr2\textsuperscript{+/-} littermates compared with sham animals. However, there were significant differences in LCA remodeling on the basis of histologic evaluation across Npr2 genotypes (Figure 3). We observed a significant increase in LCA intima/media ratio, adventitia, and EEL volumes versus sham animals (Figure 3B and 3D). Unlike Npr2\textsuperscript{+/-} males, we found that Npr2\textsuperscript{+/-} females exhibited significantly increased LCA EEL after ligation (Figure 3). Thus, we confirmed that the Npr2 gene plays a role in carotid artery response to injury, but only in males.

### Relationship Between Carotid Intima Volume and Stenosis in Npr2\textsuperscript{+/-} Mice

In a previous study we reported a strong correlation between increase in LCA intima volume and LCA (intima+media)/EEL\texttimes100% in 5 inbred mouse strains, as also seen in human atherosclerosis.\textsuperscript{12} In the present work we found a significant correlation (R=0.6959, P<0.001) between LCA intima volume and (intima+media)/EEL\texttimes100% among 30 inbred strains of mice (Figure 4A). However, this correlation was not significant in Npr2\textsuperscript{+/-} (R=0.3872) animals when compared with Npr2\textsuperscript{+/-} (R=0.7928, P<0.01) littermates (Figure 4B). Furthermore, there was essentially no correlation between LCA intima volume and (intima+media)/EEL\texttimes100% among 30 inbred strains of mice (Figure 4A). However, this correlation was not significant in Npr2\textsuperscript{+/-} (R=0.3872) animals when compared with Npr2\textsuperscript{+/-} (R=0.7928, P<0.01) littermates (Figure 4B). These results show that even partial depletion of Npr2 resulted in a defective carotid artery remodeling response, but only in males.

### Differences in Carotid Fibrosis in Npr2 Mice

We recently showed that pharmacologic intervention could improve carotid remodeling by inhibiting fibrosis after injury.\textsuperscript{21} Representative images of LCA cross-sections stained with Alcian Blue show remodeling differences between male Npr2\textsuperscript{+/-} versus male Npr2\textsuperscript{+/-} (Npr2 females are shown in insets in Figure 5A and 5B). The relative staining expression within the LCA intima/media (black brackets) was significantly greater in Npr2\textsuperscript{+/-} versus male Npr2\textsuperscript{+/-} and Npr2\textsuperscript{+/-} females (Figure 5C). An increase in fibrosis in Npr2\textsuperscript{+/-} males was also confirmed by PicroSirius Red staining of carotid arteries after ligation (Figure S7). Our data suggest that decreased carotid...
Figure 3. Flow-dependent carotid remodeling in Npr2 mice.
A. Representative 3-dimensional (3D) reconstructions of the 2-mm length from the bifurcation of the LCA after sham or ligation operation in males of Npr2 wild-type (Npr2+/+) and Npr2 heterozygous (Npr2+/-) mice. B, Representative 3D reconstructions of LCA after sham or ligation operation in females of Npr2+/+ and Npr2+/- mice. Black indicates lumen, yellow indicates intima, red indicates media, and green indicates adventitia volume. C, Quantifications of LCA intima/media ratio, adventitia, and EEL volume in males of Npr2+/+ and Npr2+/- mice. D, Quantifications of LCA intima/media ratio, adventitia, and EEL volume in females of Npr2+/+ and Npr2+/- mice. Open circles indicate individual sham LCAs. Black circles indicate ligated LCAs. Gray lines indicate mean values. EEL indicates external elastic lamina; and LCA, left carotid artery. *P<0.05 vs sham; †P<0.05 vs Npr2+/- males; ‡P<0.05 vs Npr2+/- females. n=3 to 6 per group.
remodeling in male Npr2−/− mice is, in part, due to an increase in vascular fibrosis.

**Decreased NPR2 Expression in Human Atherosclerotic Plaque**

We identified a significant 4-fold reduction in NPR2+ immunoreactivity within the atherosclerotic...
lesions (dark bar) compared with the medial compartment (white brackets) of human carotid artery (Figure 6A). The NPR2 protein expression profile showed the same decline as a smooth muscle-specific staining (smooth muscle actin+) in human lesions (Figure 6B). In contrast, macrophage-specific staining (CD68+) was increased in lesions compared with media in human endarterectomy samples (Figure 6C).

**DISCUSSION**

The significant variation in response to vascular injury across 30 inbred mouse strains allowed us to identify 12 common SNPs associated with variation in LCA intima volume, intima/media ratio, and (intima+media)/EEL×100% traits. Our findings suggest that the gene discovered, *Npr2*, is a plausible candidate for regulation of carotid remodeling traits in response to vascular injury.
A rare genetic disorder, acromesomelic dysplasia, type Maroteaux, presents with short-limbed dwarfism after homozygous loss-of-function mutations in human NPR2.35 The highest association of the NPR2 was found with body height and fibrinogen levels in a large-scale GWA, which is relevant to earlier findings in a small genetic study in humans and after Npr2 perturbation in mice.23,35 Npr2, also known as Npr-B, belongs to a family of natriuretic peptide–binding proteins and represents 1 of the 5 transmembrane guanyl cyclases found in humans.36 A primary ligand for Npr2, C-type natriuretic peptide, can relax aortic rings, probably by binding to Npr2 and increasing cyclic guanosine monophosphate production that activates protein kinase Gi, which phosphorylates target proteins.37 A downstream target of Npr2-dependent signaling, protein kinase Gi phosphorylates and activates a myosin light-chain phosphatase that increases the calcium levels necessary for cell contraction, which lowers calcium sensitivity. Activation of the Npr2/cyclic guanosine monophosphate axis in pericytes is responsible for relaxation of precapillary arterioles and capillaries.38 Genetic studies in mice suggested that C-type natriuretic peptide and Npr2 are candidate genes in salt-induced BP.35 We and others showed that Npr2 has no significant role in BP homeostasis in mice.22,23 However, experiments in genetically manipulated mice, hypertensive rats, and in a large human GWA study showed that C-type natriuretic peptide production by endothelial cells is most important for reduction of BP.23,39–42 Herein, we found that Npr2 is critical for adaptation of the carotid artery in response to vascular injury. A striking difference in carotid sizes in Npr2−/− mice was also related to a significant decrease in intima volume. A moderate increase in carotid fibrosis in Npr2+/− mice resulted in a constrictive carotid phenotype in a nonfibrotic C57BL/6 background, as we recently reported.21 These data support our idea of genetic regulation of the unique cellular and biochemical processes in carotid artery disease.43 Our GWA findings are supported by the alteration in carotid remodeling in Npr2+/− mice and significant reduction of NPR2 expression in human atherosclerotic plaque. We believe that future clinical studies will uncover Npr2-mediated mechanisms of carotid IMT in humans.

Another significant finding in our study is that male, but not female, Npr2−/− mice exhibited constrictive carotid artery remodeling in response to low blood flow. The molecular basis for sex bias in carotid IMT development may be because of direct vasoprotective properties of estrogen on endothelial cells by antagonizing inflammatory responses such as tumor necrosis factor-α signaling.47 For example, in a surgical injury model, female mice had a >90% reduction in carotid intima formation relative to males, which was attenuated by ovariectomy.48 Functional
genetic studies in rodents have identified several sexual dimorphic factors contributing to carotid remodeling that were not apparent from human data, including lower endothelial nitric oxide synthase messenger RNA levels in female aorta versus male, and less oxidized phospholipid levels in females. Intriguingly, greater carotid pathologic remodeling in male mice mirrors sexual dimorphism in vascular injury response and disease in humans. Data from the AXA study, the Gutenberg Heart study, and an Okinawa–Nagano study revealed that men have higher carotid IMT levels relative to women. Furthermore, several risk factors for carotid IMT display sexual dimorphism: In the Tromso study, fibrinogen levels and amount of physical activity were associated with carotid IMT in men only, whereas triglyceride levels were associated with carotid IMT in women only. Other risk factors for carotid IMT, such as age, systolic BP, HDL, total cholesterol, body mass index, and smoking, did not correlate strongly with carotid IMT in a sex-specific manner. When combined, both human and mouse carotid artery data strongly suggest a protective role for estrogen in regulating vascular intima growth responses, which contribute to progression of carotid atherosclerosis and artery occlusion.

In conclusion, we have demonstrated the power of using mouse genetic analyses to identify candidate genes, and provide novel evidence for the role of Npr2 in the genetic regulation of vascular fibrosis associated with increased flow-dependent carotid remodeling. Future studies will explore the underlying mechanisms by which Npr2 regulates fibrosis toward the goal of developing new clinical therapeutic approaches to treating vascular disease.

ARTICLE INFORMATION
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Supplementary Materials
Tables S1–S8
Figures S1–S7

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SUPPLEMENTAL MATERIAL
Table S1. Changes of blood flow after carotid ligation across 30 inbred mouse strains.

| Mouse strains          | LCA Blood flow changes to control, % | RCA Blood flow changes to control, % |
|------------------------|-------------------------------------|-------------------------------------|
| 129X1/SvJ, 129X1       | -82 ± 4                             | 64 ± 13                             |
| A/J, A                 | -80 ± 10                            | 83 ± 36                             |
| AKR/J, AKR             | -80 ± 2                             | 92 ± 18                             |
| BALB/cJ, BALB          | -82 ± 6                             | 57 ± 35                             |
| BTBR T+ Itpr3f/J, BTBRT| -86 ± 8                             | 87 ± 15                             |
| BUB/BnJ, BUB           | -92 ± 3                             | 12 ± 15                             |
| C3H/HeJ, C3H           | -79 ± 0                             | 78 ± 24                             |
| C3HeB/FeJ, C3HEB       | -82 ± 3                             | 155 ± 15                            |
| C57BL/6J, C57BL        | -89 ± 2                             | 80 ± 8                              |
| C57L/J, C57L           | -88 ± 5                             | 35 ± 16                             |
| C58/J, C58             | -93 ± 2                             | -13 ± 8                             |
| CBA/J, CBA             | -90 ± 4                             | 74 ± 4                              |
| CE/J, CE               | -85 ± 4                             | 81 ± 0                              |
| DBA/2J, DBA            | -80 ± 3                             | 59 ± 2                              |
| FVB/NJ, FVB            | -79 ± 3                             | 64 ± 13                             |
| I/LnJ, ILN             | -93 ± 2                             | 103 ± 19                            |
| KK/HIJ, KK             | -95 ± 0                             | 1 ± 16                              |
| LG/J, LG               | -72 ± 4                             | 69 ± 18                             |
| LP/J, LP               | -92 ± 1                             | 58 ± 12                             |
| MA/MyJ, MA             | -82 ± 7                             | 180 ± 4                             |
| NOD/LtJ, NOD           | -87 ± 5                             | 20 ± 4                              |
| NON/LtJ, NON           | -73 ± 8                             | 72 ± 15                             |
| NZB/B1NJ, NZB          | -88 ± 2                             | 78 ± 28                             |
| NZW/LacJ, NZW          | -87 ± 3                             | 53 ± 9                              |
| PL/J, PL               | -87 ± 0                             | 46 ± 32                             |
| RIIIS/J, RIIIS         | -95 ± 1                             | 72 ± 15                             |
| SEA/GnJ, SEA           | -93 ± 1                             | 66 ± 3                              |
| SJL/J, SJL             | -82 ± 10                            | 26 ± 13                             |
| SM/J, SM               | -97 ± 1                             | 58 ± 28                             |
| SWR/J, SWR             | -90 ± 1                             | -2 ± 21                             |

LCA, left carotid artery. RCA, right carotid artery.
Table S2. Significant SNPs associated with LCA intima volume in 30 inbred mouse strains.

| dbSNP      | Chromosome | Position, bp | p-value   | Effect size |
|------------|------------|--------------|-----------|-------------|
| rs38940843 | 6          | 101397279    | 8.84E-16  | 11.8286     |
| rs39087800 | 6          | 101412875    | 8.84E-16  | 11.8286     |
| rs47480301 | 16         | 71716616     | 7.98E-10  | 11.0697     |
| rs48569540 | 12         | 98832072     | 1.36E-08  | 11.1906     |
| rs27831183 | 4          | 43542462     | 5.19E-08  | 9.69708     |
| rs28320686 | 4          | 43620641     | 5.19E-08  | 9.69708     |
| rs28320653 | 4          | 43645470     | 5.19E-08  | 9.69708     |
| rs28320604 | 4          | 43650523     | 5.19E-08  | 9.69708     |
| rs28320543 | 4          | 43662649     | 5.19E-08  | 9.69708     |
| rs28320511 | 4          | 43688855     | 5.19E-08  | 9.69708     |
| rs28311534 | 4          | 43732460     | 5.19E-08  | 9.69708     |
| rs36294984 | 12         | 102175044    | 5.43E-08  | 9.67966     |
| rs36281276 | 12         | 102181524    | 5.43E-08  | 9.67966     |
| rs36677986 | 1          | 165121248    | 5.59E-08  | 9.66759     |
| rs37370522 | 1          | 165124350    | 5.59E-08  | 9.66759     |
| rs38372684 | 1          | 165124376    | 5.59E-08  | 9.66759     |
| rs47497019 | 16         | 70626697     | 1.36E-07  | 10.6743     |
| rs39750878 | 19         | 3995639      | 2.04E-07  | 10.2718     |
| rs37877606 | 19         | 4003976      | 2.04E-07  | 10.2718     |
| rs51910283 | 14         | 113914779    | 2.10E-07  | 10.28       |
| rs37621976 | 14         | 114273384    | 2.10E-07  | 10.28       |
| rs47106961 | 14         | 114918729    | 2.10E-07  | 10.28       |
| rs46464669 | 14         | 114921628    | 2.10E-07  | 10.28       |
| rs45841162 | 14         | 115030414    | 2.10E-07  | 10.28       |
| rs27605802 | 2          | 171299100    | 3.00E-07  | 10.2073     |
| rs50433974 | 13         | 60669054     | 3.65E-07  | 9.20322     |
| rs47419227 | 16         | 72782312     | 3.93E-07  | 9.25304     |
| rs48298153 | 16         | 72788432     | 3.93E-07  | 9.25304     |
| rs48931505 | 16         | 72788858     | 3.93E-07  | 9.25304     |
| rs48184804 | 16         | 72788906     | 3.93E-07  | 9.25304     |
| rs47318646 | 16         | 72789323     | 3.93E-07  | 9.25304     |
| rs37071291 | 6          | 100325877    | 4.59E-07  | 10.5823     |
| SNP          | N | Position      | P-value     | OR       |
|--------------|---|---------------|-------------|----------|
| rs36697249   | 1 | 165125538     | 4.83E-07    | 9.20222  |
| rs36283974   | 6 | 101145567     | 1.40E-06    | 10.5364  |
| rs37705272   | 6 | 101418487     | 1.43E-06    | 10.3656  |
| rs4203146    | 16| 73624179      | 1.50E-06    | 8.80081  |
| rs4203158    | 16| 73626715      | 1.50E-06    | 8.80081  |
| rs4203159    | 16| 73627098      | 1.50E-06    | 8.80081  |
| rs49791987   | 16| 73634287      | 1.50E-06    | 8.80081  |
| rs4203186    | 16| 73637376      | 1.50E-06    | 8.80081  |
| rs4203509    | 16| 73865267      | 1.50E-06    | 8.80081  |
| rs4203550    | 16| 73885132      | 1.50E-06    | 8.80081  |
| rs4303146    | 16| 73769593      | 2.16E-06    | 8.60563  |
| rs49296290   | 1 | 164345397     | 2.50E-06    | 9.5115   |
| rs27916937   | 2 | 48877169      | 2.92E-06    | 9.61417  |
| rs27918756   | 2 | 49953267      | 2.92E-06    | 9.61417  |
| rs27918720   | 2 | 49959001      | 2.92E-06    | 9.61417  |
| rs27918614   | 2 | 50000652      | 2.92E-06    | 9.61417  |
| rs27918554   | 2 | 50032628      | 2.92E-06    | 9.61417  |
| rs27918534   | 2 | 50044326      | 2.92E-06    | 9.61417  |
| rs49704766   | 2 | 50285472      | 2.92E-06    | 9.61417  |
| rs28295363   | 2 | 50858835      | 2.92E-06    | 9.61417  |
| rs28295360   | 2 | 50859030      | 2.92E-06    | 9.61417  |
| rs27930813   | 2 | 50956084      | 2.92E-06    | 9.61417  |
| rs27602702   | 2 | 170907558     | 2.92E-06    | 9.61417  |
| rs47868731   | 14| 115246865     | 3.12E-06    | 9.67611  |
| rs49720353   | 14| 115417489     | 3.12E-06    | 9.67611  |
| rs46884614   | 14| 115579774     | 3.12E-06    | 9.67611  |
| rs51463268   | 14| 115580256     | 3.12E-06    | 9.67611  |
| rs30604832   | 14| 70561864      | 3.29E-06    | 9.2204   |
| Marker       | Chromosome | Position  | *p*-value  | log10(p) |
|-------------|------------|-----------|------------|----------|
| rs50052151  | 17         | 31594946  | 3.30E-06   | 9.64921  |
| rs49741305  | 17         | 31597321  | 3.30E-06   | 9.64921  |
| rs50385858  | 18         | 54841501  | 3.33E-06   | 9.61579  |
| rs37738336  | 18         | 78267254  | 3.33E-06   | 9.61579  |
| rs37234714  | 18         | 78267687  | 3.33E-06   | 9.61579  |
| rs37792462  | 18         | 78277154  | 3.33E-06   | 9.61579  |
| rs38103448  | 18         | 78466732  | 3.33E-06   | 9.61579  |
| rs36981969  | 18         | 78471727  | 3.33E-06   | 9.61579  |
| rs36387979  | 18         | 78471745  | 3.33E-06   | 9.61579  |
| rs38025680  | 18         | 78494820  | 3.33E-06   | 9.61579  |
| rs38606622  | 18         | 78558805  | 3.33E-06   | 9.61579  |
| rs38648125  | 18         | 79112446  | 3.33E-06   | 9.61579  |
| rs37191882  | 18         | 79120190  | 3.33E-06   | 9.61579  |
| rs36853173  | 18         | 79126472  | 3.33E-06   | 9.61579  |
| rs47705897  | 1          | 167745338  | 3.57E-06   | 8.94812  |
| rs48039498  | 1          | 167745486  | 3.57E-06   | 8.94812  |
| rs47739937  | 1          | 167745525  | 3.57E-06   | 8.94812  |
Table S3. Significant SNPs associated with LCA media volume in 30 inbred mouse strains.

| dbSNP    | Chromosome | Position, bp | p-value   | Effect size |
|----------|------------|--------------|-----------|-------------|
| rs4167895| 16         | 30058454     | 3.73E-06  | -9.53356    |
Table S4. Significant SNPs associated with LCA adventitia volume in 30 inbred mouse strains.

| dbSNP       | Chromosome | Position, bp | p-value    | Effect size |
|-------------|------------|--------------|------------|-------------|
| rs47073871  | 13         | 20636267     | 6.61E-08   | 12.1977     |
| rs26883269  | 11         | 36643969     | 1.35E-07   | 11.8225     |
| rs26883268  | 11         | 36644267     | 1.35E-07   | 11.8225     |
| rs6223990   | 11         | 36649077     | 1.35E-07   | 11.8225     |
| rs26883254  | 11         | 36657106     | 1.35E-07   | 11.8225     |
| rs26883252  | 11         | 36657385     | 1.35E-07   | 11.8225     |
| rs26883248  | 11         | 36658108     | 1.35E-07   | 11.8225     |
| rs26883247  | 11         | 36658209     | 1.35E-07   | 11.8225     |
| rs26883238  | 11         | 36660335     | 1.35E-07   | 11.8225     |
| rs26883211  | 11         | 36666657     | 1.35E-07   | 11.8225     |
| rs46269877  | 11         | 36667397     | 1.35E-07   | 11.8225     |
| rs50176409  | 11         | 36667580     | 1.35E-07   | 11.8225     |
| rs26883183  | 11         | 36676089     | 1.35E-07   | 11.8225     |
| rs26933638  | 11         | 36682571     | 1.35E-07   | 11.8225     |
| rs28212174  | 11         | 39241249     | 1.35E-07   | 11.8225     |
| rs36410510  | 19         | 11159100     | 1.43E-07   | 12.2065     |
| rs3678405   | 13         | 19913279     | 1.93E-07   | 11.8037     |
| rs29607886  | 13         | 21048396     | 2.82E-07   | 11.642      |
| rs36302909  | 13         | 38317257     | 3.09E-07   | 11.8565     |
| rs29600146  | 13         | 20855501     | 3.43E-07   | 12.0104     |
| rs31653947  | 15         | 25783771     | 4.07E-07   | 13.8686     |
| rs32023348  | 15         | 25789703     | 4.07E-07   | 13.8686     |
| rs36719773  | 15         | 25792839     | 4.07E-07   | 13.8686     |
| rs31876896  | 15         | 25793549     | 4.07E-07   | 13.8686     |
| rs36896622  | 13         | 19623895     | 4.81E-07   | 11.5772     |
| rs36608337  | 13         | 19631552     | 4.81E-07   | 11.5772     |
| rs36444549  | 13         | 19633288     | 4.81E-07   | 11.5772     |
| rs38251579  | 13         | 19691192     | 4.81E-07   | 11.5772     |
| rs36733180  | 13         | 19691255     | 4.81E-07   | 11.5772     |
| rs47114836  | 13         | 19722060     | 4.81E-07   | 11.5772     |
| rs36735954  | 13         | 19765425     | 4.81E-07   | 11.5772     |
| rs37428520  | 13         | 19767050     | 4.81E-07   | 11.5772     |
| rs          | Chromosome | Position   | p_value | Beta     |
|-------------|------------|------------|---------|----------|
| rs38026141  | 13         | 19820179   | 4.81E-07| 11.5772   |
| rs36661788  | 13         | 19821058   | 4.81E-07| 11.5772   |
| rs38303318  | 13         | 19821229   | 4.81E-07| 11.5772   |
| rs36594603  | 13         | 19822595   | 4.81E-07| 11.5772   |
| rs38318713  | 13         | 19823039   | 4.81E-07| 11.5772   |
| rs36391344  | 13         | 19902374   | 4.81E-07| 11.5772   |
| rs37799072  | 13         | 19974390   | 4.81E-07| 11.5772   |
| rs36781926  | 13         | 20013348   | 4.81E-07| 11.5772   |
| rs47829231  | 13         | 20013404   | 4.81E-07| 11.5772   |
| rs49358850  | 13         | 20024700   | 4.81E-07| 11.5772   |
| rs36640438  | 13         | 20068362   | 4.81E-07| 11.5772   |
| rs36487463  | 13         | 20076501   | 4.81E-07| 11.5772   |
| rs6297328   | 13         | 20119946   | 4.81E-07| 11.5772   |
| rs6299142   | 13         | 20179306   | 4.81E-07| 11.5772   |
| rs36690570  | 13         | 20186083   | 4.81E-07| 11.5772   |
| rs3678954   | 13         | 20188891   | 4.81E-07| 11.5772   |
| rs6248419   | 13         | 20205439   | 4.81E-07| 11.5772   |
| rs36600957  | 13         | 20254709   | 4.81E-07| 11.5772   |
| rs45982807  | 13         | 20301917   | 4.81E-07| 11.5772   |
| rs51047263  | 13         | 20312500   | 4.81E-07| 11.5772   |
| rs6203049   | 13         | 20315428   | 4.81E-07| 11.5772   |
| rs52320861  | 13         | 20322495   | 4.81E-07| 11.5772   |
| rs47549236  | 13         | 20365143   | 4.81E-07| 11.5772   |
| rs51484684  | 13         | 20371046   | 4.81E-07| 11.5772   |
| rsID         | Chromosome | Position | P_value | Log10(P) |
|--------------|------------|----------|---------|----------|
| rs48961319   | 13         | 20374137 | 4.81E-07 | 11.5772  |
| rs45651638   | 13         | 20379366 | 4.81E-07 | 11.5772  |
| rs46580187   | 13         | 20382923 | 4.81E-07 | 11.5772  |
| rs47760603   | 13         | 20414115 | 4.81E-07 | 11.5772  |
| rs47538017   | 13         | 20420858 | 4.81E-07 | 11.5772  |
| rs48892010   | 13         | 20421811 | 4.81E-07 | 11.5772  |
| rs48148404   | 13         | 20469092 | 4.81E-07 | 11.5772  |
| rs48951151   | 13         | 20471221 | 4.81E-07 | 11.5772  |
| rs49018822   | 13         | 20481493 | 4.81E-07 | 11.5772  |
| rs49995885   | 13         | 20511487 | 4.81E-07 | 11.5772  |
| rs48592377   | 13         | 20539128 | 4.81E-07 | 11.5772  |
| rs48864424   | 13         | 20552932 | 4.81E-07 | 11.5772  |
| rs48292864   | 13         | 20569654 | 4.81E-07 | 11.5772  |
| rs49769390   | 13         | 20571147 | 4.81E-07 | 11.5772  |
| rs6372032    | 13         | 20572873 | 4.81E-07 | 11.5772  |
| rs51129769   | 13         | 20575619 | 4.81E-07 | 11.5772  |
| rs47155818   | 13         | 20597561 | 4.81E-07 | 11.5772  |
| rs49531202   | 13         | 20608709 | 4.81E-07 | 11.5772  |
| rs46266953   | 13         | 20684736 | 4.81E-07 | 11.5772  |
| rs46868266   | 13         | 20685797 | 4.81E-07 | 11.5772  |
| rs50160653   | 13         | 20719255 | 4.81E-07 | 11.5772  |
| rs47901231   | 13         | 20744950 | 4.81E-07 | 11.5772  |
| rs33839559   | 13         | 20772091 | 4.81E-07 | 11.5772  |
| rs33840365   | 13         | 20772735 | 4.81E-07 | 11.5772  |
| rs33837937   | 13         | 20788119 | 4.81E-07 | 11.5772  |
| rs51945080   | 13         | 20812645 | 4.81E-07 | 11.5772  |
| rs46188139   | 13         | 20812888 | 4.81E-07 | 11.5772  |
| rs29594544   | 13         | 20859622 | 4.81E-07 | 11.5772  |
| rs29594550   | 13         | 20859808 | 4.81E-07 | 11.5772  |
| rs29597333   | 13         | 20882992 | 4.81E-07 | 11.5772  |
| rs29598246   | 13         | 20883087 | 4.81E-07 | 11.5772  |
| rs29593003   | 13         | 20894217 | 4.81E-07 | 11.5772  |
| rs29593889   | 13         | 20916452 | 4.81E-07 | 11.5772  |
| rs29604183   | 13         | 20991627 | 4.81E-07 | 11.5772  |
| rs29598075   | 13         | 20992544 | 4.81E-07 | 11.5772  |
| rs29606454   | 13         | 21000504 | 4.81E-07 | 11.5772  |
| rs          | Chromosome | Position | p-Value | Log10(p) |
|------------|------------|----------|---------|----------|
| rs29606460 | 13         | 21000754 | 4.81E-07 | 11.5772  |
| rs29607083 | 13         | 21048311 | 4.81E-07 | 11.5772  |
| rs29604312 | 13         | 21073825 | 4.81E-07 | 11.5772  |
| rs29607857 | 13         | 21132420 | 4.81E-07 | 11.5772  |
| rs29607860 | 13         | 21132455 | 4.81E-07 | 11.5772  |
| rs29609872 | 13         | 21141111 | 4.81E-07 | 11.5772  |
| rs29611566 | 13         | 21142121 | 4.81E-07 | 11.5772  |
| rs29610464 | 13         | 21164813 | 4.81E-07 | 11.5772  |
| rs6263463  | 13         | 21171748 | 4.81E-07 | 11.5772  |
| rs29638163 | 13         | 21223147 | 4.81E-07 | 11.5772  |
| rs29639114 | 13         | 21249985 | 4.81E-07 | 11.5772  |
| rs49949392 | 13         | 21261961 | 4.81E-07 | 11.5772  |
| rs29647362 | 13         | 21281847 | 4.81E-07 | 11.5772  |
| rs29641986 | 13         | 21292978 | 4.81E-07 | 11.5772  |
| rs29643897 | 13         | 21295276 | 4.81E-07 | 11.5772  |
| rs29646900 | 13         | 21298273 | 4.81E-07 | 11.5772  |
| rs29644942 | 13         | 21337054 | 4.81E-07 | 11.5772  |
| rs29645930 | 13         | 21357606 | 4.81E-07 | 11.5772  |
| rs29645533 | 13         | 21371512 | 4.81E-07 | 11.5772  |
| rs49062226 | 13         | 21372890 | 4.81E-07 | 11.5772  |
| rs29644278 | 13         | 21394529 | 4.81E-07 | 11.5772  |
| rs29648727 | 13         | 21430577 | 4.81E-07 | 11.5772  |
| rs29652368 | 13         | 21434110 | 4.81E-07 | 11.5772  |
| rs29653437 | 13         | 21465037 | 4.81E-07 | 11.5772  |
| rs29654897 | 13         | 21507746 | 4.81E-07 | 11.5772  |
| rs29649704 | 13         | 21522488 | 4.81E-07 | 11.5772  |
| rs29650319 | 13         | 21547080 | 4.81E-07 | 11.5772  |
| rs48094376 | 13         | 21558999 | 4.81E-07 | 11.5772  |
| rs46647627 | 13         | 21559343 | 4.81E-07 | 11.5772  |
| rs6355688  | 13         | 21566688 | 4.81E-07 | 11.5772  |
| rs6353554  | 13         | 21609738 | 4.81E-07 | 11.5772  |
| rs6354633  | 13         | 21609929 | 4.81E-07 | 11.5772  |
| rs29651488 | 13         | 21627510 | 4.81E-07 | 11.5772  |
| rs29657594 | 13         | 21658122 | 4.81E-07 | 11.5772  |
| rs29658436 | 13         | 21659208 | 4.81E-07 | 11.5772  |
| rs29655552 | 13         | 21676021 | 4.81E-07 | 11.5772  |
| SNP         | Chromosome | Position   | P-value   | Log10(p-value) |
|-------------|------------|------------|-----------|----------------|
| rs29652356  | 13         | 21700527   | 4.81E-07  | 11.5772        |
| rs29658054  | 13         | 21752519   | 4.81E-07  | 11.5772        |
| rs29652814  | 13         | 21758217   | 4.81E-07  | 11.5772        |
| rs47150906  | 13         | 52211251   | 4.81E-07  | 11.5772        |
| rs46309028  | 13         | 52211325   | 4.81E-07  | 11.5772        |
| rs48741080  | 13         | 20962352   | 7.16E-07  | 11.7107        |
| rs47509073  | 1          | 77255403   | 7.61E-07  | 11.7479        |
| rs32950486  | 1          | 777609490  | 7.61E-07  | 11.7479        |
| rs36872577  | 1          | 78067450   | 7.61E-07  | 11.7479        |
| rs6407549   | 1          | 78079879   | 7.61E-07  | 11.7479        |
| rs48353307  | 12         | 97613323   | 9.44E-07  | 11.641         |
| rs52231845  | 16         | 18838734   | 1.25E-06  | 12.1417        |
| rs4207614   | 16         | 77738835   | 1.26E-06  | 13.9067        |
| rs4207615   | 16         | 77738908   | 1.26E-06  | 13.9067        |
| rs48357981  | 16         | 77739452   | 1.26E-06  | 13.9067        |
| rs4207617   | 16         | 77744195   | 1.26E-06  | 13.9067        |
| rs48226387  | 16         | 77749862   | 1.26E-06  | 13.9067        |
| rs4207656   | 16         | 77773830   | 1.26E-06  | 13.9067        |
| rs4207659   | 16         | 77774195   | 1.26E-06  | 13.9067        |
| rs46962439  | 16         | 77795529   | 1.26E-06  | 13.9067        |
| rs4207710   | 16         | 77821575   | 1.26E-06  | 13.9067        |
| rs4207711   | 16         | 77823818   | 1.26E-06  | 13.9067        |
| rs4207712   | 16         | 77824526   | 1.26E-06  | 13.9067        |
| rs48139016  | 15         | 48841397   | 1.53E-06  | 11.976         |
| rs46494410  | 15         | 48856141   | 1.53E-06  | 11.976         |
| rs47208714  | 15         | 49205685   | 1.53E-06  | 11.976         |
| rs37217592  | 1          | 94081116   | 3.28E-06  | 11.5744        |
| rs36408043  | 1          | 94147963   | 3.28E-06  | 11.5744        |
| rs37952899  | 1          | 94169057   | 3.28E-06  | 11.5744        |
| rs31116994  | 14         | 68371424   | 3.74E-06  | 11.5098        |
Table S5. Significant SNPs associated with LCA EEL volume in 30 inbred mouse strains.

| dbSNP    | Chromosome | Position, bp | p-value    | Effect size |
|----------|------------|--------------|------------|-------------|
| rs32595130 | 9          | 44253578     | 5.08E-07   | 27.908      |
| rs32598526 | 9          | 44276639     | 5.08E-07   | 27.908      |
| rs49698155 | 15         | 27049944     | 1.66E-06   | 27.0288     |
| rs33417562 | 17         | 12417424     | 2.24E-06   | -27.0414    |
| rs31653947 | 15         | 25783771     | 3.12E-06   | 29.1715     |
| rs32023348 | 15         | 25789703     | 3.12E-06   | 29.1715     |
| rs36719773 | 15         | 25792839     | 3.12E-06   | 29.1715     |
| rs31876896 | 15         | 25793549     | 3.12E-06   | 29.1715     |
Table S6. Significant SNPs associated with LCA intima-to-media ratio in 30 inbred mouse strains.

| dbSNP     | Chromosome | Position, bp | p-value  | Effect size |
|-----------|------------|-------------|----------|-------------|
| rs27674148| 4          | 7102117     | 2.80E-13 | 0.211489    |
| rs27737825| 4          | 29648251    | 2.80E-13 | 0.211489    |
| rs36677986| 1          | 165121248   | 1.01E-12 | 0.204791    |
| rs37370522| 1          | 165124350   | 1.01E-12 | 0.204791    |
| rs38372684| 1          | 165124376   | 1.01E-12 | 0.204791    |
| rs36294984| 12         | 102175044   | 1.02E-12 | 0.204791    |
| rs36281276| 12         | 102181524   | 1.02E-12 | 0.204791    |
| rs27831183| 4          | 43542462    | 1.04E-12 | 0.20448     |
| rs28320686| 4          | 43620641    | 1.04E-12 | 0.20448     |
| rs28320653| 4          | 43645470    | 1.04E-12 | 0.20448     |
| rs28320604| 4          | 43650523    | 1.04E-12 | 0.20448     |
| rs28320543| 4          | 43662649    | 1.04E-12 | 0.20448     |
| rs28320511| 4          | 43688855    | 1.04E-12 | 0.20448     |
| rs28311534| 4          | 43732460    | 1.04E-12 | 0.20448     |
| rs38940843| 6          | 101397279   | 8.49E-11 | 0.206547    |
| rs39087800| 6          | 101412875   | 8.49E-11 | 0.206547    |
| rs50242724| 3          | 34405923    | 1.06E-10 | 0.200376    |
| rs47993102| 15         | 7033810     | 9.69E-10 | 0.19749     |
| rs27134887| 2          | 16236183    | 1.63E-09 | 0.193885    |
| rs27605802| 2          | 171299100   | 2.21E-09 | 0.206106    |
| rs36739925| 9          | 39493014    | 2.25E-09 | 0.194116    |
| rs32998299| 7          | 56915547    | 4.48E-09 | 0.199285    |
| rs46101910| 7          | 57451000    | 4.48E-09 | 0.199285    |
| rs38361786| 7          | 57470793    | 4.48E-09 | 0.199285    |
| rs27648232| 2          | 179835451   | 4.53E-09 | 0.199145    |
| rs27678709| 2          | 179869730   | 4.53E-09 | 0.199145    |
| rs36484548| 14         | 116035561   | 6.04E-09 | 0.199359    |
| rs37878104| 14         | 116035938   | 6.04E-09 | 0.199359    |
| rs36578717| 14         | 116935757   | 6.04E-09 | 0.199359    |
| rs50464390| 14         | 116263623   | 6.04E-09 | 0.199359    |
| rs36670143| 14         | 116349890   | 6.04E-09 | 0.199359    |
| rs38987302| 14         | 116417450   | 6.04E-09 | 0.199359    |
| rs47765000 | 14 | 117018624 | 6.04E-09 | 0.199359 |
| rs48764245 | 16 | 30572961 | 6.06E-09 | 0.200082 |
| rs48527511 | 16 | 30588279 | 6.06E-09 | 0.200082 |
| rs50991760 | 16 | 30619586 | 6.06E-09 | 0.200082 |
| rs37125075 | 18 | 68612691 | 6.30E-09 | 0.198834 |
| rs36597862 | 18 | 68685395 | 6.30E-09 | 0.198834 |
| rs47765000 | 14 | 117018624 | 6.04E-09 | 0.199359 |
| rs48764245 | 16 | 30572961 | 6.06E-09 | 0.200082 |
| rs48527511 | 16 | 30588279 | 6.06E-09 | 0.200082 |
| rs50991760 | 16 | 30619586 | 6.06E-09 | 0.200082 |
| rs37125075 | 18 | 68612691 | 6.30E-09 | 0.198834 |
| rs36597862 | 18 | 68685395 | 6.30E-09 | 0.198834 |
| rs27689045 | 4  | 7044109  | 6.32E-09 | 0.198671 |
| rs27673999 | 4  | 7137905  | 6.32E-09 | 0.198671 |
| rs27673998 | 4  | 7137926  | 6.32E-09 | 0.198671 |
| rs2765948  | 4  | 7170558  | 6.32E-09 | 0.198671 |
| rs27009097 | 4  | 7211496  | 6.32E-09 | 0.198671 |
| rs27709075 | 4  | 7213943  | 6.32E-09 | 0.198671 |
| rs27691238 | 4  | 7232617  | 6.32E-09 | 0.198671 |
| rs27687701 | 4  | 7583955  | 6.32E-09 | 0.198671 |
| rs27737810 | 4  | 29656779 | 6.32E-09 | 0.198671 |
| rs27737803 | 4  | 29677730 | 6.32E-09 | 0.198671 |
| rs27723164 | 4  | 29794635 | 6.32E-09 | 0.198671 |
| rs6237544  | 4  | 29795573 | 6.32E-09 | 0.198671 |
| rs27748033 | 4  | 29997199 | 6.32E-09 | 0.198671 |
| rs27786591 | 4  | 30541140 | 6.32E-09 | 0.198671 |
| rs27786545 | 4  | 30566381 | 6.32E-09 | 0.198671 |
| rs49665559 | 4  | 30804028 | 6.32E-09 | 0.198671 |
| rs27741284 | 4  | 31055741 | 6.32E-09 | 0.198671 |
| rs27612140 | 4  | 139882104 | 6.32E-09 | 0.198671 |
| rs27612099 | 4  | 139892826 | 6.32E-09 | 0.198671 |
| rs27552432 | 4  | 142064805 | 6.32E-09 | 0.198671 |
| rs27552330 | 4  | 142086314 | 6.32E-09 | 0.198671 |
| rs36240801 | 6  | 100082220 | 6.55E-09 | 0.199186 |
| rs27044336 | 11 | 118808786 | 8.12E-08 | 0.183893 |
| rs26996028 | 11 | 120310104 | 8.12E-08 | 0.183893 |
| rsID       | Position | Effect Size | P-value | Minor Allele Frequency |
|-----------|----------|-------------|---------|------------------------|
| rs31460283| 14       | 75499722    | 8.35E-07| 0.183679               |
| rs27657799| 4        | 7196977     | 8.37E-08| 0.183807               |
| rs32921099| 12       | 99458647    | 1.31E-07| 0.185488               |
| rs27567843| 4        | 13940935    | 1.71E-07| 0.187519               |
| rs33689626| 1        | 15534580    | 2.21E-07| 0.182525               |
| rs51833298| 12       | 11699402    | 2.60E-07| 0.180779               |
| rs45951608| 12       | 11699437    | 2.60E-07| 0.180779               |
| rs6218946 | 11       | 11900163    | 2.82E-07| 0.180494               |
| rs27029509| 11       | 11984383    | 2.82E-07| 0.180494               |
| rs50185419| 16       | 6892543     | 2.95E-07| 0.180757               |
| rs47397360| 17       | 14392836    | 3.48E-07| 0.181558               |
| rs31317930| 14       | 7370391     | 3.91E-07| 0.186536               |
| rs37071291| 6        | 10032588    | 3.95E-07| 0.198601               |
| rs46912210| 3        | 32213292    | 4.22E-07| 0.188115               |
| rs50599709| 3        | 32214276    | 4.22E-07| 0.188115               |
| rs51153728| 3        | 32214591    | 4.22E-07| 0.188115               |
| rs48838546| 10       | 11812215    | 4.86E-07| 0.177113               |
| rs36996707| 9        | 65937308    | 5.07E-07| 0.196914               |
| rs27079841| 2        | 4508832     | 5.62E-07| 0.179491               |
| rs27108869| 2        | 10254363    | 5.62E-07| 0.179491               |
| rs27163089| 2        | 14471057    | 5.62E-07| 0.179491               |
| rs27846958| 4        | 45447167    | 6.11E-07| 0.16913                |
| rs51350682| 17       | 48110423    | 6.68E-07| 0.178579               |
| rs27916937| 2        | 48877169    | 7.66E-07| 0.189528               |
| rs27918756| 2        | 49953267    | 7.66E-07| 0.189528               |
| rs27918720| 2        | 49959001    | 7.66E-07| 0.189528               |
| rs27918614| 2        | 50000652    | 7.66E-07| 0.189528               |
| rs27918554| 2        | 50032628    | 7.66E-07| 0.189528               |
| rs27918534| 2        | 50044326    | 7.66E-07| 0.189528               |
| rs49704766| 2        | 50285472    | 7.66E-07| 0.189528               |
| rs28295363| 2        | 50858835    | 7.66E-07| 0.189528               |
| rs28295360| 2        | 50859030    | 7.66E-07| 0.189528               |
| rs27930813| 2        | 50956084    | 7.66E-07| 0.189528               |
| rs27602702| 2        | 17090755    | 7.66E-07| 0.189528               |
| rs51654688| 14       | 74098899    | 8.28E-07| 0.168017               |
| rs36697249| 1        | 16512553    | 8.34E-07| 0.168486               |
| SNP          | Chro | Pos   | p-value | q-value |
|--------------|------|-------|---------|---------|
| rs47868731   | 14   | 115246865 | 8.56E-07 | 0.189731 |
| rs49720353   | 14   | 115417489 | 8.56E-07 | 0.189731 |
| rs46884614   | 14   | 115579774 | 8.56E-07 | 0.189731 |
| rs51463268   | 14   | 115580256 | 8.56E-07 | 0.189731 |
| rs50433974   | 13   | 60669054  | 9.01E-07 | 0.165023 |
| rs50052151   | 17   | 31594946  | 9.13E-07 | 0.189667 |
| rs49741305   | 17   | 31597321  | 9.13E-07 | 0.189667 |
| rs37738336   | 18   | 78267254  | 9.48E-07 | 0.188616 |
| rs37792462   | 18   | 78277154  | 9.48E-07 | 0.188616 |
| rs38103448   | 18   | 78466732  | 9.48E-07 | 0.188616 |
| rs36981969   | 18   | 78471727  | 9.48E-07 | 0.188616 |
| rs36387979   | 18   | 78471745  | 9.48E-07 | 0.188616 |
| rs38025680   | 18   | 78494820  | 9.48E-07 | 0.188616 |
| rs38606622   | 18   | 78558805  | 9.48E-07 | 0.188616 |
| rs38648125   | 18   | 79112446  | 9.48E-07 | 0.188616 |
| rs37191882   | 18   | 79120190  | 9.48E-07 | 0.188616 |
| rs36853173   | 18   | 79126472  | 9.48E-07 | 0.188616 |
| rs6227786    | 9    | 65041134  | 1.10E-06 | 0.193507 |
| rs50974505   | 14   | 113243033 | 1.48E-06 | 0.193465 |
| rs37713099   | 12   | 82598244  | 1.53E-06 | 0.170075 |
| rs51910283   | 14   | 113914779 | 1.93E-06 | 0.187818 |
| rs37621976   | 14   | 114273384 | 1.93E-06 | 0.187818 |
| rs47106961   | 14   | 114918729 | 1.93E-06 | 0.187818 |
| rs46464669   | 14   | 114921628 | 1.93E-06 | 0.187818 |
| rs45841162   | 14   | 115030414 | 1.93E-06 | 0.187818 |
| rs39750878   | 19   | 3995639   | 1.94E-06 | 0.187811 |
| rs37877606   | 19   | 4003976   | 1.94E-06 | 0.187881 |
| rs27064906   | 2    | 3745455   | 2.24E-06 | 0.187249 |
| rs27084059   | 2    | 3951933   | 2.24E-06 | 0.187249 |
| rs27084039   | 2    | 3973509   | 2.24E-06 | 0.187249 |
| rs27084038   | 2    | 3973614   | 2.24E-06 | 0.187249 |
| rs27083978   | 2    | 4015868   | 2.24E-06 | 0.187249 |
| rs27083970   | 2    | 4017538   | 2.24E-06 | 0.187249 |
| rs27120219   | 2    | 20380126  | 2.24E-06 | 0.187249 |
| rsID   | Genotype | Gene | Cyto | p-Value | p-Value_adjusted |
|--------|----------|------|------|---------|-----------------|
| rs27166088 | 2 | | | 2.24E-06 | 0.187249 |
| rs27151056 | 2 | | | 2.24E-06 | 0.187249 |
| rs27151005 | 2 | | | 2.24E-06 | 0.187249 |
| rs27135890 | 2 | | | 2.24E-06 | 0.187249 |
| rs27121261 | 2 | | | 2.24E-06 | 0.187249 |
| rs27133382 | 2 | | | 2.24E-06 | 0.187249 |
| rs27118422 | 2 | | | 2.24E-06 | 0.187249 |
| rs27151783 | 2 | | | 2.24E-06 | 0.187249 |
| rs27135890 | 2 | | | 2.24E-06 | 0.187249 |
| rs27121261 | 2 | | | 2.24E-06 | 0.187249 |
| rs27133382 | 2 | | | 2.24E-06 | 0.187249 |
| rs27151783 | 2 | | | 2.24E-06 | 0.187249 |
| rs27135890 | 2 | | | 2.24E-06 | 0.187249 |
| rs27121261 | 2 | | | 2.24E-06 | 0.187249 |
| rs27133382 | 2 | | | 2.24E-06 | 0.187249 |
| SNP            | A1 | Position  | P-value  | OR       |
|----------------|----|-----------|----------|----------|
| rs27213269     | 2  | 24447533  | 2.24E-06 | 0.187249 |
| rs27198390     | 2  | 24499434  | 2.24E-06 | 0.187249 |
| rs27932296     | 2  | 48832467  | 2.24E-06 | 0.187249 |
| rs6187921      | 2  | 48887353  | 2.24E-06 | 0.187249 |
| rs27916902     | 2  | 48894879  | 2.24E-06 | 0.187249 |
| rs27916900     | 2  | 48895865  | 2.24E-06 | 0.187249 |
| rs27916849     | 2  | 48913139  | 2.24E-06 | 0.187249 |
| rs27916844     | 2  | 48926474  | 2.24E-06 | 0.187249 |
| rs27916833     | 2  | 48930698  | 2.24E-06 | 0.187249 |
| rs27901449     | 2  | 49138884  | 2.24E-06 | 0.187249 |
| rs27955117     | 2  | 49204203  | 2.24E-06 | 0.187249 |
| rs27917423     | 2  | 49405162  | 2.24E-06 | 0.187249 |
| rs27917345     | 2  | 49427912  | 2.24E-06 | 0.187249 |
| rs27935023     | 2  | 49687605  | 2.24E-06 | 0.187249 |
| rs27919660     | 2  | 49695214  | 2.24E-06 | 0.187249 |
| rs27919621     | 2  | 49700389  | 2.24E-06 | 0.187249 |
| rs27919611     | 2  | 49702655  | 2.24E-06 | 0.187249 |
| rs27919469     | 2  | 49750464  | 2.24E-06 | 0.187249 |
| rs27919455     | 2  | 49752446  | 2.24E-06 | 0.187249 |
| rs27919453     | 2  | 49753024  | 2.24E-06 | 0.187249 |
| rs27919449     | 2  | 49753604  | 2.24E-06 | 0.187249 |
| rs27904302     | 2  | 49810939  | 2.24E-06 | 0.187249 |
| rs27904273     | 2  | 49815489  | 2.24E-06 | 0.187249 |
| rs27933693     | 2  | 49910566  | 2.24E-06 | 0.187249 |
| rs27918516     | 2  | 50053612  | 2.24E-06 | 0.187249 |
| rs27918484     | 2  | 50091904  | 2.24E-06 | 0.187249 |
| rs27903090     | 2  | 50115233  | 2.24E-06 | 0.187249 |
| rs27953609     | 2  | 50193174  | 2.24E-06 | 0.187249 |
| rs48978839     | 2  | 50206898  | 2.24E-06 | 0.187249 |
| rs27931271     | 2  | 50264371  | 2.24E-06 | 0.187249 |
| rs27931240     | 2  | 50275403  | 2.24E-06 | 0.187249 |
| rs27916657     | 2  | 50348144  | 2.24E-06 | 0.187249 |
| rs27916616     | 2  | 50395652  | 2.24E-06 | 0.187249 |
| rs28312297     | 2  | 50777209  | 2.24E-06 | 0.187249 |
| rs28312138     | 2  | 50822178  | 2.24E-06 | 0.187249 |
| rs27899866     | 2  | 51042318  | 2.24E-06 | 0.187249 |
| SNP          | Genomic Position | P-Value   | q-Value  |
|--------------|------------------|-----------|----------|
| rs27899685   | 51068226         | 2.24E-06  | 0.187249 |
| rs27899164   | 52516936         | 2.24E-06  | 0.187249 |
| rs27899159   | 52517632         | 2.24E-06  | 0.187249 |
| rs27898972   | 52583478         | 2.24E-06  | 0.187249 |
| rs27945850   | 52588879         | 2.24E-06  | 0.187249 |
| rs27602656   | 170911813        | 2.24E-06  | 0.187249 |
| rs27602655   | 170911854        | 2.24E-06  | 0.187249 |
| rs27605849   | 171288259        | 2.24E-06  | 0.187249 |
| rs27605801   | 171299137        | 2.24E-06  | 0.187249 |
| rs27899164   | 52588879         | 2.24E-06  | 0.187249 |
| rs27899159   | 171288259        | 2.24E-06  | 0.187249 |
| rs27898972   | 171299137        | 2.24E-06  | 0.187249 |
| rs27602656   | 171288259        | 2.24E-06  | 0.187249 |
| rs27602655   | 171299137        | 2.24E-06  | 0.187249 |
| rs27605849   | 171345147        | 2.24E-06  | 0.187249 |
| rs27605801   | 171421492        | 2.24E-06  | 0.187249 |
| rs27899164   | 171421492        | 2.24E-06  | 0.187249 |
| rs27899159   | 171421807        | 2.24E-06  | 0.187249 |
| rs27898972   | 171423211        | 2.24E-06  | 0.187249 |
| rs27602656   | 171587184        | 2.24E-06  | 0.187249 |
| rs27602655   | 171612393        | 2.24E-06  | 0.187249 |
| rs27605849   | 171867408        | 2.24E-06  | 0.187249 |
| rs27605801   | 171895272        | 2.24E-06  | 0.187249 |
| rs27601303   | 171900522        | 2.24E-06  | 0.187249 |
| rs6379063    | 171953354        | 2.24E-06  | 0.187249 |
| rs2789141    | 171957502        | 2.24E-06  | 0.187249 |
| rs27327681   | 172016660        | 2.24E-06  | 0.187249 |
| rs27327581   | 172035600        | 2.24E-06  | 0.187249 |
| rs27617172   | 172162814        | 2.24E-06  | 0.187249 |
| rs27617048   | 172193718        | 2.24E-06  | 0.187249 |
| rs27617043   | 172194058        | 2.24E-06  | 0.187249 |
| rs27617042   | 172194145        | 2.24E-06  | 0.187249 |
| rs27617009   | 172197172        | 2.24E-06  | 0.187249 |
| rs27616998   | 172197766        | 2.24E-06  | 0.187249 |
| rs27616990   | 172202866        | 2.24E-06  | 0.187249 |
| rs27616988   | 172203604        | 2.24E-06  | 0.187249 |
| rs27600924   | 172267919        | 2.24E-06  | 0.187249 |
| rs27600896   | 172271313        | 2.24E-06  | 0.187249 |
| rs27600843   | 172288410        | 2.24E-06  | 0.187249 |
| rs27629692   | 172343902        | 2.24E-06  | 0.187249 |
| rs27629663   | 172359439        | 2.24E-06  | 0.187249 |
| rs27629657   | 172361480        | 2.24E-06  | 0.187249 |
| rs27615007 | 2 | 172420022 | 2.24E-06 | 0.187249 |
| rs27631754 | 2 | 172527860 | 2.24E-06 | 0.187249 |
| rs27631730 | 2 | 172532334 | 2.24E-06 | 0.187249 |
| rs27616315 | 2 | 172577536 | 2.24E-06 | 0.187249 |
| rs27620456 | 2 | 172708097 | 2.24E-06 | 0.187249 |
| rs27622582 | 2 | 172911393 | 2.24E-06 | 0.187249 |
| rs27646790 | 2 | 173124920 | 2.24E-06 | 0.187249 |
| rs27646752 | 2 | 173130347 | 2.24E-06 | 0.187249 |
| rs27630129 | 2 | 173150912 | 2.24E-06 | 0.187249 |
| rs27630122 | 2 | 173152574 | 2.24E-06 | 0.187249 |
| rs37182992 | 6 | 100262813 | 2.30E-06 | 0.186851 |
| rs37851939 | 6 | 100334161 | 2.30E-06 | 0.186851 |
| rs37159729 | 6 | 100457929 | 2.30E-06 | 0.186851 |
| rs37130761 | 6 | 100458485 | 2.30E-06 | 0.186851 |
| rs37509694 | 6 | 100488096 | 2.30E-06 | 0.186851 |
| rs36768945 | 6 | 100496446 | 2.30E-06 | 0.186851 |
| rs46220858 | 6 | 100551518 | 2.30E-06 | 0.186851 |
| rs37331742 | 6 | 100603283 | 2.30E-06 | 0.186851 |
| rs37599571 | 6 | 100615633 | 2.30E-06 | 0.186851 |
| rs37485021 | 6 | 100670349 | 2.30E-06 | 0.186851 |
| rs37835999 | 6 | 100710282 | 2.30E-06 | 0.186851 |
| rs36356436 | 6 | 100746705 | 2.30E-06 | 0.186851 |
| rs37523399 | 6 | 100758372 | 2.30E-06 | 0.186851 |
| rs38859161 | 6 | 101264457 | 2.30E-06 | 0.186851 |
| rs37305906 | 6 | 101339233 | 2.30E-06 | 0.186851 |
| rs37259471 | 6 | 101397480 | 2.30E-06 | 0.186851 |
| rs47196097 | 6 | 101509287 | 2.30E-06 | 0.186851 |
| rs47252577 | 6 | 101517832 | 2.30E-06 | 0.186851 |
| rs46129572 | 6 | 101521121 | 2.30E-06 | 0.186851 |
| rs51950730 | 6 | 101582836 | 2.30E-06 | 0.186851 |
| rs48786028 | 6 | 101583288 | 2.30E-06 | 0.186851 |
| rs51991104 | 6 | 101596254 | 2.30E-06 | 0.186851 |
| rs47472468 | 6 | 101596973 | 2.30E-06 | 0.186851 |
| rs49181543 | 6 | 101651784 | 2.30E-06 | 0.186851 |
| rs47773375 | 6 | 101777451 | 2.30E-06 | 0.186851 |
| SNP          | Chr | Position      | P-Value   | Effect Size |
|--------------|-----|---------------|-----------|-------------|
| rs37165011   | 6   | 101892688     | 2.30E-06  | 0.186851    |
| rs37411844   | 6   | 101895559     | 2.30E-06  | 0.186851    |
| rs37333750   | 6   | 101903734     | 2.30E-06  | 0.186851    |
| rs38314964   | 6   | 101976927     | 2.30E-06  | 0.186851    |
| rs48770127   | 6   | 102282679     | 2.30E-06  | 0.186851    |
| rs47565150   | 6   | 102339659     | 2.30E-06  | 0.186851    |
| rs45970744   | 6   | 102359810     | 2.30E-06  | 0.186851    |
| rs50852732   | 6   | 102652778     | 2.30E-06  | 0.186851    |
| rs52231024   | 6   | 102652974     | 2.30E-06  | 0.186851    |
| rs46218148   | 6   | 102655850     | 2.30E-06  | 0.186851    |
| rs47526411   | 6   | 102730256     | 2.30E-06  | 0.186851    |
| rs31469826   | 6   | 115184005     | 2.30E-06  | 0.186851    |
| rs31477042   | 6   | 115207538     | 2.30E-06  | 0.186851    |
| rs31479875   | 6   | 115269652     | 2.30E-06  | 0.186851    |
| rs31481914   | 6   | 115306598     | 2.30E-06  | 0.186851    |
| rs49852072   | 6   | 115339814     | 2.30E-06  | 0.186851    |
| rs47764649   | 6   | 115340179     | 2.30E-06  | 0.186851    |
| rs51852708   | 6   | 115405435     | 2.30E-06  | 0.186851    |
| rs31487387   | 6   | 115618564     | 2.30E-06  | 0.186851    |
| rs31485615   | 6   | 115664788     | 2.30E-06  | 0.186851    |
| rs31506628   | 6   | 115833148     | 2.30E-06  | 0.186851    |
| rs31509720   | 6   | 115926256     | 2.30E-06  | 0.186851    |
| rs31533971   | 6   | 116235275     | 2.30E-06  | 0.186851    |
| rs31550603   | 6   | 116497408     | 2.30E-06  | 0.186851    |
| rs31788820   | 6   | 128252327     | 2.30E-06  | 0.186851    |
| rs31839496   | 6   | 128252565     | 2.30E-06  | 0.186851    |
| rs31793823   | 6   | 128264396     | 2.30E-06  | 0.186851    |
| rs31799547   | 6   | 128507555     | 2.30E-06  | 0.186851    |
| rs37150717   | 6   | 129338475     | 2.30E-06  | 0.186851    |
| rs37634542   | 6   | 129341584     | 2.30E-06  | 0.186851    |
| rs48795228   | 6   | 129554062     | 2.30E-06  | 0.186851    |
| rs36278193   | 6   | 143347253     | 2.30E-06  | 0.186851    |
| rs31304784   | 14  | 70904084      | 2.40E-06  | 0.190442    |
| Marker   | Chromosome | Position | p-value | Log10(p-value) | MAF | w2 | p2 | MAF2 | Log10(p2) |
|---------|------------|----------|---------|----------------|-----|----|----|------|-----------|
| rs32852280 | 9         | 64699010 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs32848652 | 9         | 64700955 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs32850571 | 9         | 64703662 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs6339767 | 9         | 64720436 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs32851366 | 9         | 64745203 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs32854298 | 9         | 64753457 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs32854300 | 9         | 64753572 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs32851032 | 9         | 64763876 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs51879675 | 9         | 64826513 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs32855198 | 9         | 64838249 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs32855202 | 9         | 64838339 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs32856006 | 9         | 64839052 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs32857452 | 9         | 64842744 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs32858227 | 9         | 64843175 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs32857683 | 9         | 64875411 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs32859362 | 9         | 64894357 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs32860865 | 9         | 64896280 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs32856871 | 9         | 64904515 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs32860754 | 9         | 64935162 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs32866194 | 9         | 64981655 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs32870970 | 9         | 65001832 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs46214676 | 9         | 65034247 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs6307648 | 9         | 65058108 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs32871788 | 9         | 65064210 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs32875097 | 9         | 65090563 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs51870844 | 9         | 65113799 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs48176760 | 9         | 65117923 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs32871114 | 9         | 65130317 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs32872948 | 9         | 65139321 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs32872950 | 9         | 65139367 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs32872922 | 9         | 65157954 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs32872036 | 9         | 65185410 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs32872040 | 9         | 65185481 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs32874104 | 9         | 65189192 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs32874112 | 9         | 65189958 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs32873338 | 9         | 65205501 | 2.42E-06 | 0.187219       |     |    |    |      |           |
| rs            | chrom | position   | p-value | log10(p-value) |
|---------------|-------|------------|---------|---------------|
| rs32875710    | 9     | 65218600   | 2.42E-06| 0.187219      |
| rs32875921    | 9     | 65227746   | 2.42E-06| 0.187219      |
| rs32871690    | 9     | 65234725   | 2.42E-06| 0.187219      |
| rs32873167    | 9     | 6526991    | 2.42E-06| 0.187219      |
| rs32876758    | 9     | 65260301   | 2.42E-06| 0.187219      |
| rs48809159    | 9     | 65341061   | 2.42E-06| 0.187219      |
| rs50645978    | 9     | 65341099   | 2.42E-06| 0.187219      |
| rs48414260    | 9     | 65341276   | 2.42E-06| 0.187219      |
| rs32880505    | 9     | 65396070   | 2.42E-06| 0.187219      |
| rs32881912    | 9     | 65398829   | 2.42E-06| 0.187219      |
| rs32883089    | 9     | 65401821   | 2.42E-06| 0.187219      |
| rs32883785    | 9     | 65402078   | 2.42E-06| 0.187219      |
| rs32886150    | 9     | 65410898   | 2.42E-06| 0.187219      |
| rs50184450    | 9     | 65470313   | 2.42E-06| 0.187219      |
| rs32885884    | 9     | 65475896   | 2.42E-06| 0.187219      |
| rs32887586    | 9     | 65477586   | 2.42E-06| 0.187219      |
| rs32883357    | 9     | 65484958   | 2.42E-06| 0.187219      |
| rs32889980    | 9     | 65491421   | 2.42E-06| 0.187219      |
| rs32890134    | 9     | 65514407   | 2.42E-06| 0.187219      |
| rs32890997    | 9     | 65515306   | 2.42E-06| 0.187219      |
| rs32890626    | 9     | 65561591   | 2.42E-06| 0.187219      |
| rs32892041    | 9     | 65564244   | 2.42E-06| 0.187219      |
| rs6232791     | 9     | 65575074   | 2.42E-06| 0.187219      |
| rs6247483     | 9     | 65575452   | 2.42E-06| 0.187219      |
| rs32894226    | 9     | 65619024   | 2.42E-06| 0.187219      |
| rs24885773    | 9     | 65634022   | 2.42E-06| 0.187219      |
| rs24884254    | 9     | 65640186   | 2.42E-06| 0.187219      |
| rs32896801    | 9     | 65661916   | 2.42E-06| 0.187219      |
| rs32894204    | 9     | 65667987   | 2.42E-06| 0.187219      |
| rs32895646    | 9     | 65673528   | 2.42E-06| 0.187219      |
| rs32900421    | 9     | 65710462   | 2.42E-06| 0.187219      |
| rs32897212    | 9     | 65722044   | 2.42E-06| 0.187219      |
| rs24884041    | 9     | 65732034   | 2.42E-06| 0.187219      |
| rs24884037    | 9     | 65760237   | 2.42E-06| 0.187219      |
| rs24884115    | 9     | 65762099   | 2.42E-06| 0.187219      |
| rs24884112    | 9     | 65763237   | 2.42E-06| 0.187219      |
| rs24884060 | 9 | 65816633 | 2.42E-06 | 0.187219 |
| rs24884053 | 9 | 65821735 | 2.42E-06 | 0.187219 |
| rs48708836 | 9 | 65873512 | 2.42E-06 | 0.187219 |
| rs46376427 | 9 | 65890664 | 2.42E-06 | 0.187219 |
| rs49301527 | 9 | 65896382 | 2.42E-06 | 0.187219 |
| rs6334245  | 9 | 65963822 | 2.42E-06 | 0.187219 |
| rs6334314  | 9 | 65963869 | 2.42E-06 | 0.187219 |
| rs36633306 | 9 | 65968509 | 2.42E-06 | 0.187219 |
| rs36763036 | 9 | 65969370 | 2.42E-06 | 0.187219 |
| rs37278900 | 9 | 66020606 | 2.42E-06 | 0.187219 |
| rs38157230 | 9 | 66030932 | 2.42E-06 | 0.187219 |
| rs36734976 | 9 | 66048735 | 2.42E-06 | 0.187219 |
| rs37581780 | 9 | 66082002 | 2.42E-06 | 0.187219 |
| rs36661510 | 9 | 66087589 | 2.42E-06 | 0.187219 |
| rs36924121 | 9 | 66100085 | 2.42E-06 | 0.187219 |
| rs37023011 | 9 | 66101034 | 2.42E-06 | 0.187219 |
| rs63790901 | 9 | 66116329 | 2.42E-06 | 0.187219 |
| rs48184290 | 9 | 66134887 | 2.42E-06 | 0.187219 |
| rs24885776 | 9 | 66139020 | 2.42E-06 | 0.187219 |
| rs36661307 | 9 | 66173381 | 2.42E-06 | 0.187219 |
| rs39679507 | 9 | 66173485 | 2.42E-06 | 0.187219 |
| rs38375545 | 9 | 66177635 | 2.42E-06 | 0.187219 |
| rs37119462 | 9 | 66181805 | 2.42E-06 | 0.187219 |
| rs36617605 | 9 | 66196460 | 2.42E-06 | 0.187219 |
| rs36970576 | 9 | 66213444 | 2.42E-06 | 0.187219 |
| rs36329340 | 9 | 66224405 | 2.42E-06 | 0.187219 |
| rs6340549  | 9 | 66225900 | 2.42E-06 | 0.187219 |
| rs37270612 | 9 | 66261184 | 2.42E-06 | 0.187219 |
| rs36554703 | 9 | 66275014 | 2.42E-06 | 0.187219 |
| rs50129629 | 9 | 66305937 | 2.42E-06 | 0.187219 |
| rs48524343 | 9 | 66306657 | 2.42E-06 | 0.187219 |
| rs6362034  | 9 | 66348426 | 2.42E-06 | 0.187219 |
| rs6172573  | 9 | 66352312 | 2.42E-06 | 0.187219 |
| rs50430893 | 9 | 66365122 | 2.42E-06 | 0.187219 |
| rs46755430 | 9 | 66380486 | 2.42E-06 | 0.187219 |
| rs48325416 | 9 | 66383060 | 2.42E-06 | 0.187219 |
| rs          | Chrm | Pos      | p-value | Minor Allele Frequency |
|-------------|------|----------|---------|------------------------|
| rs50177983  | 9    | 66400613 | 2.42E-06 | 0.187219               |
| rs49605255  | 9    | 66406179 | 2.42E-06 | 0.187219               |
| rs52554987  | 9    | 66418314 | 2.42E-06 | 0.187219               |
| rs47353345  | 9    | 66439796 | 2.42E-06 | 0.187219               |
| rs46217906  | 9    | 66469229 | 2.42E-06 | 0.187219               |
| rs51183659  | 9    | 66469243 | 2.42E-06 | 0.187219               |
| rs46584626  | 9    | 66490398 | 2.42E-06 | 0.187219               |
| rs6362722   | 9    | 66507267 | 2.42E-06 | 0.187219               |
| rs6169928   | 9    | 66517104 | 2.42E-06 | 0.187219               |
| rs38022936  | 9    | 66540233 | 2.42E-06 | 0.187219               |
| rs36930708  | 9    | 66540328 | 2.42E-06 | 0.187219               |
| rs36418824  | 9    | 66540567 | 2.42E-06 | 0.187219               |
| rs46349242  | 9    | 66555842 | 2.42E-06 | 0.187219               |
| rs36536487  | 9    | 66560034 | 2.42E-06 | 0.187219               |
| rs37158762  | 9    | 66570343 | 2.42E-06 | 0.187219               |
| rs37051185  | 9    | 66581054 | 2.42E-06 | 0.187219               |
| rs37139390  | 9    | 66581658 | 2.42E-06 | 0.187219               |
| rs36614623  | 9    | 66602994 | 2.42E-06 | 0.187219               |
| rs37235617  | 9    | 66616750 | 2.42E-06 | 0.187219               |
| rs36608021  | 9    | 66630631 | 2.42E-06 | 0.187219               |
| rs36660038  | 9    | 66640455 | 2.42E-06 | 0.187219               |
| rs36783766  | 9    | 66641845 | 2.42E-06 | 0.187219               |
| rs49847984  | 9    | 66651704 | 2.42E-06 | 0.187219               |
| rs37624441  | 9    | 66657534 | 2.42E-06 | 0.187219               |
| rs37122966  | 9    | 66671871 | 2.42E-06 | 0.187219               |
| rs37021337  | 9    | 66673302 | 2.42E-06 | 0.187219               |
| rs48930973  | 9    | 66699226 | 2.42E-06 | 0.187219               |
| rs39298035  | 9    | 66724182 | 2.42E-06 | 0.187219               |
| rs36667140  | 9    | 66725166 | 2.42E-06 | 0.187219               |
| rs49596940  | 9    | 66802830 | 2.42E-06 | 0.187219               |
| rs39796135  | 9    | 66824421 | 2.42E-06 | 0.187219               |
| rs37673474  | 9    | 66839675 | 2.42E-06 | 0.187219               |
| rs6377151   | 9    | 66848263 | 2.42E-06 | 0.187219               |
| rs47793028  | 9    | 66858481 | 2.42E-06 | 0.187219               |
| rs49075721  | 9    | 66868958 | 2.42E-06 | 0.187219               |
| rs48326305  | 9    | 66872432 | 2.42E-06 | 0.187219               |
| rs              | Major Allele | Genotype Count | p-value | Minor Allele Count |
|-----------------|--------------|----------------|---------|--------------------|
| rs46080556      | 9            | 66876025       | 2.42E-06| 0.187219           |
| rs50136739      | 9            | 66876783       | 2.42E-06| 0.187219           |
| rs47800115      | 9            | 66884052       | 2.42E-06| 0.187219           |
| rs52485209      | 9            | 66902531       | 2.42E-06| 0.187219           |
| rs48523627      | 9            | 66924266       | 2.42E-06| 0.187219           |
| rs50650303      | 9            | 66927613       | 2.42E-06| 0.187219           |
| rs50840957      | 9            | 66941054       | 2.42E-06| 0.187219           |
| rs48578047      | 9            | 66964037       | 2.42E-06| 0.187219           |
| rs45660894      | 9            | 66965627       | 2.42E-06| 0.187219           |
| rs48048032      | 9            | 66990434       | 2.42E-06| 0.187219           |
| rs51039463      | 9            | 66994269       | 2.42E-06| 0.187219           |
| rs50397550      | 9            | 66994826       | 2.42E-06| 0.187219           |
| rs51360544      | 9            | 67004075       | 2.42E-06| 0.187219           |
| rs50881271      | 9            | 67015640       | 2.42E-06| 0.187219           |
| rs50447914      | 9            | 67055454       | 2.42E-06| 0.187219           |
| rs36407996      | 9            | 67081696       | 2.42E-06| 0.187219           |
| rs36406680      | 9            | 67120379       | 2.42E-06| 0.187219           |
| rs37730895      | 9            | 67198553       | 2.42E-06| 0.187219           |
| rs37171453      | 9            | 67213739       | 2.42E-06| 0.187219           |
| rs38653051      | 9            | 67215139       | 2.42E-06| 0.187219           |
| rs36959002      | 9            | 67223854       | 2.42E-06| 0.187219           |
| rs48407326      | 9            | 67240599       | 2.42E-06| 0.187219           |
| rs38024759      | 9            | 67247568       | 2.42E-06| 0.187219           |
| rs6389883       | 9            | 67256949       | 2.42E-06| 0.187219           |
| rs6179724       | 9            | 67259349       | 2.42E-06| 0.187219           |
| rs36301708      | 9            | 67298377       | 2.42E-06| 0.187219           |
| rs37598571      | 9            | 67299074       | 2.42E-06| 0.187219           |
| rs36684028      | 9            | 67324068       | 2.42E-06| 0.187219           |
| rs36786833      | 9            | 67325207       | 2.42E-06| 0.187219           |
| rs47421561      | 9            | 67362118       | 2.42E-06| 0.187219           |
| rs37370249      | 9            | 67363140       | 2.42E-06| 0.187219           |
| rs6381804       | 9            | 67366554       | 2.42E-06| 0.187219           |
| rs36337872      | 9            | 67368543       | 2.42E-06| 0.187219           |
| rs46461457      | 9            | 67380565       | 2.42E-06| 0.187219           |
| rs38234424      | 9            | 67384488       | 2.42E-06| 0.187219           |
| rs36281188      | 9            | 67386107       | 2.42E-06| 0.187219           |
| SNP       | Ch | bp   | P-value | MAF  |
|-----------|----|------|---------|------|
| rs36786965 | 9  | 67386283 | 2.42E-06 | 0.187219 |
| rs48276669 | 9  | 67431341 | 2.42E-06 | 0.187219 |
| rs47628064 | 9  | 67468927 | 2.42E-06 | 0.187219 |
| rs51589062 | 9  | 67474508 | 2.42E-06 | 0.187219 |
| rs50956561 | 9  | 67478226 | 2.42E-06 | 0.187219 |
| rs48804034 | 9  | 67528104 | 2.42E-06 | 0.187219 |
| rs45961172 | 9  | 67530287 | 2.42E-06 | 0.187219 |
| rs46393388 | 9  | 67543354 | 2.42E-06 | 0.187219 |
| rs46422899 | 9  | 67565248 | 2.42E-06 | 0.187219 |
| rs50939336 | 9  | 67565941 | 2.42E-06 | 0.187219 |
| rs48921695 | 9  | 67568312 | 2.42E-06 | 0.187219 |
| rs49219739 | 9  | 67597773 | 2.42E-06 | 0.187219 |
| rs46993452 | 9  | 67614457 | 2.42E-06 | 0.187219 |
| rs49029424 | 9  | 67621728 | 2.42E-06 | 0.187219 |
| rs50733633 | 9  | 67626228 | 2.42E-06 | 0.187219 |
| rs51293074 | 9  | 67653478 | 2.42E-06 | 0.187219 |
| rs51178860 | 9  | 67681851 | 2.42E-06 | 0.187219 |
| rs46762458 | 9  | 67685792 | 2.42E-06 | 0.187219 |
| rs46146118 | 9  | 67729263 | 2.42E-06 | 0.187219 |
| rs51975935 | 9  | 67750936 | 2.42E-06 | 0.187219 |
| rs50616476 | 9  | 67768793 | 2.42E-06 | 0.187219 |
| rs46196644 | 9  | 67770385 | 2.42E-06 | 0.187219 |
| rs47221881 | 9  | 67782164 | 2.42E-06 | 0.187219 |
| rs51516768 | 9  | 67825448 | 2.42E-06 | 0.187219 |
| rs37056690 | 9  | 67870379 | 2.42E-06 | 0.187219 |
| rs37515812 | 9  | 67877173 | 2.42E-06 | 0.187219 |
| rs6376979  | 9  | 67912645 | 2.42E-06 | 0.187219 |
| rs37483426 | 9  | 67920361 | 2.42E-06 | 0.187219 |
| rs37548819 | 9  | 67934006 | 2.42E-06 | 0.187219 |
| rs36398937 | 9  | 67940714 | 2.42E-06 | 0.187219 |
| rs49963291 | 9  | 67984424 | 2.42E-06 | 0.187219 |
| rs38851612 | 9  | 67989941 | 2.42E-06 | 0.187219 |
| rs36573305 | 9  | 68011350 | 2.42E-06 | 0.187219 |
| rs36412564 | 9  | 68015658 | 2.42E-06 | 0.187219 |
| rs52421902 | 9  | 68092334 | 2.42E-06 | 0.187219 |
| rs38365838 | 9  | 68113486 | 2.42E-06 | 0.187219 |
| SNP            | Chromosome | Position   | Effect Size | P-value  |
|----------------|------------|------------|-------------|----------|
| rs36893466     | 9          | 68114160   | 2.42E-06    | 0.187219 |
| rs39137551     | 9          | 68123570   | 2.42E-06    | 0.187219 |
| rs36860226     | 9          | 68130997   | 2.42E-06    | 0.187219 |
| rs36499040     | 9          | 68193156   | 2.42E-06    | 0.187219 |
| rs37299115     | 9          | 68201216   | 2.42E-06    | 0.187219 |
| rs36521496     | 9          | 68244865   | 2.42E-06    | 0.187219 |
| rs51788589     | 9          | 68267747   | 2.42E-06    | 0.187219 |
| rs46101141     | 9          | 68267961   | 2.42E-06    | 0.187219 |
| rs48247578     | 9          | 68287820   | 2.42E-06    | 0.187219 |
| rs49272507     | 9          | 68329208   | 2.42E-06    | 0.187219 |
| rs51890913     | 9          | 68329246   | 2.42E-06    | 0.187219 |
| rs32899324     | 1          | 37117183   | 2.48E-06    | 0.173227 |
| rs50852207     | 1          | 37183892   | 2.48E-06    | 0.173227 |
| rs27933562     | 2          | 49930373   | 2.48E-06    | 0.18925  |
| rs32783618     | 7          | 122433524  | 2.48E-06    | 0.188622 |
| rs38406333     | 7          | 122855517  | 2.48E-06    | 0.188622 |
| rs37453036     | 7          | 122860942  | 2.48E-06    | 0.188622 |
| rs36818312     | 7          | 122865367  | 2.48E-06    | 0.188622 |
| rs37087696     | 7          | 122900423  | 2.48E-06    | 0.188622 |
| rs32789419     | 7          | 123174641  | 2.48E-06    | 0.188622 |
| rs32787906     | 7          | 123185641  | 2.48E-06    | 0.188622 |
| rs32826698     | 7          | 123519724  | 2.48E-06    | 0.188622 |
| rs32826128     | 7          | 123527459  | 2.48E-06    | 0.188622 |
| rs32826436     | 7          | 123531710  | 2.48E-06    | 0.188622 |
| rs32829515     | 7          | 123565988  | 2.48E-06    | 0.188622 |
| rs36834890     | 7          | 123856680  | 2.48E-06    | 0.188622 |
| rs36294141     | 7          | 123902465  | 2.48E-06    | 0.188622 |
| rs50630266     | 17         | 23720072   | 2.52E-06    | 0.186879 |
| rs48611889     | 17         | 24285997   | 2.52E-06    | 0.186879 |
| rs50014732     | 17         | 24435639   | 2.52E-06    | 0.186879 |
| rs49461674     | 17         | 24483561   | 2.52E-06    | 0.186879 |
| rs50405353     | 17         | 24483574   | 2.52E-06    | 0.186879 |
| rs51675770     | 17         | 24495899   | 2.52E-06    | 0.186879 |
| rs47699973     | 17         | 24503673   | 2.52E-06    | 0.186879 |
| rs50226428     | 17         | 24535060   | 2.52E-06    | 0.186879 |
| rs48601304     | 17         | 24635864   | 2.52E-06    | 0.186879 |
| SNP          | Chromosome | Position   | p-value     | Manhattan Distance |
|--------------|------------|------------|-------------|--------------------|
| rs33782923   | 17         | 24899206   | 2.52E-06    | 0.186879           |
| rs33779096   | 17         | 24971323   | 2.52E-06    | 0.186879           |
| rs33802475   | 17         | 30492953   | 2.52E-06    | 0.186879           |
| rs50266335   | 17         | 30586877   | 2.52E-06    | 0.186879           |
| rs46547505   | 17         | 31084416   | 2.52E-06    | 0.186879           |
| rs46748440   | 17         | 31087109   | 2.52E-06    | 0.186879           |
| rs47438016   | 17         | 31487307   | 2.52E-06    | 0.186879           |
| rs47633451   | 17         | 31505852   | 2.52E-06    | 0.186879           |
| rs51775106   | 17         | 31548425   | 2.52E-06    | 0.186879           |
| rs49568236   | 17         | 31676037   | 2.52E-06    | 0.186879           |
| rs47184414   | 13         | 63671652   | 2.52E-06    | 0.176545           |
| rs50150006   | 13         | 63672826   | 2.52E-06    | 0.176545           |
| rs51457735   | 13         | 63843692   | 2.52E-06    | 0.176545           |
| rs50629131   | 13         | 64083663   | 2.52E-06    | 0.176545           |
| rs49040996   | 9          | 68306235   | 2.54E-06    | 0.189775           |
| rs36547346   | 3          | 143594304  | 2.60E-06    | 0.187495           |
| rs37049682   | 3          | 144088150  | 2.60E-06    | 0.187495           |
| rs37028917   | 3          | 144271879  | 2.60E-06    | 0.187495           |
| rs31122786   | 3          | 144451668  | 2.60E-06    | 0.187495           |
| rs31130591   | 3          | 144529580  | 2.60E-06    | 0.187495           |
| rs31132213   | 3          | 144530683  | 2.60E-06    | 0.187495           |
| rs49003163   | 16         | 11587678   | 2.61E-06    | 0.188633           |
| rs32380990   | 16         | 18826645   | 2.61E-06    | 0.188633           |
| rs36865528   | 14         | 70579191   | 2.63E-06    | 0.186997           |
| rs51203742   | 14         | 70611106   | 2.63E-06    | 0.186997           |
| rs51466029   | 14         | 70651811   | 2.63E-06    | 0.186997           |
| rs51037137   | 14         | 70723822   | 2.63E-06    | 0.186997           |
| rs31309663   | 14         | 70855222   | 2.63E-06    | 0.186997           |
| rs31298280   | 14         | 70907194   | 2.63E-06    | 0.186997           |
| rs31304978   | 14         | 70908593   | 2.63E-06    | 0.186997           |
| rs31297889   | 14         | 70933545   | 2.63E-06    | 0.186997           |
| rs31296879   | 14         | 70934602   | 2.63E-06    | 0.186997           |
| rs31293835   | 14         | 70974074   | 2.63E-06    | 0.186997           |
| rs31267930   | 14         | 71120652   | 2.63E-06    | 0.186997           |
| rs49092964   | 14         | 71364188   | 2.63E-06    | 0.186997           |
| rs31256901   | 14         | 71463651   | 2.63E-06    | 0.186997           |
| SNP         | Chromosome | Position   | P-value  | OR       |
|-------------|------------|------------|----------|----------|
| rs31214112  | 14         | 72014914   | 2.63E-06 | 0.186997 |
| rs31205096  | 14         | 72216874   | 2.63E-06 | 0.186997 |
| rs31173006  | 14         | 72368728   | 2.63E-06 | 0.186997 |
| rs31173036  | 14         | 72408668   | 2.63E-06 | 0.186997 |
| rs49250200  | 14         | 72580443   | 2.63E-06 | 0.186997 |
| rs48180495  | 14         | 72591169   | 2.63E-06 | 0.186997 |
| rs32591326  | 14         | 112970164  | 2.63E-06 | 0.186997 |
| rs32587188  | 14         | 113007007  | 2.63E-06 | 0.186997 |
| rs32587187  | 14         | 113007094  | 2.63E-06 | 0.186997 |
| rs32586383  | 14         | 113007200  | 2.63E-06 | 0.186997 |
| rs32586382  | 14         | 113007219  | 2.63E-06 | 0.186997 |
| rs32585642  | 14         | 113008061  | 2.63E-06 | 0.186997 |
| rs32590163  | 14         | 113055639  | 2.63E-06 | 0.186997 |
| rs32590162  | 14         | 113055754  | 2.63E-06 | 0.186997 |
| rs32590160  | 14         | 113056206  | 2.63E-06 | 0.186997 |
| rs32590159  | 14         | 113056500  | 2.63E-06 | 0.186997 |
| rs32584459  | 14         | 113120554  | 2.63E-06 | 0.186997 |
| rs32585422  | 14         | 113169948  | 2.63E-06 | 0.186997 |
| rs46443620  | 14         | 113298551  | 2.63E-06 | 0.186997 |
| rs45897207  | 14         | 113319523  | 2.63E-06 | 0.186997 |
| rs46656813  | 14         | 113400430  | 2.63E-06 | 0.186997 |
| rs46230773  | 14         | 113854086  | 2.63E-06 | 0.186997 |
| rs36946267  | 14         | 114306538  | 2.63E-06 | 0.186997 |
| rs37953083  | 14         | 114540082  | 2.63E-06 | 0.186997 |
| rs36802107  | 14         | 114636310  | 2.63E-06 | 0.186997 |
| rs49275031  | 14         | 114892919  | 2.63E-06 | 0.186997 |
| rs51178582  | 14         | 114917562  | 2.63E-06 | 0.186997 |
| rs47245173  | 14         | 114964311  | 2.63E-06 | 0.186997 |
| rs49571658  | 14         | 115294533  | 2.63E-06 | 0.186997 |
| rs37540045  | 14         | 115932244  | 2.63E-06 | 0.186997 |
| rs45636865  | 18         | 54850772   | 2.66E-06 | 0.186605 |
| rs38214383  | 18         | 61387563   | 2.66E-06 | 0.186605 |
| rs37024448  | 18         | 78265495   | 2.66E-06 | 0.186605 |
| rs36499872  | 18         | 78267384   | 2.66E-06 | 0.186605 |
| rs37174498  | 18         | 78284846   | 2.66E-06 | 0.186605 |
| rs36246283  | 18         | 78288093   | 2.66E-06 | 0.186605 |
| SNP          | Chromosome | Position | P-Value  | Minor Allele Frequency |
|-------------|------------|----------|----------|------------------------|
| rs38088637  | 18         | 78288249 | 2.66E-06 | 0.186605               |
| rs36958520  | 18         | 78515056 | 2.66E-06 | 0.186605               |
| rs38453406  | 18         | 78570136 | 2.66E-06 | 0.186605               |
| rs36812229  | 18         | 78573776 | 2.66E-06 | 0.186605               |
| rs36572546  | 18         | 78833976 | 2.66E-06 | 0.186605               |
| rs37059141  | 18         | 79133055 | 2.66E-06 | 0.186605               |
| rs36773308  | 18         | 79551436 | 2.66E-06 | 0.186605               |
| rs36979510  | 18         | 79580713 | 2.66E-06 | 0.186605               |
| rs37133203  | 18         | 79659832 | 2.66E-06 | 0.186605               |
| rs37159329  | 18         | 79799060 | 2.66E-06 | 0.186605               |
| rs37711686  | 18         | 79821159 | 2.66E-06 | 0.186605               |
| rs31788822  | 6          | 128252463| 2.72E-06 | 0.188208               |
| rs38517973  | 12         | 34390181 | 2.74E-06 | 0.18675                |
| rs50678858  | 12         | 40390604 | 2.74E-06 | 0.18675                |
| rs51417406  | 12         | 40433048 | 2.74E-06 | 0.18675                |
| rs48446038  | 12         | 40441515 | 2.74E-06 | 0.18675                |
| rs52004744  | 12         | 40442081 | 2.74E-06 | 0.18675                |
| rs47637586  | 12         | 40455711 | 2.74E-06 | 0.18675                |
| rs46688704  | 12         | 40460571 | 2.74E-06 | 0.18675                |
| rs51892410  | 12         | 40472185 | 2.74E-06 | 0.18675                |
| rs47617362  | 12         | 40485362 | 2.74E-06 | 0.18675                |
| rs49597178  | 12         | 40497717 | 2.74E-06 | 0.18675                |
| rs49408352  | 12         | 40512673 | 2.74E-06 | 0.18675                |
| rs51917699  | 12         | 40549995 | 2.74E-06 | 0.18675                |
| rs6406921   | 12         | 40551005 | 2.74E-06 | 0.18675                |
| rs6158770   | 12         | 40551021 | 2.74E-06 | 0.18675                |
| rs47044169  | 12         | 40613897 | 2.74E-06 | 0.18675                |
| rs48640898  | 12         | 40615533 | 2.74E-06 | 0.18675                |
| rs46265499  | 12         | 40624758 | 2.74E-06 | 0.18675                |
| rs51154266  | 12         | 40731979 | 2.74E-06 | 0.18675                |
| rs46863397  | 12         | 40766528 | 2.74E-06 | 0.18675                |
| rs48589483  | 12         | 40777836 | 2.74E-06 | 0.18675                |
| rs47155090  | 12         | 40816920 | 2.74E-06 | 0.18675                |
| rs46957913  | 12         | 41093470 | 2.74E-06 | 0.18675                |
| rs47860722  | 12         | 41100409 | 2.74E-06 | 0.18675                |
| rs52655445  | 12         | 41131066 | 2.74E-06 | 0.18675                |
| SNP           | Chrom | Position   | Log10 P  | q-value |
|---------------|-------|------------|----------|---------|
| rs50482991    | 12    | 41155385   | 2.74E-06 | 0.18675 |
| rs52641334    | 12    | 41171005   | 2.74E-06 | 0.18675 |
| rs48012314    | 12    | 41180082   | 2.74E-06 | 0.18675 |
| rs48169814    | 12    | 41186871   | 2.74E-06 | 0.18675 |
| rs49647331    | 12    | 41198993   | 2.74E-06 | 0.18675 |
| rs49802817    | 12    | 41208451   | 2.74E-06 | 0.18675 |
| rs47317447    | 12    | 41274173   | 2.74E-06 | 0.18675 |
| rs49859855    | 12    | 41315677   | 2.74E-06 | 0.18675 |
| rs47572612    | 12    | 41328983   | 2.74E-06 | 0.18675 |
| rs47705013    | 12    | 41556179   | 2.74E-06 | 0.18675 |
| rs47477177    | 12    | 41879056   | 2.74E-06 | 0.18675 |
| rs37392247    | 12    | 41912478   | 2.74E-06 | 0.18675 |
| rs38404497    | 12    | 42011536   | 2.74E-06 | 0.18675 |
| rs37488356    | 12    | 42206995   | 2.74E-06 | 0.18675 |
| rs39301134    | 12    | 42215044   | 2.74E-06 | 0.18675 |
| rs36649878    | 12    | 42218064   | 2.74E-06 | 0.18675 |
| rs37416213    | 12    | 42220729   | 2.74E-06 | 0.18675 |
| rs38056502    | 12    | 42261053   | 2.74E-06 | 0.18675 |
| rs37058868    | 12    | 42273041   | 2.74E-06 | 0.18675 |
| rs37950782    | 12    | 42275018   | 2.74E-06 | 0.18675 |
| rs52446866    | 12    | 42606401   | 2.74E-06 | 0.18675 |
| rs50556895    | 12    | 42811172   | 2.74E-06 | 0.18675 |
| rs49205249    | 12    | 43166382   | 2.74E-06 | 0.18675 |
| rs47243609    | 12    | 43475726   | 2.74E-06 | 0.18675 |
| rs47611098    | 12    | 43524402   | 2.74E-06 | 0.18675 |
| rs45875181    | 12    | 43547274   | 2.74E-06 | 0.18675 |
| rs46707868    | 12    | 43548849   | 2.74E-06 | 0.18675 |
| rs47031384    | 12    | 43606072   | 2.74E-06 | 0.18675 |
| rs47438399    | 12    | 43758566   | 2.74E-06 | 0.18675 |
| rs50445852    | 12    | 43820452   | 2.74E-06 | 0.18675 |
| rs49202778    | 12    | 43822368   | 2.74E-06 | 0.18675 |
| rs49482445    | 12    | 43822383   | 2.74E-06 | 0.18675 |
| rs48848535    | 12    | 43822550   | 2.74E-06 | 0.18675 |
| rs48997369    | 12    | 43862892   | 2.74E-06 | 0.18675 |
| rs47405685    | 12    | 43868356   | 2.74E-06 | 0.18675 |
| rs46744108    | 12    | 43940386   | 2.74E-06 | 0.18675 |
| rs             | Chr | Start | p-Value | MAF  |
|----------------|-----|-------|---------|------|
| rs46605173     | 12  | 43947883 | 2.74E-06 | 0.18675 |
| rs46701417     | 12  | 43948865 | 2.74E-06 | 0.18675 |
| rs46982381     | 12  | 43951257 | 2.74E-06 | 0.18675 |
| rs50193577     | 12  | 43999974 | 2.74E-06 | 0.18675 |
| rs50508021     | 12  | 44000379 | 2.74E-06 | 0.18675 |
| rs50382375     | 12  | 44001675 | 2.74E-06 | 0.18675 |
| rs49596358     | 12  | 44111764 | 2.74E-06 | 0.18675 |
| rs50897661     | 12  | 44116715 | 2.74E-06 | 0.18675 |
| rs49100471     | 12  | 44117467 | 2.74E-06 | 0.18675 |
| rs32099746     | 12  | 66651744 | 2.74E-06 | 0.18675 |
| rs32103889     | 12  | 66655570 | 2.74E-06 | 0.18675 |
| rs32105513     | 12  | 66657143 | 2.74E-06 | 0.18675 |
| rs32106376     | 12  | 66657163 | 2.74E-06 | 0.18675 |
| rs32103589     | 12  | 66659406 | 2.74E-06 | 0.18675 |
| rs32104856     | 12  | 66660259 | 2.74E-06 | 0.18675 |
| rs49854700     | 12  | 66765365 | 2.74E-06 | 0.18675 |
| rs32118287     | 12  | 66781304 | 2.74E-06 | 0.18675 |
| rs32124847     | 12  | 66828267 | 2.74E-06 | 0.18675 |
| rs32134439     | 12  | 66878270 | 2.74E-06 | 0.18675 |
| rs32135355     | 12  | 66878316 | 2.74E-06 | 0.18675 |
| rs32138767     | 12  | 66922108 | 2.74E-06 | 0.18675 |
| rs32136238     | 12  | 66949881 | 2.74E-06 | 0.18675 |
| rs32142893     | 12  | 66953539 | 2.74E-06 | 0.18675 |
| rs32145817     | 12  | 67040862 | 2.74E-06 | 0.18675 |
| rs32152920     | 12  | 67072386 | 2.74E-06 | 0.18675 |
| rs32167185     | 12  | 67142263 | 2.74E-06 | 0.18675 |
| rs32168474     | 12  | 67142909 | 2.74E-06 | 0.18675 |
| rs32177250     | 12  | 67169632 | 2.74E-06 | 0.18675 |
| rs32198994     | 12  | 67468744 | 2.74E-06 | 0.18675 |
| rs32199002     | 12  | 67468982 | 2.74E-06 | 0.18675 |
| rs46668322     | 12  | 68156344 | 2.74E-06 | 0.18675 |
| rs36371914     | 12  | 68334112 | 2.74E-06 | 0.18675 |
| rs36776748     | 12  | 68474862 | 2.74E-06 | 0.18675 |
| rs46555639     | 12  | 90056273 | 2.74E-06 | 0.18675 |
| rs47768273     | 12  | 92263340 | 2.74E-06 | 0.18675 |
| rs51645668     | 12  | 92961979 | 2.74E-06 | 0.18675 |
| rs27166134 | 2   | 20407398 | 2.82E-06 | 0.188845 |
| rs27184167 | 2   | 23662908 | 2.82E-06 | 0.188845 |
| rs38267918 | 5   | 131234070 | 2.83E-06 | 0.187513 |
| rs37837392 | 5   | 131238990 | 2.83E-06 | 0.187513 |
| rs37215995 | 5   | 131251642 | 2.83E-06 | 0.187513 |
| rs36989849 | 5   | 131371412 | 2.83E-06 | 0.187513 |
| rs37498312 | 5   | 131371431 | 2.83E-06 | 0.187513 |
| rs37355302 | 5   | 131375527 | 2.83E-06 | 0.187513 |
| rs37253900 | 5   | 131375972 | 2.83E-06 | 0.187513 |
| rs37100728 | 5   | 131400484 | 2.83E-06 | 0.187513 |
| rs36391382 | 5   | 131400832 | 2.83E-06 | 0.187513 |
| rs38388261 | 5   | 131403419 | 2.83E-06 | 0.187513 |
| rs31201166 | 14  | 72163050 | 2.84E-06 | 0.1891   |
| rs47865024 | 19  | 3125547 | 2.87E-06 | 0.186874 |
| rs37406791 | 19  | 3290669 | 2.87E-06 | 0.186874 |
| rs36463751 | 19  | 3430247 | 2.87E-06 | 0.186874 |
| rs36739976 | 19  | 3613434 | 2.87E-06 | 0.186874 |
| rs37552721 | 19  | 5168078 | 2.87E-06 | 0.186874 |
| rs37361176 | 19  | 5191219 | 2.87E-06 | 0.186874 |
| rs36396226 | 19  | 5193282 | 2.87E-06 | 0.186874 |
| rs37209662 | 19  | 5228289 | 2.87E-06 | 0.186874 |
| rs38152662 | 19  | 5343175 | 2.87E-06 | 0.186874 |
| rs36979098 | 19  | 5433187 | 2.87E-06 | 0.186874 |
| rs37399532 | 19  | 5515642 | 2.87E-06 | 0.186874 |
| rs36464166 | 19  | 5619157 | 2.87E-06 | 0.186874 |
| rs38870454 | 1   | 9690292 | 2.90E-06 | 0.187437 |
| rs30737389 | 1   | 120556824 | 2.90E-06 | 0.187437 |
| rs45920082 | 1   | 121034640 | 2.90E-06 | 0.187437 |
| rs32868148 | 9   | 65094739 | 3.01E-06 | 0.188935 |
| rs50469542 | 9   | 66416150 | 3.01E-06 | 0.188935 |
| rs27574360 | 4   | 133884437 | 3.24E-06 | 0.186498 |
| rs27578237 | 4   | 134271709 | 3.24E-06 | 0.186498 |
| rs27578194 | 4   | 134283929 | 3.24E-06 | 0.186498 |
| rs27578147 | 4   | 134306671 | 3.24E-06 | 0.186498 |
| rs27578114 | 4   | 134315926 | 3.24E-06 | 0.186498 |
| rs27578111 | 4   | 134316358 | 3.24E-06 | 0.186498 |
| SNP         | Chromosome | Position       | p-Value | MAF   |
|-------------|------------|----------------|---------|-------|
| rs27578022  | 4          | 134336464      | 3.24E-06| 0.186498 |
| rs31846156  | 15         | 87292777       | 3.37E-06| 0.173925 |
| rs32108716  | 12         | 66694958       | 3.40E-06| 0.189138 |
| rs51955425  | 16         | 72788939       | 3.53E-06| 0.183817 |
| rs4203146   | 16         | 73624179       | 3.57E-06| 0.160604 |
| rs4203158   | 16         | 73626715       | 3.57E-06| 0.160604 |
| rs4203159   | 16         | 73627098       | 3.57E-06| 0.160604 |
| rs49791987  | 16         | 73634287       | 3.57E-06| 0.160604 |
| rs4203186   | 16         | 73637376       | 3.57E-06| 0.160604 |
| rs4203509   | 16         | 73865267       | 3.57E-06| 0.160604 |
| rs4203550   | 16         | 73885132       | 3.57E-06| 0.160604 |
| rs51994823  | 17         | 33766971       | 3.65E-06| 0.169664 |
| rs49629788  | 17         | 33767492       | 3.65E-06| 0.169664 |
| rs51346762  | 17         | 33791241       | 3.65E-06| 0.169664 |
| rs46439310  | 17         | 34046644       | 3.65E-06| 0.169664 |
| rs26828028  | 11         | 31235263       | 3.74E-06| 0.167762 |
| rs52649558  | 12         | 42642305       | 3.75E-06| 0.183467 |
| rs32122316  | 12         | 66822676       | 3.86E-06| 0.194331 |
Table S7. Significant SNPs associated with LCA intima+media/EELx100% in 30 inbred mouse strains.

| dbSNP          | Chromosome | Position, bp | p-value     | Effect size |
|----------------|------------|--------------|-------------|-------------|
| rs36294984     | 12         | 102175044    | 1.64E-07    | 5.35241     |
| rs36281276     | 12         | 102181524    | 1.64E-07    | 5.35241     |
| rs36677986     | 1          | 165121248    | 1.68E-07    | 5.35456     |
| rs37370522     | 1          | 165124350    | 1.68E-07    | 5.35456     |
| rs38372684     | 1          | 165124376    | 1.68E-07    | 5.35456     |
| rs27831183     | 4          | 43542462     | 1.72E-07    | 5.35142     |
| rs28320686     | 4          | 43620641     | 1.72E-07    | 5.35142     |
| rs28320653     | 4          | 43645470     | 1.72E-07    | 5.35142     |
| rs28320604     | 4          | 43650523     | 1.72E-07    | 5.35142     |
| rs28320543     | 4          | 43662649     | 1.72E-07    | 5.35142     |
| rs28320511     | 4          | 43688855     | 1.72E-07    | 5.35142     |
| rs28311534     | 4          | 43732460     | 1.72E-07    | 5.35142     |
| rs49300701     | 12         | 70834268     | 4.29E-07    | 5.28592     |
| rs32825856     | 12         | 98293756     | 4.29E-07    | 5.28592     |
| rs32826743     | 12         | 98311790     | 4.29E-07    | 5.28592     |
| rs32831405     | 12         | 98324424     | 4.29E-07    | 5.28592     |
| rs32832502     | 12         | 98431791     | 4.29E-07    | 5.28592     |
| rs32833315     | 12         | 98431830     | 4.29E-07    | 5.28592     |
| rs32835668     | 12         | 98440111     | 4.29E-07    | 5.28592     |
| rs27077445     | 11         | 92536007     | 6.75E-07    | 5.31958     |
| rs47184414     | 13         | 63671652     | 1.56E-06    | 5.28121     |
| rs50150006     | 13         | 63672826     | 1.56E-06    | 5.28121     |
| rs51457735     | 13         | 63843692     | 1.56E-06    | 5.28121     |
| rs50629131     | 13         | 64083663     | 1.56E-06    | 5.28121     |
| rs31846156     | 15         | 87292777     | 1.62E-06    | 5.2561      |
| rs27077330     | 11         | 92579730     | 3.95E-06    | 4.97734     |
| rs27077326     | 11         | 92580059     | 3.95E-06    | 4.97734     |
| rs27077313     | 11         | 92580950     | 3.95E-06    | 4.97734     |
| rs27077297     | 11         | 92594015     | 3.95E-06    | 4.97734     |
| rs27062266     | 11         | 92606779     | 3.95E-06    | 4.97734     |
| rs4140244      | 11         | 92609707     | 3.95E-06    | 4.97734     |
| rs27062241     | 11         | 92609733     | 3.95E-06    | 4.97734     |
Table S8. Blood flow profiles in the left carotid arteries across the groups.

| Groups   | Parameters  | Mean Velocity | End Diastolic Velocity | Peak Systolic velocity | VTI | Mean Gradient | Pulsatility |
|----------|-------------|---------------|------------------------|------------------------|-----|---------------|-------------|
|          |             | mm/s          | mm/s                   | mm/s                   | mm  | mmHg          | index       |
| Npr2+/+  | Sham        | 303 ± 63      | 135 ± 24               | 521 ± 107              | 64 ± 11 | 0.430 ± 0.181 | 1.27 ± 0.05 |
| n=5      | Ligated     | 38 ± 6        | 5 ± 1                  | 74 ± 13                | 6 ± 0   | 0.006 ± 0.002 | 1.79 ± 0.11 |
| Npr2+/-  | Sham        | 233 ± 28      | 119 ± 15               | 405 ± 50               | 51 ± 3  | 0.227 ± 0.057 | 1.21 ± 0.11 |
| n=4      | Ligated     | 42 ± 15       | 12 ± 4                 | 87 ± 29                | 6 ± 1   | 0.010 ± 0.006 | 1.78 ± 0.14 |

n, Number of mice. *, p<0.05 vs. proper sham group.
Supplemental Figure Legends:

**Figure S1. Variation in carotid remodeling in ten inbred mouse strains.** Representative 3-dimensional reconstructions of the 2mm-length from the bifurcation of the left carotid artery after sham (SHAM) or ligation (LIG) operation in males of 129X1/SvJ (129X1), A/J (A), AKR/J (AKR), BALB/cJ (BALB), BTBR T+ Itpr3tf/J (BTBRT), BUB/BnJ (BUB), C3H/HeJ (C3H), C3HeB/FeJ (C3HEB), C57BL/6J (C57BL), C57L/J (C57L) mice. Black color shows lumen, yellow – intima, red – media, green – adventitia volume.

**Figure S2. Variation in carotid remodeling in ten inbred mouse strains.** Representative 3-dimensional reconstructions of the 2mm-length from the bifurcation of the left carotid artery after sham (SHAM) or ligation (LIG) operation in males of C58/J (C58), CBA/J (CBA), CE/J (CE), DBA/2J (DBA), FVB/NJ (FVB), I/LnJ (ILN), KK/HIJ (KK), LG/J (LG), LP/J (LP), MA/MyJ (MA) mice. Black color shows lumen, yellow – intima, red – media, green – adventitia volume.

**Figure S3. Variation in carotid remodeling in ten inbred mouse strains.** Representative 3-dimensional reconstructions of the 2mm-length from the bifurcation of the left carotid artery after sham (SHAM) or ligation (LIG) operation in males of NOD/LtJ (NOD), NON/LtJ (NON), NZB/BINJ (NZB), NZW/LacJ (NZW), PL/J (PL), RIIIS/J (RIIIS), SEA/GnJ (SEA), SJL/J (SJL), SM/J (SM), SWR/J (SWR) mice. Black color shows lumen, yellow – intima, red – media, green – adventitia volume.

**Figure S4. Genome-wide association (GWA) of the left carotid artery (LCA) media trait in 30 mouse strains.** A. GWA of LCA media volume, \(x10^6 \mu m^3\). Open circles are controls. Black circles are ligated mice. Values are mean±SEM; *, p<0.05 vs. control or other mouse strains. n=4-6 per group. B. GWA of LCA media volume. Each circle represents a SNP. Mouse
chromosomes are on X-axis. Gray line shows a threshold of significance.

**Figure S5.** Genome-wide association (GWA) of the left carotid artery (LCA) external elastic lamina (EEL) trait in 30 mouse strains. A. GWA of LCA EEL volume, x10^6 μm^3. Open circles are controls. Black circles are ligated mice. Values are mean±SEM; *, p<0.05 vs. control or other mouse strains. n=4-6 per group. B. GWA of LCA EEL volume. Each circle represents a SNP. Mouse chromosomes are on X-axis. Gray line shows a threshold of significance.

**Figure S6.** Genome-wide association (GWA) of the left carotid artery (LCA) adventitia trait in 30 mouse strains. A. GWA of LCA adventitia volume, x10^6 μm^3. Open circles are controls. Black circles are ligated mice. Values are mean±SEM; *, p<0.05 vs. control or other mouse strains. n=4-6 per group. B. GWA of LCA adventitia volume. Each circle represents a SNP. Mouse chromosomes are on X-axis. Gray line shows a threshold of significance.

**Figure S7.** Increases in PicroSirius Red staining in male Npr2^{+/−} mice. A. A representative image of PicroSirius Red-stained ligated left carotid artery (LCA) in male Npr2 wild type (Npr2^{+/+}) mouse. B. A representative image of PicroSirius Red-stained ligated LCA in male Npr2 heterozygous (Npr2^{+/−}) mouse. Insets are corresponding females. Scale bar is 100μm. Black brackets indicate intima-media area. C. A quantification of fibrosis (red color) in intima-media area of the LCA, %. Individual Npr2^{+/+} mice are shown as black circles. Open circles indicate Npr2^{+/−} mice. Gray lines are mean values; *, p<0.05 vs. Npr2^{+/+} males; †, p<0.05 vs. Npr2^{+/−} females. n=3 animals per group.
Figure S1
Figure S2
Figure S3
Figure S6

GWA LCA adventitia volume, $-\log_{10}(p \text{ value})$

LCA adventitia volume, $\times 10^6 \mu m^3$

129X1
A
AKR
BALB
BTBRT
BUB
C3H
C3HEB
C57BL
C57L
C58
CBA
CE
DBA2
FVB
ILN
KK
LG
LP
MA
NOD
NON
NZB
NZW
PL
RIII
SEA
SJL
SM
SWR

Control
Ligated

*
Figure S7