Association of Genetic Risk Variants with Expression of Proximal Genes Identifies Novel Susceptibility Genes for Cardiovascular Disease

Running title: Folkersen et al.; Association of risk variants and gene expression

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Abstract:

**Background** - Population-based genome-wide association studies (GWAS) have identified several single-nucleotide polymorphisms (SNPs) associated with cardiovascular disease or its risk factors. Genes in close proximity to these risk-SNPs are often thought to be pathogenetically important based on their location alone. However, the actual connections between SNPs and disease mechanisms remain largely unknown.

**Methods and Results** - To identify novel susceptibility genes, we investigated how 166 SNPs previously found to be associated with increased cardiovascular risk and/or predisposing metabolic traits, relate to the expression of nearby genes. Gene expression in 577 samples of aorta, liver, mammary artery and carotid atherosclerotic plaque was measured using expression arrays. For 47 SNPs, the expression levels of proximal genes (located within 200 kb) were affected ($P < 0.005$). More than 20 of these genes had not previously been identified as candidate genes for cardiovascular or related metabolic traits. SNP-associated gene effects were tissue-specific and the tissue specificity was phenotype-dependent.

**Conclusions** - This study demonstrates several instances of association between risk-SNPs and genes immediately adjacent to them. It also demonstrates instances where the associated gene is not the immediately proximal and obvious candidate gene for disease. This shows the necessity of careful studies of genetic marker data as a first step towards application of GWAS findings in a clinical setting.

**Key words:** genetics, genes, myocardial infarction, molecular biology
Introduction

It is incompletely understood how SNPs mediate their impact on pathobiology. The majority of disease-associated SNPs are located in non-coding regions of the genome. It is therefore speculated that genetic variants in promoter and enhancer regions are likely to affect gene expression levels. Such relations have previously been shown to exists using a candidate-gene driven approach [1-2]. Furthermore, genome-wide studies using gene expression levels as quantitative traits (eQTLs) have indicated a widespread regulation of gene expression by cis-acting SNPs [3-6]. Marked differences in association patterns between different cell types have also been observed in studies using stable cell lines, i.e. fibroblasts, T-cells and immortalized lymphoblastoid cells. In these studies 69 to 80% of the regulatory variants were identified only in specific cell types [4]. With the exception of one study on post-mortem liver tissue [5], the majority of eQTL studies have used readily available cell lines. However, for SNPs associated with a particular disease phenotype, eQTL associations should primarily be detectable in biopsies from tissues known to be involved in the pathogenesis of the disease. We therefore hypothesized that the mechanisms of cardiovascular and metabolic risk-SNPs can be deduced by use of gene expression data from relevant tissues. To this end we determined the association of risk-SNPs with gene expression levels in samples from liver, aorta (medial and adventitial portions), mammary artery, and carotid plaque obtained from two biobanks, each containing more than 200 samples from carotid endarterectomy and aortic valve disease patients, respectively.
Materials and Methods

Sample collection

Biobank materials were generated after informed consent from all participants had been obtained according to the declaration of Helsinki and with approval by the ethics committee of the Karolinska Institute (application numbers 02-147 and 2006/784-31/1). The Advanced Study of Aortic Pathology (ASAP) study included patients undergoing aortic valve surgery at the Karolinska University Hospital, Stockholm, Sweden. Biopsies were obtained at surgery from liver, mammary artery and dilated and non-dilated ascending aorta. The medial and adventitial layers of the vascular specimens were isolated by adventicectomy, incubated with RNA later (Ambion) and homogenized with a FastPrep (Qbiogene, Irvine, CA) using Lysing Matrix D tubes (Invitro cat.no. 6913-100). The Biobank of Karolinska Endarterectomies (BiKE) study included atherosclerotic tissue collected from patients undergoing carotid endarterectomy at the Karolinska University Hospital, Stockholm, Sweden. For both biobanks, total RNA was isolated using Trizol (BRL Life Technologies) and RNeasy Mini kit (Qiagen) including treatment with RNase-free DNase set (Qiagen) according the manufacturer’s instructions. The quality of RNA was analyzed with an Agilent 2100 bioanalyzer (Agilent Technologies Inc., Paolo Alto, CA, USA) and quantity was measured by a NanoDrop (Thermo Scientific). The ASAP and BiKE databases are independent of each other, but several overlaps exist between the individual ASAP data sets: In ASAP altogether 223 different patients had microarray measurements made on aortic medial tissue, aortic adventitia, liver and mammary artery. Information on sample size and distribution of all samples with both RNA expression measurements and DNA genotyping can be found in table 1.

Genotyping and expression analysis
The BiKE and ASAP RNA samples were hybridized and scanned at the Karolinska Institute Affymetrix core facility. For samples from the BiKE biobank Affymetrix HG-U133 plus 2.0 arrays and protocols were used, whereas Affymetrix GeneChip® Human Exon 1.0 ST arrays and protocols were used for samples from the ASAP biobank.

For probe set and meta probe set level investigations, i.e. the analysis of whole-gene variation with genotype, cel files were pre-processed using Robust Multichip Average (RMA) [7] normalization as implemented in the Affymetrix Power Tools 1.10.2 package apt-probeset-summarize. All expression measurements were log2 transformed as part of the RMA normalization. Using HG-U133 plus 2.0 arrays all probe sets were included and using Exon 1.0 ST arrays the investigation was performed in the extended subset of Affymetrix meta probe sets. Expression of sex specific transcripts were checked for concordance with database-registered sex. Microarray probes containing SNPs are potential sources of error. However, on investigation it was found that results were largely similar with or without these probes. All presented expression data is filtered for probes containing known SNPs from build 131 of NCBI dbSNP.

DNA samples from ASAP and BiKE patients were genotyped using Illumina Human 610W-Quad Beadarrays at the SNP technology platform at Uppsala University. The GenomeStudio™ software from Illumina was used for genotype calling and quality control. The average call rate per SNP was 99.84%. Replicate genotyping of twelve samples showed an overall concordance of 99.99 %. Data for 8 SNPs that had previously been genotyped with a taqman PCR-based method (Applied Biosystems) in 89 samples from the BiKE cohort showed only one discrepant genotype, corresponding to a concordance rate of 99.86%

Of the 168 initially selected SNPs, 114 (67.5%) were either genotyped directly on the Beadarray or had a perfect proxy (LD of \( R^2 = 1 \)) that was genotyped. Most of the remaining SNPs (51) could be imputed using the PLINK software with an INFO value of 0.8 or above.
The investigated SNPs were in Hardy-Weinberg equilibrium at $P > 0.01$. Information on the imputed SNPs and LD-block structures is available in Supplementary table 1. Of all SNPs, 31 were found to be linked in 13 groups with other investigated SNPs (at $R^2 > 0.8$) effectively giving 148 different investigated loci. Each SNP is treated individually in figure 1. SNPs in high LD are indicated together in table 2.

Selection of neighboring genes

In order to reduce the multiple testing, a limited number of neighboring genes were selected for association testing with each SNP. These genes were selected to be harbored within a region of 400 kb centered on each SNP. This width of the selection window was based on the fact that none of the investigated SNPs were found to be in an LD of $R^2 > 0.8$ with other SNPs further than 200 kb away (median distance was 34 kb) in the HapMap CEU population. This choice is further supported by previously published data in which the majority of associations are found within a 200 kb window [4]. All positions of genes are from ENSEMBL 56 (GRCh37 assembly) and all positions of SNPs are from ENSEMBL variation 56 (dbSNP130 assembly) [8]. Data was retrieved using the biomaRt package [9] available through the Bioconductor repository [10].

Statistics

All association tests between genotype and gene expression level were performed using additive (0-1-2) and dominant/recessive (0-0-1 and 0-1-1) models. The additive model encodes each heterozygote patient as 1 and each of the two homozygote types as 0 or 2. A linear model is fitted to the expression level of each gene, using this genotype value as effect. The additive model was not applied to genotypes with only one homozygote form present in a data set. The dominant/recessive models group the heterozygote samples with one of the homozygotes and compare the expression level of a gene using Student’s t-test. Multiple testing issues are limited by a directed choice of risk-SNPs and the use of a narrow search
window for nearby genes. On average for each data set 703 tests were applied to 131 SNPs using an additive model. A p-value cutoff of 0.005 corresponds to an overall false discovery rate of 0.1 calculated using the qvalue package from Bioconductor. Another indication of false discovery rates, obtained from a more realistic background of random samplings of SNP associations can be found in figure 1. False positive rates at $P < 0.005$ calculated from these samplings are 0.022 for exon arrays and 0.038 for HG-U133 plus 2.0 arrays. This difference from standard FDR is likely due to the interdependence of testing the same genes in similar tissues. In any case, we have sought to avoid a hard threshold for significance. Instead we present and discuss all p-values as raw and unmodified.

**Results**

The risk SNPs were selected from genome-wide association studies (GWAS) investigating cardiovascular risk factors for which relevant tissue were available to us. These included serum LDL, HDL, triglyceride concentrations and waist-circumference (liver), myocardial infarction, aneurysm formation, atherosclerosis, and hypertension (vessel wall, plaque). All larger studies of caucasians catalogued under relevant trait headers in the Catalog of Published Genome-Wide Association Studies [11] were trawled, and SNPs were included in the analysis if they had been found to be significantly or borderline significantly associated with the phenotype according to the statistical considerations employed by the authors of each article [6, 12-22]. A total of 168 SNPs were identified, but after imputation 166 SNPs remained to be studied. An overview of the included SNPs together with data on proxy-selection, LD-block size and association with expression is provided in supporting information in table S1.

In general, the selected SNPs showed stronger associations with gene expression levels than expected by chance alone. In figure 1 the association trends are compared between GWAS
risk-SNPs and random samples of SNPs. Here the association of one group of randomly selected SNPs was related to the expression of nearby genes and another group of randomly selected SNPs was related to randomly selected genes. As motivated in the methods section, nearby genes were defined as being located within 200 kb of a SNP. Generally SNPs showed stronger associations with the expression of nearby genes than with the expression of randomly selected genes, but the specific set of SNPs selected from GWAS showed much stronger associations. This finding supports the initial hypothesis that risk-SNPs frequently act by influencing the expression levels of nearby genes. Of all investigated risk-SNPs, 47 were associated with the expression level of a nearby gene at $P < 0.005$ in one or more of the investigated tissue types. Particularly strong associations were seen in the liver samples, but also plaque samples and the intimal / medial portions of the aortic samples showed association levels above those expected for randomly selected SNPs. The tissue distribution of associations depended on the phenotype investigated. The majority of risk-SNPs associated with lipid phenotypes were found to be associated with gene expression levels in the liver, and more than half of these SNP-expression level associations were confined to the liver only. SNPs associated with phenotypes that are more directly related to the vessel wall were more frequently associated with gene expression levels in vascular tissues (figure 2).

Based on the distance between SNPs and the associated genes, four different classes of associations between SNPs and gene expression levels emerged. Approximately half of the SNPs were located in close proximity to or within the associated genes (figure 3). However, in 22 instances, the SNPs were not located within <35 kb of the genes. Of these associations, 9 are explained by linked SNPs in closer proximity to the gene (figure 4a). However, for 7 other associations, there were no SNPs in LD at $R^2 > 0.4$ in closer proximity to the associated gene (figure 4b). A fourth complex class of SNPs is exemplified by rs6450415 (figure 4c).
This SNP associates with the expression levels of MAP3K1, GPBP1 and MIER3 in mammary artery tissue at P-values between 0.0044 and 0.009. The expression levels of these three genes show high degree of correlation (Pearson correlation coefficient > 0.75 for all pair-wise comparisons), which, because of the proximity, is likely to indicate a co-regulatory mechanism of the SNP. The three genes are found at distances of 157 kb and 136 kb centromeric and 121 kb telomeric from the risk-SNP, and since there are no SNPs in LD of R² > 0.4 further than 30 kb away, this observation is not explained by an LD-block. This finding is of general interest since there are several other similar observations, for example the associations of the SNP rs413016 with SRR, SMG6 and METT10D and those of rs6922269 with PLEKHG1 and MTHFD1L (see also table 2 and supporting information S2). The implication of the existence of four classes of SNP-gene expression associations is that genes located next to identified risk-SNPs do not necessarily participate in the disease mechanism.

It is of special clinical relevance to discuss examples of risk-SNPs associated with the important phenotype of MI [12-14, 23-24]. As shown in a previous analysis of this data set, no association with proximal gene expression is found for the chr9p21.3 locus [25]. In contrast, the rs646776 SNP shows a strong association with the expression level of SORT1 (P = 8.14e-62). This association has previously been shown in liver [5-6]. Our present data shows that the SORT1 association is remarkably liver-specific, even though SORT1 shows high expression levels in all the investigated tissues. An example of novel association with gene expression is seen for the rs6725887 SNP, which has previously been reported to be associated with MI, with WDR12 as the reported culprit gene [14]. As shown in figure 4b, however, the expression of the NBEAL1 gene, located at a distance of 134 kb, gives a stronger association signal with the genotype of the rs6725887 SNP. This distance span is of the LD-block spanning class and the P-value for the association signal is < 0.005 in all
vascular tissues included in the analysis. The NBEAL1 gene encodes the neurobeachin-like 1 protein, which has previously only been implicated in glioma [26]. Our findings suggest it as a novel research target. Other MI-specific examples of novel SNP-expression level associations are listed in table 2.

Discussion

GWAS provide valuable indications of novel potential pathophysiological mechanisms for complex diseases. However, it should be underscored that GWAS are designed to discover links between disease and genetic markers, not necessarily between disease and actual genes. We show here that the most proximal gene is often not the culprit gene. Also, an important observation in our study is the high degree of tissue specificity. The effects of the majority of SNPs associated with lipid levels were seen in liver tissue and many of them solely there. SNPs associated with MI showed gene expression associations that were specific for vessel wall tissue, particularly aortic intima/media. The corollary is that tissue diversity is essential for future eQTL studies. Tissue types thought to be involved in the pathogenesis of an investigated disease are of primary interest, but it cannot be excluded that broader investigations will uncover novel pathophysiological mechanisms.

Several SNPs did not show association with expression levels of any nearby genes. There are several explanations for how these SNPs could influence the first step of a mechanism, examples being alteration of protein-sequence (directly or indirectly through linkage), expression changes in other tissues, not included in this analysis, or effects outside of the search window. Although 200 kb was the size of the largest LD-block encountered in this study, we observed associations with the expression levels of genes outside the reach of LD-blocks. Finally, more complex regulation patterns could be responsible. For example, mechanisms suggested to be responsible for the much-investigated chr9p21 ANRIL SNP
association include miRNA and epigenetics, expression patterns limited temporally to
discrete developmental stages, and a complex transcript isoform structure [25, 27].

An important promise of the GWAS is the ability to identify novel pathways of pathogenesis
and eventually new concepts for therapy. Accurate knowledge of the functional consequences
of genetic variation is essential to achieve this goal. The multiple instances where the
associated gene is not the immediately obvious candidate gene for disease, demonstrates the
necessity of careful studies of genetic marker data as a first step towards application of
GWAS knowledge in a clinical setting.

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**Conflict of Interest Disclosures:** None

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Table 1  Overview of analyzed datasets

<table>
<thead>
<tr>
<th>Name</th>
<th>Tissue</th>
<th>Sample number</th>
<th>Expression array type</th>
<th>Female gender</th>
<th>Mean age ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>BiKE database</td>
<td>Carotid plaque tissue</td>
<td>117</td>
<td>Affymetrix HG-U133 plus 2.0</td>
<td>19.8%</td>
<td>70.0 ± 8.87</td>
</tr>
<tr>
<td>ASAP MMed database</td>
<td>Medial mammary artery tissue</td>
<td>88</td>
<td>Affymetrix Human Exon 1.0 ST</td>
<td>37.5%</td>
<td>65.0 ± 11.3</td>
</tr>
<tr>
<td>ASAP AAdv database</td>
<td>Adventitial aortic tissue</td>
<td>103</td>
<td>Affymetrix Human Exon 1.0 ST</td>
<td>29.1%</td>
<td>62.2 ± 12.2</td>
</tr>
<tr>
<td>ASAP AMed database</td>
<td>Medial aortic tissue</td>
<td>117</td>
<td>Affymetrix Human Exon 1.0 ST</td>
<td>25.6%</td>
<td>61.6 ± 11.3</td>
</tr>
<tr>
<td>ASAP L  database</td>
<td>Liver samples</td>
<td>152</td>
<td>Affymetrix Human Exon 1.0 ST</td>
<td>27.0%</td>
<td>63.9 ± 11.4</td>
</tr>
</tbody>
</table>
Table 2: Curated list of SNPs that are associated with whole-gene expression levels in one or more data sets

<table>
<thead>
<tr>
<th>SNP(s)</th>
<th>GWAS</th>
<th>Chr</th>
<th>Pos. (MB)</th>
<th>Distance to gene</th>
<th>Transcript association</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs10903129</td>
<td>Total cholesterol [15]</td>
<td>1</td>
<td>25.8</td>
<td>175 kb, borderline same LD-block</td>
<td>C1orf63 (liver P = 4.58e-08, also other vessel tissues)</td>
</tr>
<tr>
<td>rs1167998</td>
<td>Total cholesterol and TG [15]</td>
<td>1</td>
<td>62.9</td>
<td>0 kb</td>
<td>DOCK7 (plaque P = 1.51e-09)</td>
</tr>
<tr>
<td>rs646776</td>
<td>MTHFD1 [14], LDL [15-16], total cholesterol [15], LDL [6]</td>
<td>1</td>
<td>109.8</td>
<td>34 kb to SORT1, not same LD-block</td>
<td>SORT1 (P = 8.14e-62), PSRC1 (P = 8.33e-27), CELSR2 (P = 3.55e-06) - all liver</td>
</tr>
<tr>
<td>rs9818870</td>
<td>MTHFD1 [13]</td>
<td>1</td>
<td>138.1</td>
<td>0 kb</td>
<td>MRAS (aorta media P = 5.12e-16, mammary media P = 2.44e-09, aorta adv. P = 0.00395)</td>
</tr>
<tr>
<td>rs4846914</td>
<td>HDL [6]</td>
<td>1</td>
<td>230.3</td>
<td>0 kb</td>
<td>GALNT2 (plaque P = 0.001, liver P = 0.00206)</td>
</tr>
<tr>
<td>rs6725887</td>
<td>MTHFD1 [14]</td>
<td>2</td>
<td>203.7</td>
<td>134 kb, same LD-block</td>
<td>NBEAL1 (aorta media P = 4.23e-05, mammary media P = 0.000274, aorta adv. P = 0.00188)</td>
</tr>
<tr>
<td>rs9815354</td>
<td>Diastolic blood pressure [17-18]</td>
<td>3</td>
<td>41.9</td>
<td>0 kb</td>
<td>ULK4 (aorta media P = 1.01e-06, mammary media P = 3.02e-05, aorta adv. P = 0.000199)</td>
</tr>
<tr>
<td>rs7442295</td>
<td>Uric acid [19], TG [15]</td>
<td>4</td>
<td>10</td>
<td>0 kb</td>
<td>SLC2A9 (liver P = 0.000917)</td>
</tr>
<tr>
<td>rs6450415</td>
<td>Left ventricular mass [20]</td>
<td>5</td>
<td>56.3</td>
<td>See fig 4C</td>
<td>MIER3 (P = 0.00435), CPBP1 (P = 0.03161), MAP3K1 (P = 0.00394) - all mammary media</td>
</tr>
<tr>
<td>rs6922269</td>
<td>Mi [12]</td>
<td>6</td>
<td>151.3</td>
<td>0 kb</td>
<td>MTHFD1L (plaque P = u.00548)</td>
</tr>
<tr>
<td>rs2240466</td>
<td>TG [15]</td>
<td>7</td>
<td>72.9</td>
<td>133 kb, not same LD block</td>
<td>NUX5 (mammary media P = 4e-18 by 0-1-1 model)</td>
</tr>
<tr>
<td>rs6961069</td>
<td>Left ventricular mass [20]</td>
<td>7</td>
<td>80.2</td>
<td>0 kb</td>
<td>CD36 (liver P = 0.00128)</td>
</tr>
<tr>
<td>rs10498859</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rs2245667</td>
<td>Waist-circumference [21]</td>
<td>8</td>
<td>17.46</td>
<td>0 kb</td>
<td>DGCR1 (mammary media P = 0.00795)</td>
</tr>
<tr>
<td>rs6987702</td>
<td>Total cholesterol [15]</td>
<td>8</td>
<td>126.5</td>
<td>125 kb, not same LD-block</td>
<td>NSMCI (aorta media P = 3.00626)</td>
</tr>
<tr>
<td>rs471364</td>
<td>HDL [6]</td>
<td>9</td>
<td>15.3</td>
<td>0 kb</td>
<td>TTC19B (plaque P = 2.01e-05, liver P = 6.47e-05) *</td>
</tr>
<tr>
<td>rs1004467</td>
<td>Diastolic blood pressure [17-18]</td>
<td>10</td>
<td>104.6</td>
<td>96 kb, same LD-block</td>
<td>SFXN2 (liver P = 0.00215)</td>
</tr>
<tr>
<td>rs11014166</td>
<td>Diastolic blood pressure [17]</td>
<td>10</td>
<td>18.7</td>
<td>126 kb, not same LD-block</td>
<td>NSUN6 (liver P = 0.00251)</td>
</tr>
<tr>
<td>rs174547</td>
<td>HDL and TG [6]</td>
<td>11</td>
<td>61.6</td>
<td>0 kb to FADS1</td>
<td>FADS1 (liver P = 3.66e-06), FADS2 (plaque P = 3.57e-05), C11orf9 (liver P = 0.000195) *</td>
</tr>
<tr>
<td>rs174570</td>
<td>Total cholesterol and LDL [15]</td>
<td>11</td>
<td>61.6</td>
<td>41 kb, not same LD-block</td>
<td>C11orf9 (liver P = 0.000292)</td>
</tr>
<tr>
<td>rs3819100</td>
<td>Abdominal aortic aneurysm [22]</td>
<td>11</td>
<td>114.2</td>
<td>46 kb, not same LD-block</td>
<td>ZBTB16 (liver P = 0.000495, aorta adv. P = 0.00142)</td>
</tr>
<tr>
<td>rs12272004</td>
<td>TG [15]</td>
<td>11</td>
<td>116.6</td>
<td>45 kb, same LD-block</td>
<td>ZNF259 (aorta adv. P = 0.000278)</td>
</tr>
<tr>
<td>rs608501</td>
<td>Waist-hip-ratio [21]</td>
<td>11</td>
<td>125.3</td>
<td>0 kb</td>
<td>PKNOX2 (plaque P = 0.000548)</td>
</tr>
<tr>
<td>rs6487924</td>
<td>Waist-hip-ratio and Waist-circumference [21]</td>
<td>12</td>
<td>30.79</td>
<td>77 kb, same LD-block</td>
<td>CAPRIN2 (liver P = 0.00205)</td>
</tr>
<tr>
<td>rs2338104</td>
<td>HDL [6]</td>
<td>12</td>
<td>109.9</td>
<td>96 kb, same LD-block</td>
<td>MMAB (liver P = 2.42e-08, aorta media P = 0.000293, mammary media P = 0.000324) *</td>
</tr>
<tr>
<td>rs8003379</td>
<td>Abdominal aortic aneurysm [22]</td>
<td>14</td>
<td>64.9</td>
<td>0 kb</td>
<td>MTHFD1 (mammary media P = 0.00153, aorta media P = 0.00221, aorta adv. P = 0.00717)</td>
</tr>
<tr>
<td>rs2414500</td>
<td>Waist-circumference [21]</td>
<td>15</td>
<td>57.6</td>
<td>14 kb</td>
<td>TCF12 (aorta media P = 0.000425)</td>
</tr>
<tr>
<td>rs1532085</td>
<td>HDL [15], HDL [13]</td>
<td>15</td>
<td>58.7</td>
<td>0-19 kb</td>
<td>LIPC (liver P = 0.00622) *</td>
</tr>
</tbody>
</table>
All loci with an association with the expression of a gene at $P < 0.005$ using an additive model are listed. A few interesting examples with lower significance or significance under different models are also included. A complete list of all SNPs with association $P$-values for all nearby genes in all data set under all three association models can be found in supporting information table S1. Presence in same LD-block is defined as close to any SNP in LD of $R^2 > 0.6$. * previously shown eQTL from [6].
Figure Legends:

Figure 1 – Observed test statistics for investigated SNPs compared with random sample SNPs
The y-axis shows the -log10(P) significance of associations between SNPs and the most significantly associated nearby genes using an additive model. The x-axis is the sorted rank of each y-axis value. Black dots show the distribution of P-values for the investigated set of risk-SNPs identified from the literature. Blue dots represent random equally sized samples of SNPs and the strongest association with expression of one of the genes within a 400 kb search window. There are no significant differences in distance between SNPs and genes in the risk-SNP group and the corresponding distances in groups of random SNPs. Red dots represent random equally sized samples of SNPs and the strongest association with the expression of one of the genes sampled from randomly selected 400 kb search windows. Each of the two random sampling sets has been repeated ten times. For clarity, the plot has been cropped to maximally show a -log10(P) value of 7. This leaves out several highly significant data points but allows focus on the general trend of higher P-values for SNPs identified in GWAS.

Figure 2 - Tissue specificity relates to phenotype
Number of times SNPs are found to be associated with gene expression in a given tissue, stratified by the phenotype previously found to be associated with these SNPs. Association is based on the interpretation given in table 2. Basing association on a hard cutoff, such as \( P < 0.005 \), gives a similar trend but omits cases of recessive/dominant effects and cases with interpreted clear high-significant dominance of one tissue type. Lipids phenotypes are defined as HDL, LDL, TG, or total cholesterol. Vessel wall-related phenotypes are broadly defined as anything related to diastolic blood pressure, internal left ventricular diastolic dimensions, left ventricular mass, systolic blood pressure, left ventricular systolic dysfunction, or left ventricular wall thickness. However, the trend is the same in each of these subsets when analyzed separately.

Figure 3 – Tissue specific association between genotype and expression level of all genes within a 400 kb search window.
In each plot the y-axis shows the -log10(P) calculated for the association between genotype and expression level using an additive model. The x-axis shows the data sets listed in table 2. In this table n is also listed. Each colored line shows the association level for one gene across different tissue types. The relative expression level of a gene in the tissue type is indicated by the dot size. Relative location of genes, SNP and LD boundaries are indicated by the map below each plot. Different shades of grey indicate the most distal SNPs in LD of R² 0.8, 0.6 and 0.4, respectively. A) A simple example of the notation used in tissue specific plots: the rs1532085 and its association with the expression of LIPC. Since this is the only gene close to the SNP, there is only one colored line. As can be seen from the height of this line, the association is highly liver-specific. In addition, the dot sizes show that LIPC is only expressed in the liver. The rs1532085 SNP has previously been associated with HDL levels [15]. B) Example of association between a SNP and its harboring gene. The association between rs1167998 and the expression of DOCK7 is seen in plaque tissue only. This SNP has previously been associated with serum cholesterol and triglyceride (TG) concentrations [15].

Figure 4 – Three classes of association between genotype and distal gene expression.
See figure 3 for plot description. A) Example of long-range association that is a result of LD-block span. The rs6725887 SNP is associated with the vessel wall expression of NBEAL1. The SNP-to-gene distance is 134 kb but a perfect proxy is found inside the gene. This SNP has been found to be associated with risk of MI [14]. B) Example of longer-range association without more proximal SNPs in LD. The rs174570 SNP and the expression levels of C11orf9 are associated in liver. However, the SNP-to-gene distance is 41 kb. No other SNPs in LD of R² > 0.4 are found closer to the gene. C) Example of a complex interaction. The rs6450415 SNP, previously associated with left ventricular mass [20], associates with the expression of MIER3, GPBP1, and MAP3K1 in mammary artery.
Association of Genetic Risk Variants with Expression of Proximal Genes Identifies Novel Susceptibility Genes for Cardiovascular Disease
Lasse Folsersen, Ferdinand van't Hooft, Ekaterina Chernogubova, Hanna E. Agardh, Göran K. Hansson, Ulf Hedin, Jan Liska, Ann-Christine Syyänen, Gabrielle Paulsson-Berne, Anders Franco-Cereceda, Anders Hamsten, Anders Gabrielsen and Per Eriksson

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SUPPLEMENTAL MATERIAL

Association of genetic risk variants with expression of proximal genes identifies novel susceptibility genes for cardiovascular disease

Lasse Folkersen¹,², Ferdinand van’t Hooft¹, Ekaterina Chernogubova¹, Hanna E Agardh², Göran K Hansson², Ulf Hedin³, Jan Liska⁴, Ann-Christine Syvänen⁵, Gabrielle Paulssson-Berne², Anders Franco-Cereceda⁴, Anders Hamsten¹, Anders Gabrielsen²*, Per Eriksson¹*, on behalf of the BiKE and ASAP study groups

*Contributed equally, corresponding authors AG for BiKE-database and PE for ASAP-database.

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⁵Molecular Medicine, Department of Medical Sciences, Uppsala University, 751 85, Uppsala, Sweden.

SNP-entries sorted by most significant p-value. Missing data points are fully explained in supplementary data sheet. Likely explanations are lack of annotated probe sets for array type or lack of two homozygotes for 0-1-2 model.
SNP located on chr chr1 at 109.8 Mb. The rs646776 which is in LD 1 was used as proxy.

Gene and distance to SNP:
- TAF13 (−199 kb)
- TMEM167B (−178 kb)
- SCARNA2 (−174 kb)
- C1orf194 (−161 kb)
- KIAA1324 (−68 kb)
- SARS (−37 kb)
- CELSR2 (0 kb)
- PSRC1 (5 kb)
- MYBPHL (17 kb)
- SORT1 (35 kb)
- PSMA5 (127 kb)
- SYPL2 (192 kb)

Expression levels:
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

rs12740374 relation by 0–1–2 model
Identifying GWAS: LDL (8, 15)
rs646776 relation by 0−1−2 model

SNP located on chr chr1 at 109.8 MB. This SNP was measured on array.
Identifying GWAS: LDL (15, 2), MI (11), Total cholesterol (2)
rs599839 relation by 0−1−2 model

Identifying GWAS: LDL (17, 15), MI (14)

SNP located on chr chr1 at 109.8 MB. This SNP was imputed.

expression level
• 1st quartile
• 2nd quartile
• 3rd quartile
• 4th quartile

gene and distance to SNP
- TMEM167B (−183 kb)
- SCARNA2 (−179 kb)
- C1orf194 (−166 kb)
- KIAA1324 (−73 kb)
- SARS (−41 kb)
- CELSR2 (−4 kb)
- PSRC1 (0 kb)
- MYBPHL (13 kb)
- SORT1 (30 kb)
- PSMA5 (122 kb)
- SYPL2 (187 kb)
rs9818870 relation by 0−1−2 model

SNP located on chr chr3 at 138.1 MB. The rs1199338 which is in LD 1 was used as proxy.

Identifying GWAS: MI (4)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- ARMC8 (~105 kb)
- TXNDC6 (~73 kb)
- MRAS (0 kb)
- ESYT3 (31 kb)
- CEP70 (91 kb)
SNP located on chr chr1 at 62.93 Mb. This SNP was measured on array.

Identifying GWAS: TG (2), Total cholesterol (2)

rs1167998 relation by 0−1−2 model

expression level

- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

DOCK7

KANK4 (−147 kb)

USP1 (−14 kb)

DOCK7 (0 kb)

ANGPTL3 (132 kb)

rs1167998

rs1167998

expressed level

1st quartile

2nd quartile

3rd quartile

4th quartile

expression level

KANK4

USP1

ANGPTL3

position

62700000 62800000 62900000 63000000 63100000

KANK4

USP1

DOCK7

ANGPTL3

rs1167998

AA, AC, CC
rs10889353 relation by 0−1−2 model

SNP located on chr chr1 at 63.12 MB. This SNP was measured on array.

Identifying GWAS: TG (2, 8), Total cholesterol (2)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- DOCK7 (0 kb)
- ANGPTL3 (−46 kb)
- ATG4C (132 kb)
rs2338104 relation by 0–1–2 model
SNP located on chr chr12 at 109.9 MB. The rs2058804 which is in LD 1 was used as proxy.
Identifying GWAS: HDL (8)
rs10903129 relation by 0−1−2 model
SNP located on chr chr1 at 25.77 MB. This SNP was measured on array.
Identifying GWAS: Total cholesterol (2)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- C1orf63 (−175 kb)
- RHD (−112 kb)
- TMEM50A (−80 kb)
- RHCE (−12 kb)
- TMEM57 (0 kb)
- LDLRAP1 (101 kb)
- MAN1C1 (175 kb)
rs9815354 relation by 0−1−2 model

SNP located on chr 3 at 41.91 MB. The rs10212536 which is in LD 1 was used as proxy.

Identifying GWAS: Diastolic blood pressure (9)

expression level
• 1st quartile
• 2nd quartile
• 3rd quartile
• 4th quartile

gene and distance to SNP
- ULK4 (0 kb)
- TRAK1 (143 kb)

Identification of GWAS:
- Diastolic blood pressure (9)
- SNP located on chr 3 at 41.91 MB.
- The rs10212536 which is in LD 1 was used as proxy.

Position of SNPs:
- ASAP MMed: 61 AA / 26 AG / 1 GG
- ASAP L: 107 AA / 43 AG / 1 GG
- ASAP AMed: 72 AA / 29 AG / 2 GG
- ASAP AAdv: 59 AA / 29 AG / 2 GG
- Bike plaque hgu133plus2: 78 AA / 28 AG

Expression levels:
- ULK4 (0 kb)
- TRAK1 (143 kb)

Gene distances to SNP:
- ULK4 (0 kb)
- TRAK1 (143 kb)
rs174547 relation by 0−1−2 model
SNP located on chr chr11 at 61.57 MB. The rs174537 which is in LD 1 was used as proxy.
Identifying GWAS: HDL (8), TG (8)
rs7679 relation by 0–1–2 model

SNP located on chr chr20 at 44.58 MB. This SNP was measured on array.
Identifying GWAS: HDL (8), TG (8)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
WFDC3 (−156 kb)
SPINT2 (−198 kb)
DNTTIP1 (−136 kb)
UBE2C (−131 kb)
TNCC2 (−114 kb)
SNX21 (−102 kb)
ACOT8 (−90 kb)
C20orf165 (−60 kb)
NEURL2 (−57 kb)
CTSA (−49 kb)
PLTP (−36 kb)
PCIF1 (0 kb)
FTLP (27 kb)
FTLP (27 kb)
ZNF335 (1 kb)
FTLP (27 kb)
MMP9 (61 kb)
SLC12A5 (74 kb)
NCOA5 (113 kb)
RPL13P2 (152 kb)
CD40 (170 kb)
rs471364 relation by 0−1−1 model
SNP located on chr chr9 at 15.29 MB. The rs3933785 which is in LD 1 was used as proxy.
Identifying GWAS: HDL (8)
rs4523957 relation by 0−1−2 model

SNP located on chr chr17 at 2.209 MB. This SNP was imputed.

Identifying GWAS: Aortic root size (16)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- SMG6 (−2 kb)
- SRR (0 kb)
- TSR1 (17 kb)
- SNORD91B (24 kb)
- SNORD91A (25 kb)
- SGSM2 (32 kb)
- MNT (78 kb)
- METT10D (110 kb)
rs2240466 relation by 0−1−1 model
SNP located on chr chr7 at 72.86 MB. This SNP was measured on array.
rs439401 relation by 0–1–2 model

SNP located on chr chr19 at 45.41 MB. This SNP was measured on array.

Identifying GWAS: TG (2)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- BCL3 (−151 kb)
- CBLC (−111 kb)
- BCAM (−90 kb)
- PVRL2 (−22 kb)
- TOMM40 (−8 kb)
- APOE (−2 kb)
- APOC1 (3 kb)
- APOC4 (31 kb)
- APOC2 (35 kb)
- CLPTM1 (44 kb)
- RELB (90 kb)
- SFRS16 (128 kb)
- ZNF296 (160 kb)
- GEMIN7 (168 kb)
- LRRC68 (182 kb)
rs4675310 relation by 0–1–2 model
SNP located on chr chr2 at 203.9 MB. The rs6725887 which is in LD 1 was used as proxy.
Identifying GWAS: MI (11)

SNP located on chr chr2 at 203.9 MB. The rs6725887 which is in LD 1 was used as proxy.

ICA1L (−144 kb)
WDR12 (−1 kb)
ALS2CR8 (−30 kb)
NBEAL1 (0 kb)

expression level
● 1st quartile
● 2nd quartile
● 3rd quartile
● 4th quartile

gene and distance to SNP
ICA1L (−144 kb)
WDR12 (−1 kb)
ALS2CR8 (−30 kb)
NBEAL1 (0 kb)
rs10852932 relation by 0–1–2 model
SNP located on chr17 at 2.143 MB. This SNP was imputed.
Identifying GWAS: Aortic root size (16)
rs413016 relation by 0–1–2 model

SNP located on chr chr17 at 2,237 MB. This SNP was measured on array.

Identifying GWAS: Aortic root size (16)

Expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

Gene and distance to SNP
- SMG6 (~30 kb)
- SRR (~9 kb)
- TSR1 (0 kb)
- SNORD91B (~5 kb)
- SNORD91A (~4 kb)
- SGSM2 (3 kb)
- MNT (50 kb)
- METT10D (82 kb)
rs2235487 relation by 0–1–2 model
SNP located on chr chr16 at 1,73 MB. This SNP was measured on array.
Identifying GWAS: Systolic dysfunction (16)

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<th>Gene</th>
<th>AA</th>
<th>AG</th>
<th>GG</th>
</tr>
</thead>
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<tr>
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<td>37</td>
<td>5</td>
</tr>
<tr>
<td>ASAP_L</td>
<td>91</td>
<td>53</td>
<td>7</td>
</tr>
<tr>
<td>ASAP_AMed</td>
<td>50</td>
<td>36</td>
<td>4</td>
</tr>
<tr>
<td>ASAP_AAdv</td>
<td>49</td>
<td>34</td>
<td>5</td>
</tr>
<tr>
<td>bike_plaque_hgu133plus2</td>
<td>60</td>
<td>33</td>
<td>13</td>
</tr>
</tbody>
</table>

- **rs2235487**
- **chr16**
- **1,73 MB**
- **AA** 6.5
- **AG** 7.5
- **GG**
Identifying GWAS: MI (11)

rs9982601 relation by 0–1–1 model
SNP located on chr chr21 at 35.6 MB. This SNP was imputed.
rs12272004 relation by 0–1–2 model

SNP located on chr chr11 at 116.6 MB. This SNP was measured on array.

Identifying GWAS: TG (2)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP

BUD13 (15 kb)
ZNF259 (45 kb)
APOA5 (56 kb)
APOA4 (88 kb)
APOC3 (97 kb)
APOA1 (103 kb)
SIK3 (110 kb)
rs174570 relation by 0–1–2 model

SNP located on chr chr11 at 61.6 MB. This SNP was measured on array.

Identifying GWAS: LDL (2), Total cholesterol (2)

-5log10(P)

<table>
<thead>
<tr>
<th>Gene</th>
<th>Expression level</th>
<th>Distance to SNP</th>
</tr>
</thead>
<tbody>
<tr>
<td>RPLP0P2</td>
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<td>−190 kb</td>
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<tr>
<td>DAGLA</td>
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<td>−83 kb</td>
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<tr>
<td>C11orf9</td>
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<tr>
<td>C11orf10</td>
<td>4th quartile</td>
<td>−37 kb</td>
</tr>
<tr>
<td>MIR611</td>
<td>(−37 kb)</td>
<td></td>
</tr>
<tr>
<td>FEN1</td>
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<td></td>
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<tr>
<td>FADS1</td>
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<tr>
<td>MIR1908</td>
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<tr>
<td>RAB3IL1</td>
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<tr>
<td>BEST1</td>
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<tr>
<td>FTH1</td>
<td>(135 kb)</td>
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</table>

Position:

61400000 61500000 61600000 61700000 61800000
rs2414500 relation by 0−1−2 model

SNP located on chr chr15 at 57.6 MB. This SNP was imputed.

Identifying GWAS: Waist-circumference (10)

gene and distance to SNP

- TCF12 (−14 kb)
- CGNL1 (72 kb)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile
rs3819100 relation by 0–1–2 model
SNP located on chr chr11 at 114.2 MB. This SNP was measured on array.

Identifying GWAS: Abdominal Aortic Aneurysm (5)

- log10(P)

ASAP_MMed
38 AA // 41 AG // 9 GG

ASAP_L
69 AA // 72 AG // 10 GG

ASAP_AMed
54 AA // 41 AG // 8 GG

ASAP_AAdv
45 AA // 40 AG // 5 GG

bike_plaque_hgu133plus2
62 AA // 36 AG // 8 GG

ZBTB16 (−46 kb)
NNMT (0 kb)
C11orf71 (95 kb)
RBM7 (104 kb)
REXO2 (143 kb)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- ZBTB16
- NNMT
- C11orf71
- RBM7
- REXO2

position
rs608501 relation by 0−1−2 model
SNP located on chr chr11 at 125.3 MB. This SNP was imputed.

Identifying GWAS: Waist−hip−ratio (10)

<table>
<thead>
<tr>
<th>Gene</th>
<th>Expression Level</th>
<th>Distance to SNP</th>
</tr>
</thead>
<tbody>
<tr>
<td>PKNOX2</td>
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<td>0 kb</td>
</tr>
<tr>
<td>FEZ1</td>
<td>24 kb</td>
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<td>EI24</td>
<td>151 kb</td>
<td>151 kb</td>
</tr>
<tr>
<td>STT3A</td>
<td>171 kb</td>
<td>171 kb</td>
</tr>
</tbody>
</table>

-log10(P)

- 0.0
- 0.5
- 1.0
- 1.5
- 2.0
- 2.5
- 3.0

AA AG GG
rs173539 relation by 0−1−2 model

SNP located on chr16 at 56.99 MB. The rs3764261 which is in LD 1 was used as proxy.

Identifying GWAS: HDL (8)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

Gene and distance to SNP
- NUP93 (−109 kb)
- MIR138−2 (−96 kb)
- SLC12A3 (−38 kb)
- HERPUD1 (−10 kb)
- CETP (8 kb)
- NLRC5 (35 kb)
- CPNE2 (138 kb)
- FAM192A (198 kb)
rs10499859 relation by 0–1–2 model

SNP located on chr chr7 at 80.26 MB. The rs1527479 which is in LD 1 was used as proxy. Identifying GWAS: Left ventricular mass (1)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- CD36 (0 kb)
- GNAT3 (−117 kb)
- SEMA3C (113 kb)

- log10(P)

<table>
<thead>
<tr>
<th>SNP</th>
<th>ASAP.MMED</th>
<th>ASAP.L</th>
<th>ASAP.AMed</th>
<th>ASAP.AAdv</th>
</tr>
</thead>
</table>

- CD36
- SEMA3C
- GNAT3

position

80000000 80100000 80200000 80300000 80400000 80500000
rs7442295 relation by 0–1–2 model

SNP located on chr chr4 at 9,966 MB. This SNP was imputed.

Identifying GWAS: Serum urate (17), TG (2)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- DRD5 (~181 kb)
- SLC2A9 (0 kb)
- WDR1 (110 kb)

Identifying GWAS: Serum urate (17), TG (2)

Identifying GWAS: Serum urate (17), TG (2)

Identifying GWAS: Serum urate (17), TG (2)
rs4846914 relation by 0–1–2 model
SNP located on chr chr1 at 230.3 MB. This SNP was imputed.
Identifying GWAS: HDL (8)

-log10(P)

GALNT2

PGBD5

expression level
• 1st quartile
● 2nd quartile
■ 3rd quartile
● 4th quartile

gene and distance to SNP
- GALNT2 (0 kb)
- PGBD5 (162 kb)

Identifying GWAS: HDL (8)

SNP located on chr chr1 at 230.3 MB. This SNP was imputed.
rs4939883 relation by 0–1–1 model

SNP located on chr chr18 at 47.17 MB. This SNP was measured on array.

Identifying GWAS: HDL (2, §)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- DYM (−180 kb)
- C18orf32 (−154 kb)
- MIR1539 (−153 kb)
- SNORD58B (−148 kb)
- RPL17 (−148 kb)
- SNORD58C (−152 kb)
- SNORD58A (−149 kb)
- LIPG (−48 kb)
- ACA2A (143 kb)
- SCARNA17 (173 kb)
- MYO5B (182 kb)
Identifying GWAS: Diastolic blood pressure (9)

SNP located on chr chr15 at 75.13 MB. This SNP was measured on array.

rs6495122 relation by 0–1–2 model

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- EDC3 (−137 kb)
- CYP1A1 (−108 kb)
- CYP1A2 (−77 kb)
- CSK (−30 kb)
- LMAN1L (−2 kb)
- CPLX3 (−2 kb)
- ULK3 (3 kb)
- SCAMP2 (10 kb)
- MPI (57 kb)
- C15orf17 (67 kb)
- COX5A (86 kb)
- RPP25 (122 kb)
- SCAMP5 (162 kb)
- PPCDC (190 kb)

Position

- 74900000 75000000 75100000 75200000 75300000

rs6495122

ASAP_MMed
ASAP_L
ASAP_AMed
ASAP_AAdv
bike_plaque_hgu133plus2

EDC3
CYP1A1
CYP1A2
CSK
LMAN1L
CPLX3
ULK3
SCAMP2
MPI
C15orf17
COX5A
RPP25
SCAMP5
PPCDC

- AA
- AC
- CC

−log10(P)
rs688 relation by 0–1–2 model

SNP located on chr chr19 at 11.23 Mb. This SNP was measured on array.

Identifying GWAS: LDL (7)
rs8003379 relation by 0–1–2 model

SNP located on chr chr14 at 64.87 MB. This SNP was measured on array.

Identifying GWAS: Abdominal Aortic Aneurysm (5)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- SYNE2 (−180 kb)
- ESR2 (−68 kb)
- MTHFD1 (0 kb)
- AKAP5 (59 kb)
- ZBTB25 (80 kb)
- ZBTB1 (98 kb)
- HSP A2 (129 kb)
- C14orf50 (143 kb)

SYNE2 (64400000 64600000 64800000 65000000 65200000 65400000)

ESR2

MTHFD1

AKAP5

ZBTB1

ZBTB25

HSP A2

C14orf50

position

64400000 64600000 64800000 65000000 65200000 65400000
rs1529729 relation by 0−1−2 model
SNP located on chr chr19 at 11.16 MB. This SNP was measured on array.
Identifying GWAS: LDL (7)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- C19orf38 (−183 kb)
- CARM1 (−130 kb)
- YIPF2 (−124 kb)
- C19orf52 (−123 kb)
- SMARCA4 (0 kb)
- LDLR (36 kb)
- SPC24 (93 kb)
- KANK2 (111 kb)
- DOCK6 (146 kb)
rs6961069 relation by 0–1–2 model

SNP located on chr chr7 at 80.22 MB. This SNP was measured on array.

Identifying GWAS: Left ventricular mass (1)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- CD36 (0 kb)
- GNAT3 (~78 kb)
- SEMA3C (153 kb)
<table>
<thead>
<tr>
<th>SNP</th>
<th>1 AA</th>
<th>20 AG</th>
<th>67 GG</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASAP_MMed</td>
<td>1 AA</td>
<td>34 AG</td>
<td>116 GG</td>
</tr>
<tr>
<td>ASAP_AMed</td>
<td>1 AA</td>
<td>28 AG</td>
<td>74 GG</td>
</tr>
<tr>
<td>ASAP_AAdv</td>
<td>1 AA</td>
<td>20 AG</td>
<td>69 GG</td>
</tr>
<tr>
<td>bike_plaque_hgu133plus2</td>
<td>1 AA</td>
<td>33 AG</td>
<td>72 GG</td>
</tr>
</tbody>
</table>

rs2271293 relation by 0−1−2 model
SNP located on chr16 at 67.9 MB. This SNP was measured on array.

Identifying GWAS: HDL (2, 8)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- C16orf86 (−199 kb)
- GFOD2 (−149 kb)
- RANBP10 (−62 kb)
- TSNAXIP1 (−40 kb)
- CENPT (−33 kb)
- THAP11 (−24 kb)
- NUTF2 (0 kb)
- EDC4 (5 kb)
- NRN1L (17 kb)
- PSKH1 (25 kb)
- CTRL (61 kb)
- PSMB10 (66 kb)
- LCAT (72 kb)
- SLC12A4 (76 kb)
- DPEP3 (107 kb)
- DPEP2 (119 kb)
- DDX28 (153 kb)
- DUS2L (155 kb)

expression levels (−log10(P))
1st quartile: 5.4
2nd quartile: 6.0
3rd quartile: 6.6
4th quartile: 7.2

Position (in kb)

<table>
<thead>
<tr>
<th>C16orf86</th>
<th>GFOD2</th>
<th>RANBP10</th>
<th>TSNAXIP1</th>
<th>CENPT</th>
<th>THAP11</th>
<th>NUTF2</th>
<th>EDC4</th>
<th>NRN1L</th>
<th>PSKH1</th>
<th>CTRL</th>
<th>PSMB10</th>
<th>LCAT</th>
<th>SLC12A4</th>
<th>DPEP3</th>
<th>DPEP2</th>
<th>DDX28</th>
<th>DUS2L</th>
</tr>
</thead>
<tbody>
<tr>
<td>67700000</td>
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</tr>
</tbody>
</table>

position
rs6487924 relation by 0−1−2 model

SNP located on chr12 at 30.79 MB. The rs10843803 which is in LD 1 was used as proxy.

Identifying GWAS: Waist-circumference (10), Waist-hip-ratio (10)

- log10(P)

<table>
<thead>
<tr>
<th>Sample</th>
<th>AA</th>
<th>AC</th>
<th>CC</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASAP_MMed</td>
<td>52 AA</td>
<td>32 AC</td>
<td>11 CC</td>
</tr>
<tr>
<td>ASAP_L</td>
<td>83 AA</td>
<td>57 AC</td>
<td>11 CC</td>
</tr>
<tr>
<td>ASAP_AMed</td>
<td>55 AA</td>
<td>39 AC</td>
<td>9 CC</td>
</tr>
<tr>
<td>ASAP_AAdv</td>
<td>48 AA</td>
<td>35 AC</td>
<td>7 CC</td>
</tr>
<tr>
<td>bike_plaque_hgu133plus2</td>
<td>69 AA</td>
<td>33 AC</td>
<td>4 CC</td>
</tr>
</tbody>
</table>

- Expression level
  - 1st quartile
  - 2nd quartile
  - 3rd quartile
  - 4th quartile

- Gene and distance to SNP
  - IPO8 (0 kb)
  - CAPRIN2 (77 kb)
Identifying GWAS: HDL (8)

SNP located on chr chr19 at 8.47 MB. This SNP was measured on array.
rs1004467 relation by 0−1–2 model
SNP located on chr chr10 at 104.6 MB. The rs17115100 which is in LD 1 was used as proxy.
Identifying GWAS: Systolic blood pressure (9, 12)

<table>
<thead>
<tr>
<th>SNP</th>
<th>Genotype Distribution</th>
<th>G</th>
<th>T</th>
<th>A</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASAP_M</td>
<td>GG TG TT</td>
<td>63</td>
<td>25</td>
<td>2</td>
</tr>
<tr>
<td>ASAP_L</td>
<td>GG TG TT</td>
<td>115</td>
<td>35</td>
<td>2</td>
</tr>
<tr>
<td>ASAP_AM</td>
<td>GG TG TT</td>
<td>76</td>
<td>25</td>
<td>2</td>
</tr>
<tr>
<td>ASAP_A</td>
<td>GG TG TT</td>
<td>68</td>
<td>21</td>
<td>1</td>
</tr>
<tr>
<td>bike_plaque_hgu133plus2</td>
<td>GG TG TT</td>
<td>89</td>
<td>16</td>
<td>1</td>
</tr>
</tbody>
</table>

expression level
• 1st quartile
• 2nd quartile
• 3rd quartile
• 4th quartile

gene and distance to SNP
- TRIM8 (−176 kb)
- ARL3 (−120 kb)
- SFXN2 (−96 kb)
- C10orf26 (−18 kb)
- CYP17A1 (0 kb)
- CYP17A1OS (0 kb)
- C10orf32 (19 kb)
- AS3MT (35 kb)
- CNNM2 (84 kb)

-10log10(P)
### rs1260326 relation by 0–1–2 model

SNP located on chr2 at 27,73 MB. This SNP was measured on array.

**Identifying GWAS: Tg (8)**

<table>
<thead>
<tr>
<th>Gene</th>
<th>Expression Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>UCN</td>
<td>1st quartile</td>
</tr>
<tr>
<td>MPV17</td>
<td>2nd quartile</td>
</tr>
<tr>
<td>GTF3C2</td>
<td>3rd quartile</td>
</tr>
<tr>
<td>EIF2B4</td>
<td>4th quartile</td>
</tr>
</tbody>
</table>

- **SNP measured on array:**
  - **ASAP_MMed**
    - CC: 39
    - TC: 42
    - TT: 7
  - **ASAP_L**
    - CC: 63
    - TC: 72
    - TT: 16
  - **ASAP_AMed**
    - CC: 44
    - TC: 47
    - TT: 12
  - **ASAP_AAdv**
    - CC: 36
    - TC: 46
    - TT: 8

**Gene and Distance to SNP**

- **UCN (−200 kb)**
- **MPV17 (−182 kb)**
- **GTF3C2 (−151 kb)**
- **EIF2B4 (−138 kb)**
- **SNX17 (−131 kb)**
- **ZNF513 (−127 kb)**
- **PPM1G (−98 kb)**
- **FTHL3 (−115 kb)**
- **NRBP1 (−66 kb)**
- **KRTCAP3 (−62 kb)**
- **IFT172 (−18 kb)**
- **FND4C (−13 kb)**
- **GCKR (0 kb)**
- **ZNF512 (75 kb)**
- **CCDC121 (118 kb)**
- **SUPT7L (143 kb)**
- **SLC4A1AP (155 kb)**

**Position**

- rs1260326

---

**Diagram:**

- **Expression Level:**
  - 1st quartile
  - 2nd quartile
  - 3rd quartile
  - 4th quartile

- **Genes and Distance:**
  - UCN (−200 kb)
  - MPV17 (−182 kb)
  - GTF3C2 (−151 kb)
  - EIF2B4 (−138 kb)
  - SNX17 (−131 kb)
  - ZNF513 (−127 kb)
  - PPM1G (−98 kb)
  - FTHL3 (−115 kb)
  - NRBP1 (−66 kb)
  - KRTCAP3 (−62 kb)
  - IFT172 (−18 kb)
  - FND4C (−13 kb)
  - GCKR (0 kb)
  - ZNF512 (75 kb)
  - CCDC121 (118 kb)
  - SUPT7L (143 kb)
  - SLC4A1AP (155 kb)

---

**Gene List:**

- **rs1260326 relation by 0–1–2 model**
- SNP located on chr2 at 27,73 MB. This SNP was measured on array.
rs157580 relation by 0–1–2 model
SNP located on chr chr19 at 45.4 MB. This SNP was measured on array.
Identifying GWAS: LDL (2), TG (2), Total cholesterol (2)
SNP located on chr chr5 at 56.35 MB. This SNP was imputed.

Identifying GWAS: Left ventricular mass (1)

rs6450415 relation by 0–1–2 model
rs1801133 relation by 0−1−2 model

SNP located on chr chr1 at 11.86 MB. This SNP was measured on array.

Identifying GWAS: Abdominal Aortic Aneurysm (5)

expression level
● 1st quartile
● 2nd quartile
● 3rd quartile
● 4th quartile

gene and distance to SNP
- FBXO2 (−141 kb)
- FBXO44 (−133 kb)
- FBXO6 (−122 kb)
- MAD2L2 (−105 kb)
- C1orf187 (−70 kb)
- AGTRAP (−42 kb)
- C1orf167 (−7 kb)
- MTHFR (0 kb)
- CLCN6 (10 kb)
- NPPAAS (45 kb)
- NPPA (49 kb)
- NPPB (61 kb)
- RNU5E (112 kb)
- KIAA2013 (115 kb)
- PLOD1 (138 kb)
- MFN2 (184 kb)

position

rs1801133

−log10(P)

ASAP_MMed
49 CC // 32 TC // 7 TT

ASAP_L
76 CC // 66 TC // 9 TT

ASAP_AMed
58 CC // 37 TC // 8 TT

ASAP_AAdv
50 CC // 33 TC // 7 TT

bike_plaque_hgu133plus2
48 CC // 48 TC // 10 TT

FBXO2
●

FBXO44
●

FBXO6
●

MAD2L2
●

C1orf187
●

AGTRAP
●

C1orf167
●

MTHFR
●

CLCN6
●

NPPAAS
●

NPPA
●

NPPB
●

RNU5E
●

KIAA2013
●

PLOD1
●

MFN2
●

CLCN6
●

NPPAAS
●

NPPA
●

NPPB
●

RNU5E
●

KIAA2013
●

PLOD1
●

MFN2
●

rs1801133

11700000 11800000 11900000 12000000

FBXO2

1st quartile
2nd quartile
3rd quartile
4th quartile
rs238688 relation by 0−1−2 model

SNP located on chrchr20 at 3.526 Mb. This SNP was imputed.

Identifying GWAS: Left ventricular mass (1)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- C20orf194 (−137 kb)
- UBE2V1P1 (−183 kb)
- ATRN (0 kb)
- SF3A3P1 (−54 kb)
- GFRA4 (114 kb)
- ADAM33 (123 kb)
- SIGLEC1 (142 kb)
- HSPA12B (188 kb)
rs16948048 relation by 0−1−2 model
SNP located on chr chr17 at 47.44 MB. This SNP was imputed.

Identifying GWAS: Diastolic blood pressure (12)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- B4GALNT2 (−193 kb)
- GNGT2 (−154 kb)
- ABI3 (−140 kb)
- PHOSPHO1 (−132 kb)
- ZNF652 (−1 kb)
- PHB (41 kb)
- NGFR (132 kb)

B4GALNT2
GNGT2
ABI3
PHOSPHO1
ZNF652
PHB
NGFR

position
47200000 47300000 47400000 47500000 47600000
rs10468017 relation by 0–1–2 model

SNP located on chr chr15 at 58.68 MB. This SNP was measured on array.

Identifying GWAS: HDL (8)

-\log_{10}(P)

ASAP_MMed
46 CC // 36 TC // 6 TT

ASAP_L
81 CC // 55 TC // 14 TT

ASAP_AMed
52 CC // 39 TC // 11 TT

ASAP_AAdv
47 CC // 32 TC // 10 TT

bike_plaque_hgu133plus2
54 CC // 43 TC // 19 TT

---

gene and distance to SNP

expression level

- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

LIPC (24 kb)

---

LIPC
rs964184 relation by 0–1–2 model

SNP located on chr chr11 at 116.6 MB. This SNP was measured on array.

Identifying GWAS: HDL (8), TG (8)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- BUD13 (−5 kb)
- ZNF259 (0 kb)
- APOA5 (11 kb)
- APOA4 (43 kb)
- APOC3 (52 kb)
- APOA1 (58 kb)
- SIK3 (65 kb)

116400000 116500000 116600000 116700000 116800000 116900000

-\log_{10}(P)
rs756529 relation by 0−1−2 model

SNP located on chr chr20 at 48.01 MB. This SNP was imputed.

Identifying GWAS: Left ventricular mass (1)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- DDX27 (−150 kb)
- ZNFX1 (−116 kb)
- C20orf199 (−105 kb)
- SNORD12C (−115 kb)
- MIR1259 (−114 kb)
- SNORD12B (−114 kb)
- SNORD12 (−114 kb)
- KCNB1 (0 kb)
- PTGIS (113 kb)
rs6429082 relation by 0–1–2 model

SNP located on chr chr1 at 235.6 MB. This SNP was imputed.

Identifying GWAS: Waist-circumreference (10)

-log10(P)

ARID4B
GGPS1
TBCE
B3GALNT2
GNG4

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- ARID4B (−109 kb)
- GGPS1 (−92 kb)
- TBCE (0 kb)
- B3GALNT2 (13 kb)
- GNG4 (111 kb)
rs6922269 relation by 0−1−2 model
SNP located on chr chr6 at 151.3 MB. This SNP was measured on array.
Identifying GWAS: MI (11, 14)
rs2304130 relation by 0–1–2 model

SNP located on chr chr19 at 19.79 MB. This SNP was measured on array.

Identifying GWAS: Total cholesterol (2)

**expression level**
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

**gene and distance to SNP**
- GATAD2A (−170 kb)
- TSSK6 (−163 kb)
- YJEFN3 (−141 kb)
- NDUFA13 (−141 kb)
- CILP2 (−132 kb)
- PBX4 (−60 kb)
- LPAR2 (−50 kb)
- GMIP (−35 kb)
- ATP13A1 (−15 kb)
- ZNF101 (0 kb)
- ZNF14 (32 kb)
- ZNF506 (107 kb)
- ZNF253 (187 kb)
- ZNF93 (187 kb)
- ZNF486 (187 kb)
- ZNF90 (187 kb)

---

Identifying GWAS: Total cholesterol (2)

SNP located on chr chr19 at 19.79 MB. This SNP was measured on array.

Identifying GWAS: Total cholesterol (2)
rs1378942 relation by 0–1–2 model

SNP located on chr chr15 at 75.08 MB. This SNP was measured on array.

Identifying GWAS: Diastolic blood pressure (12)

expression level
● 1st quartile
● 2nd quartile
● 3rd quartile
● 4th quartile

gene and distance to SNP
- ARID3B (−187 kb)
- CLK3 (−155 kb)
- EDC3 (−89 kb)
- CYP1A1 (−59 kb)
- CYP1A2 (−28 kb)
- CSK (0 kb)
- LMAN1L (28 kb)
- CPLX3 (42 kb)
- ULK3 (51 kb)
- SCAMP2 (59 kb)
- MPI (105 kb)
- C15orf17 (115 kb)
- COX5A (135 kb)
- RPP25 (170 kb)

Identifying GWAS: Diastolic blood pressure (12)
Identifying GWAS: HDL (2)

SNP located on chr chr15 at 58.68 MB. This SNP was measured on array.
rs6987702 relation by 0–1–2 model

SNP located on chr chr8 at 126.5 MB. This SNP was measured on array.

Identifying GWAS: Total cholesterol (2)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- NSMCE2 (~125 kb)
- TRIB1 (~54 kb)
rs780094 relation by 0−1−2 model

SNP located on chr chr2 at 27.74 MB. This SNP was measured on array.

Identifying GWAS: TG (17)
rs805412 relation by 0–1–2 model

SNP located on chr2 at 54.12 MB. This SNP was imputed.

Identifying GWAS: Waist–hip–ratio (10)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- ASB3 (−34 kb)
- CHAC2 (−118 kb)
- ERLEC1 (−75 kb)
- GPR75 (−34 kb)
- PSME4 (0 kb)

Identifying GWAS: Waist–hip–ratio (10)

SNP located on chr2 at 54.12 MB. This SNP was imputed.

Identifying GWAS: Waist–hip–ratio (10)
rs7970350 relation by 0−1−2 model
SNP located on chr12 at 66.36 MB. This SNP was imputed.
Identifying GWAS: Waist-circumference (10)
rs12993133 relation by 0−1−2 model

SNP located on chr2 at 10.85 MB. This SNP was imputed.

Identifying GWAS: Waist-circumference (10), Waist-hip-ratio (10)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- NOL10 (~16 kb)
- ATP6V1C2 (16 kb)
- PDIA6 (77 kb)

Identifying GWAS: Waist-circumference (10), Waist-hip-ratio (10)
rs653178 relation by 0−1−2 model
SNP located on chr chr12 at 112 MB. This SNP was measured on array.

Identifying GWAS. Diastolic blood pressure (12, 9)
rs17216525 relation by 0–1–1 model
SNP located on chr chr19 at 19.66 MB. This SNP was imputed.
Identifying GWAS: TG (8)

expression level
• 1st quartile
• 2nd quartile
• 3rd quartile
• 4th quartile

gene and distance to SNP
- KIAA0892 (−193 kb)
- GATAD2A (−42 kb)
- MIR640 (−116 kb)
- TSSK6 (−35 kb)
- YJEFN3 (−14 kb)
- NDUFA13 (−14 kb)
- CILP2 (−5 kb)
- PBX4 (10 kb)
- LPAR2 (72 kb)
- GMIP (78 kb)
- ATP13A1 (94 kb)
- ZNF101 (117 kb)
- ZNF14 (159 kb)

19500000 19600000 19700000 19800000 19900000

position
rs2245667 relation by 0–1–2 model

SNP located on chr 8 at 17.46 MB. This SNP was imputed.

Identifying GWAS: Waist-circumference (10)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- MTMR7 (~190 kb)
- SLC7A2 (~33 kb)
- PDGFRL (0 kb)
- MTUS1 (40 kb)

17200000 17300000 17400000 17500000 17600000 17700000

position
rs2083637 relation by 0–1–2 model
SNP located on chr chr8 at 19.87 MB. This SNP was measured on array.
Identifying GWAS: HDL (2), TG (2)
rs1532624 relation by 0–1–2 model
SNP located on chr chr16 at 57.01 MB. This SNP was measured on array.

Identifying GWAS: HDL (2)

expression level
• 1st quartile
• 2nd quartile
• 3rd quartile
• 4th quartile

gene and distance to SNP
- NUP93 (−127 kb)
- MIR138−2 (−113 kb)
- SLC12A3 (−56 kb)
- HERPUD1 (−28 kb)
- CETP (0 kb)
- NLRC5 (18 kb)
- CPNE2 (121 kb)
- FAM192A (181 kb)

Identifying GWAS: HDL (2)

SNP located on chr chr16 at 57.01 MB. This SNP was measured on array.

Identifying GWAS: HDL (2)

expression level
• 1st quartile
• 2nd quartile
• 3rd quartile
• 4th quartile

gene and distance to SNP
- NUP93 (−127 kb)
- MIR138−2 (−113 kb)
- SLC12A3 (−56 kb)
- HERPUD1 (−28 kb)
- CETP (0 kb)
- NLRC5 (18 kb)
- CPNE2 (121 kb)
- FAM192A (181 kb)
Identifying GWAS: Aortic root size (16)

rs17470137 relation by 0−1−2 model

SNP located on chr 5 at 122.5 MB. The rs17469907 which is in LD 1 was used as proxy.

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile
gene and distance to SNP
- SNX24 (−186 kb)
- PPIC (−159 kb)
- PRDM6 (−8 kb)
- CEP120 (149 kb)
rs819146 relation by 0−1−2 model

SNP located on chr chr20 at 32,89 MB. The rs819163 which is in LD 1 was used as proxy.

Identifying GWAS: Abdominal Aortic Aneurysm (5)

-log10(P)
rs2075650 relation by 0–1–2 model

SNP located on chr chr19 at 45.4 MB. This SNP was measured on array.

Identifying GWAS: Total cholesterol (2)
rs17367504 relation by 0–1–1 model

SNP located on chr chr1 at 11.86 MB. This SNP was measured on array.

Identifying GWAS: Systolic blood pressure (12)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- FBXO2 (−147 kb)
- FBXO44 (−139 kb)
- FBXO6 (−128 kb)
- MAD2L2 (−111 kb)
- C1orf187 (−77 kb)
- AGTRAP (−48 kb)
- C1orf167 (−13 kb)
- MTHFR (0 kb)
- CLCN6 (3 kb)
- NPPAAS (38 kb)
- NPPA (43 kb)
- NPPB (55 kb)
- RNU5E (105 kb)
- KIAA2013 (108 kb)
- PLOD1 (131 kb)
- MFN2 (177 kb)
SNP located on chr chr1 at 237.1 MB. The rs946934 which is in LD 1 was used as proxy.

Identifying GWAS: Abdominal Aortic Aneurysm (5)

rs2853523 relation by 0−1−2 model

Identifying GWAS: Abdominal Aortic Aneurysm (5)

rs2853523 relation by 0−1−2 model

Identifying GWAS: Abdominal Aortic Aneurysm (5)
SNP located on chr2 at 44.07 MB. This SNP was measured on array.
rs17608766 relation by 0–1–2 model

SNP located on chr chr17 at 45.01 Mb. This SNP was measured on array.

Identifying GWAS: Aortic root size (16)

-log10(P)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- NSF (−178 kb)
- WNT3 (−117 kb)
- WNT9B (−51 kb)
- GOSR2 (0 kb)
- RPRML (42 kb)
- CDC27 (182 kb)
rs2650000 relation by 0-1-2 model

-log10(P)

ASAP_MMed
34 GG // 33 TG // 21 TT

ASAP_L
53 GG // 70 TG // 27 TT

ASAP_AMed
38 GG // 48 TG // 17 TT

ASAP_AAdv
30 GG // 41 TG // 18 TT

bike_plaque_hgu133plus2
36 GG // 55 TG // 15 TT

HNF1A

C12orf43

OASL

P2RX7

Identifying GWAS: LDL (8)

SNP located on chr12 at 121.4 Mb. This SNP was measured on array.

expression level

1st quartile
2nd quartile
3rd quartile
4th quartile

gene and distance to SNP

HNF1A (27 kb)
C12orf43 (52 kb)
OASL (69 kb)
P2RX7 (182 kb)
rs3890182 relation by 0–1–2 model
SNP located on chr chr9 at 107.6 MB. The rs3847303 which is in LD 1 was used as proxy.

Identifying GWAS: LDL (7)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile
gene and distance to SNP
- OR13D1 (−190 kb)
- NIPSNAP3A (−125 kb)
- NIPSNAP3B (−108 kb)
- ABCA1 (0 kb)
rs89107 relation by 0−1−2 model

SNP located on chr chr6 at 118.6 MB. This SNP was measured on array.

Gene: SLC35F1

Position: 118300000 - 118900000

Expression level:
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

Gene and distance to SNP:
- SLC35F1 (0 kb)

Identifying GWAS: Internal diastolic dimensions (16)

ASAP_MMed
- 20 AA // 43 AG // 25 GG

ASAP_L
- 37 AA // 73 AG // 25 GG

ASAP_AMed
- 30 AA // 53 AG // 20 GG

ASAP_AAdv
- 23 AA // 47 AG // 20 GG

bike_plaque_hgu133plus2
- 32 AA // 54 AG // 20 GG
rs1883025 relation by 0–1–2 model
SNP located on chr chr9 at 107.7 MB. This SNP was imputed.
Identifying GWAS: HDL (8)
rs12654264 relation by 0–1–2 model

SNP located on chr chr5 at 74.65 MB. This SNP was imputed.
Identifying GWAS: LDL (7)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- ANKRD31 (−116 kb)
- HMGCR (0 kb)
- COL4A3BP (18 kb)
- POLK (159 kb)
rs10401969 relation by 0−1−2 model

SNP located on chr chr19 at 19.41 MB. This SNP was imputed.

Identifying GWAS: LDL (8)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- SLC25A42 (−184 kb)
- TMEM161A (−158 kb)
- MEF2B (−104 kb)
- RFXANK (−95 kb)
- NR2C2AP (−93 kb)
- NCAN (−45 kb)
- HAPLN4 (−34 kb)
- TM6SF2 (−24 kb)
- SF4 (0 kb)
- KIAA0892 (24 kb)
- GATAD2A (89 kb)
- MIR640 (138 kb)

position

rs10401969

80,000
100,000
120,000
140,000
160,000
180,000
200,000

19200000 19300000 19400000 19500000 19600000
Identifying GWAS: Diastolic blood pressure (12.9)

SNP located on chr chr3 at 169.2 MB. The rs6779380 which is in LD 1 was used as proxy.

- **MECOM**

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- MECOM (~179 kb)
rs10096633 relation by 0–1–2 model

SNP located on chr chr8 at 19.83 Mb. This SNP was measured on array.
Identifying GWAS: HDL (2), TG (2)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- INTS10 (~121 kb)
- LPL (~6 kb)
- SLC18A1 (171 kb)
rs1122608 relation by 0−1−2 model

SNP located on chr chr19 at 11,16 MB. This SNP was imputed.

Identifying GWAS: MI (11)
rs3788205 relation by 0–1–2 model

SNP located on chr chr21 at 46.96 MB. This SNP was measured on array.

Identifying GWAS: Abdominal Aortic Aneurysm (S)

rs3788205 / COL18A1 / NCRNA00175 / SLC19A1 / PCBP3

-log10(P)

expression level

1st quartile
2nd quartile
3rd quartile
4th quartile

gene and distance to SNP

COL18A1 (~31 kb)
NCRNA00175 (~119 kb)
SLC19A1 (0 kb)
PCBP3 (99 kb)

COL18A1
NCRNA00175
PCBP3
SLC19A1

rs3788205

position

46600000
46800000
47000000
47200000
rs2259816 relation by 0–1–2 model

SNP located on chr chr12 at 121.4 MB. The rs735396 which is in LD 1 was used as proxy.

Identifying GWAS: MI (4)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- HNF1A (0 kb)
- C12orf43 (5 kb)
- OASL (23 kb)
- P2RX7 (135 kb)
rs7543130 relation by 0–1–2 model

Identifying GWAS: Aortic root size (16)

SNP located on chr chr1 at 100 MB. This SNP was measured on array.

-log10(P)

|------|------------------------|-----------------------|-----------------------|-----------------------|-----------------------|

[Gene expression levels and distances to SNP]

expression level

- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP

- PALMD (62 kb)
- FRRS1 (124 kb)
Identifying GWAS: LDL

SNP located on chr chr16 at 57 MB. This SNP was measured on array.

rs1800775 relation by 0−1−2 model

expression level
1st quartile
2nd quartile
3rd quartile
4th quartile

gene and distance to SNP
NUP93 (−116 kb)
MIR138−2 (−103 kb)
SLC12A3 (−45 kb)
HERPUD1 (−17 kb)
CETP (1 kb)
NLRC5 (28 kb)
CPNE2 (131 kb)
FAM192A (191 kb)

position
56800000
56900000
57000000
57100000
57200000
rs1501908 relation by 0–1–2 model
SNP located on chr chr5 at 156.4 MB. This SNP was imputed.
Identifying GWAS: LDL (8)

expression level
● 1st quartile
● 2nd quartile
● 3rd quartile
● 4th quartile

gene and distance to SNP
PPP1R2P3 (−119 kb)
TIMD4 (−8 kb)
HAVCR1 (58 kb)
HAVCR2 (115 kb)
MED7 (166 kb)
FAM71B (191 kb)

PPP1R2P3
TIMD4
HAVCR1
HAVCR2
MED7
FAM71B

rs1501908

position
156200000 156300000 156400000 156500000 156600000

10−log10(P)

ASAP_MMed
ASAP_L
ASAP_AMed
ASAP_AAdv
bike_plaque_hgu133plus2

37 CC // 37 GC // 12 GG
60 CC // 71 GC // 18 GG
42 CC // 45 GC // 14 GG
33 CC // 45 GC // 10 GG
44 CC // 47 GC // 14 GG

1st quartile
2nd quartile
3rd quartile
4th quartile

PPP1R2P3 (−119 kb)
TIMD4 (−8 kb)
HAVCR1 (58 kb)
HAVCR2 (115 kb)
MED7 (166 kb)
FAM71B (191 kb)
rs7819412 relation by 0–1–2 model

SNP located on chr chr8 at 11.05 MB. The rs2409722 which is in LD 1 was used as proxy.

Identifying GWAS: TG (8)
rs10116277 relation by 0–1–2 model

SNP located on chr chr9 at 22.08 MB. This SNP was measured on array.
rs7395662 relation by 0–1–2 model

SNP located on chr chr11 at 48.52 MB. This SNP was measured on array.

Identifying GWAS: HDL (2)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- OR4S1 (−190 kb)
- OR4C3 (−169 kb)
- OR4C45 (−145 kb)
- OR4C2P (−76 kb)
- OR4C10P (−64 kb)
- OR4A47 (−8 kb)

SNP located on chr chr11 at 48.52 MB. This SNP was measured on array.

Identifying GWAS: HDL (2)
rs6892723 relation by 0−1−2 model

SNP located on chr5 at 157.2 MB. The rs1039322 which is in LD 1 was used as proxy.

Identifying GWAS: Waist-circumference (10)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- ADAM19 (−165 kb)
- SOX30 (−88 kb)
- C5orf52 (−60 kb)
- THG1L (0 kb)
- LSM11 (3 kb)
- CLINT1 (46 kb)
rs3846663 relation by 0–1–2 model

SNP located on chr chr5 at 74.66 MB. This SNP was imputed.

Identifying GWAS: LDL (8)

- ANKRD31
- HMGCR
- COL4A3BP
- POLK

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- ANKRD31 (~123 kb)
- HMGCR (0 kb)
- COL4A3BP (11 kb)
- POLK (152 kb)
rs11153768 relation by 0–1–2 model

SNP located on chr chr6 at 119 MB. This SNP was imputed.
Identifying GWAS: Internal diastolic dimensions (16)

C6orf204 (0 kb)
BRD7P3 (−163 kb)
PLN (−106 kb)
MCM9 (148 kb)
ASF1A (162 kb)
rs7557067 relation by 0–1–2 model
SNP located on chr chr2 at 21.21 MB. The rs6728178 which is in LD 1 was used as proxy.
Identifying GWAS: TG (8)

Identifying GWAS: TG (8)

C2orf43 (−185 kb) APOB (16 kb)

-Log10(P)

expression level
• 1st quartile
• 2nd quartile
• 3rd quartile
• 4th quartile

gene and distance to SNP
- C2orf43
- APOB

SNP located on chr chr2 at 21.21 MB. The rs6728178 which is in LD 1 was used as proxy.

Identifying GWAS: TG (8)
rs3846662 relation by 0–1–2 model

SNP located on chr5 at 74.65 MB. This SNP was measured on array.

Identifying GWAS: LDL (2), Total cholesterol (2)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- ANKRD31 (-118 kb)
- HMGCR (0 kb)
- COL4A3BP (16 kb)
- POLK (157 kb)

Identifying GWAS: LDL (2), Total cholesterol (2)
rs2954029 relation by 0−1−2 model

SNP located on chr chr at 126.5 MB. This SNP was imputed.

Identifying GWAS: TG (8)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- NSMCE2 (~112 kb)
- TRIB1 (~40 kb)

126200000 126400000 126600000 126800000

position

126200000 126400000 126600000 126800000

NSMCE2

TRIB1

Identifying GWAS: TG (8)
rs406796 relation by 0–1–2 model

SNP located on chr chr8 at 68.5 MB. This SNP was imputed.

Identifying GWAS: Waist–hip–ratio (10)
SNP located on chr chr12 at 111.9 MB. This SNP was measured on array.

Identifying GWAS: Diastolic blood pressure (9), Systolic blood pressure (9, 12)

rs3184504 relation by 0–1–2 model

<table>
<thead>
<tr>
<th>Gene</th>
<th>17 CC / 48 TC / 23 TT</th>
<th>37 CC / 74 TC / 40 TT</th>
<th>22 CC / 58 TC / 23 TT</th>
<th>19 CC / 47 TC / 24 TT</th>
<th>Bike plaque hgu133plus2</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASAP_MMed</td>
<td>17 CC / 48 TC / 23 TT</td>
<td>37 CC / 74 TC / 40 TT</td>
<td>22 CC / 58 TC / 23 TT</td>
<td>19 CC / 47 TC / 24 TT</td>
<td>Bike plaque hgu133plus2</td>
</tr>
<tr>
<td>ASAP_L</td>
<td>37 CC / 74 TC / 40 TT</td>
<td>22 CC / 58 TC / 23 TT</td>
<td>19 CC / 47 TC / 24 TT</td>
<td>Bike plaque hgu133plus2</td>
<td>Bike plaque hgu133plus2</td>
</tr>
<tr>
<td>ASAP_AMed</td>
<td>22 CC / 58 TC / 23 TT</td>
<td>19 CC / 47 TC / 24 TT</td>
<td>Bike plaque hgu133plus2</td>
<td>Bike plaque hgu133plus2</td>
<td>Bike plaque hgu133plus2</td>
</tr>
<tr>
<td>ASAP_AAdv</td>
<td>19 CC / 47 TC / 24 TT</td>
<td>Bike plaque hgu133plus2</td>
<td>Bike plaque hgu133plus2</td>
<td>Bike plaque hgu133plus2</td>
<td>Bike plaque hgu133plus2</td>
</tr>
</tbody>
</table>

- CUX2 (−96 kb)  
- FAM109A (−78 kb)  
- SH2B3 (0 kb)  
- ATXN2 (5 kb)  
- BRAP (195 kb)  

expression level:
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP:

- CUX2 (−96 kb)
- FAM109A (−78 kb)
- SH2B3 (0 kb)
- ATXN2 (5 kb)
- BRAP (195 kb)
rs11206510 relation by 0–1–2 model

SNP located on chr chr1 at 55.5 Mb. This SNP was measured on array.

Identifying GWAS: MI (11)

SNP located on chr chr1 at 55.5 Mb. This SNP was measured on array.

Identifying GWAS: MI (11)

Identifying GWAS: MI (11)

Identifying GWAS: MI (11)
rs2383207 relation by 0−1−2 model

SNP located on chr chr9 at 22.12 MB. This SNP was measured on array.

Identifying GWAS: MI (NA, 3)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- MTAP (−83 kb)
- C9orf53 (−148 kb)
- CDKN2A (−121 kb)
- CDKN2BAS (0 kb)
- CDKN2B (−107 kb)
rs381815 relation by 0−1−2 model

SNP located on chr chr11 at 16.9 MB. This SNP was imputed.

Identifying GWAS: Systolic blood pressure (9, 12)
rs4129218 relation by 0–1–2 model

SNP located on chr chr12 at 65.96 Mb. The rs4129217 which is in LD 1 was used as proxy.

Identifying GWAS: Left ventricular mass (1)

<table>
<thead>
<tr>
<th>SNP</th>
<th>Genotype Counts</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASAP_MMed</td>
<td>27 CC // 61 TT</td>
</tr>
<tr>
<td>ASAP_L</td>
<td>3 CC // 47 TT // 101 TT</td>
</tr>
<tr>
<td>ASAP_AMed</td>
<td>3 CC // 25 TT // 75 TT</td>
</tr>
<tr>
<td>ASAP_AAdv</td>
<td>2 CC // 24 TT // 64 TT</td>
</tr>
<tr>
<td>bike_plaque_hgu133plus2</td>
<td>1 CC // 33 TT // 72 TT</td>
</tr>
</tbody>
</table>

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- MSRB3 (~98 kb)
- RPSAP52 (193 kb)
rs3905000 relation by 0–1–2 model

SNP located on chr chr9 at 107.7 MB. This SNP was measured on array.

Identifying GWAS: HDL [2]

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- OR13D1 (−199 kb)
- NIPSNAP3A (−135 kb)
- NIPSNAP3B (−117 kb)
- ABCA1 (0 kb)

Identifying GWAS: HDL [2]

rs3905000 relation by 0–1–2 model

SNP located on chr chr9 at 107.7 MB. This SNP was measured on array.

Identifying GWAS: HDL [2]

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- OR13D1 (−199 kb)
- NIPSNAP3A (−135 kb)
- NIPSNAP3B (−117 kb)
- ABCA1 (0 kb)

Identifying GWAS: HDL [2]
rs409045 relation by 0–1–2 model
SNP located on chr chr5 at 34.63 MB. The rs377504 which is in LD 1 was used as proxy.

Identifying GWAS: Left ventricular mass (1)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- RAI14 (28 kb)

rs409045

-log10(P)
rs1833534 relation by 0−1−2 model
SNP located on chr chr5 at 162.8 MB. The rs17061586 which is in LD 1 was used as proxy.

Identifying GWAS: Left ventricular mass (1)

expression level
• 1st quartile
• 2nd quartile
• 3rd quartile
• 4th quartile

gene and distance to SNP

○ CCNG1 (44 kb)
○ NUDCD2 (60 kb)
○ HMMR (67 kb)
○ MAT2B (109 kb)
rs11970116 relation by 0–1–2 model
SNP located on chr chr6 at 55 MB. This SNP was imputed.

Identifying GWAS: Waist-circumference (10)

rs11970116

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- FAM83B (−193 kb)
- HCRTR2 (39 kb)
- GFRAL (192 kb)
rs4026608 relation by 0–1–2 model

SNP located on chr chr12 at 66.39 MB. This SNP was imputed.

Identifying GWAS: Aortic root size (16)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- RPSAP52 (−174 kb)
- HMGA2 (−35 kb)
- LLPH (122 kb)
- TMBIM4 (136 kb)
- IRAK3 (188 kb)
rs41290000 relation by 0–1–2 model
SNP located on chr12 at 65.95 MB. The rs4575324 which is in LD 1 was used as proxy.
Identifying GWAS: Left ventricular mass (1)

expression level
• 1st quartile
• 2nd quartile
• 3rd quartile
• 4th quartile

gene and distance to SNP
● MSRB3 (~93 kb)
● RPSAP52 (198 kb)
rs1530440 relation by 0−1−2 model

SNP located on chr chr10 at 63,52 MB. The rs751891 which is in LD 1 was used as proxy.

Identifying GWAS: Diastolic blood pressure (12)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- C10orf107 (0 kb)
- ARID5B (136 kb)
rs7575840 relation by 0–1–2 model

SNP located on chr chr2 at 21.27 MB. This SNP was imputed.

Identifying GWAS: LDL (8, 15)

APOB

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- APOB (~7 kb)

expression level

APOB

21240000 21260000 21280000 21300000 21320000

position

APOB

rs7575840

40 GG // 27 TG // 11 TT

62 GG // 33 TG // 15 TT

44 GG // 38 TG // 10 TT

39 GG // 32 TG // 7 TT

35 GG // 44 TG // 9 TT

bike_plaque_hgu133plus2

Identifying GWAS: LDL (8, 15)
rs714052 relation by 0−1−2 model

SNP located on chr chr7 at 72.86 MB. This SNP was measured on array.

Identifying GWAS: TG (8)

SNP: rs714052

Genes and distances to SNP:
- GTF2IRD2P: −171 kb
- POM121B: −148 kb
- NSUN5: −142 kb
- TRIM50: −123 kb
- FKBP6: −92 kb
- FZD9: −14 kb
- BAZ1B: 0 kb
- BCL7B: 86 kb
- TBL2: 119 kb
- MLXIPL: 143 kb

Expression levels:
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile
rs7048915 relation by 0–1–2 model

SNP located on chr9 at 4,206 Mb. This SNP was measured on array.

Identifying GWAS: MI (4)

- expression level
  - 1st quartile
  - 2nd quartile
  - 3rd quartile
  - 4th quartile

- gene and distance to SNP
  - GLIS3 (0 kb)

---

GLIS3

---

rs7048915

---

- ASAP_MMed
  - 4 AA // 30 AG // 54 GG

- ASAP_L
  - 6 AA // 51 AG // 94 GG

- ASAP_AMed
  - 1 AA // 32 AG // 70 GG

- ASAP_AAdv
  - 2 AA // 25 AG // 63 GG

- bike_plaque_hgu133plus2
  - 6 AA // 29 AG // 71 GG

---

- position
  - 3800000
  - 4000000
  - 4200000
  - 4400000
  - 4600000
rs673548 relation by 0−1−2 model
SNP located on chr chr2 at 21.24 MB. This SNP was measured on array.

Identifying GWAS: TG (2)

APOB

rs673548

expression level
• 1st quartile
• 2nd quartile
• 3rd quartile
• 4th quartile

gene and distance to SNP

APOB (0 kb)
rs6699397 relation by 0–1–2 model

SNP located on chr chr1 at 91.21 MB. The rs10922911 which is in LD 1 was used as proxy.

Identifying GWAS: Waist–hip–ratio (10)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- BARHL2 (−29 kb)
- ZNF644 (169 kb)
rs893817 relation by 0−1−2 model
SNP located on chr chr15 at 74,23 MB. This SNP was measured on array.

Identifying GWAS: Aortic root size (16)
rs6102059 relation by 0–1–2 model

SNP located on chr chr20 at 39,23 MB. This SNP was imputed.

Identifying GWAS: LDL (8)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- MAFB (86 kb)
rs7565161 relation by 0−1−2 model

SNP located on chr chr2 at 47.5 MB. This SNP was imputed.

Identifying GWAS: Left ventricular mass (16)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- TTC7A (~192 kb)
- CALM2 (~91 kb)
- C2orf61 (~113 kb)
- BCYRN1 (63 kb)
- EPCAM (77 kb)
- MIR559 (110 kb)
- MSH2 (135 kb)
rs11191548 relation by 0–1–2 model

SNP located on chr chr10 at 104.8 MB. The rs12411886 which is in LD 1 was used as proxy.

Identifying GWAS: Systolic blood pressure (12)

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expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- AS3MT (−185 kb)
- CNNM2 (−8 kb)
- NT5C2 (0 kb)
- INA (191 kb)
rs12670798 relation by 0–1–2 model

SNP located on chr7 at 21.61 MB. This SNP was measured on array.

Identifying GWAS: LDL (2), Total cholesterol (2)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- SP4 (~53 kb)
- MIR1183 (~97 kb)
- DNAH11 (0 kb)

SNP located on chr7 at 21.61 MB. This SNP was measured on array.

Identifying GWAS: LDL (2), Total cholesterol (2)
rs4977574 relation by 0−1−2 model
SNP located on chr chr9 at 22.1 MB. This SNP was measured on array.
Identifying GWAS: MI (NA, 3)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- MTAP (−66 kb)
- C9orf53 (−131 kb)
- CDKN2A (−103 kb)
- CDKN2BAS (0 kb)
- CDKN2B (−89 kb)

21800000 21900000 22000000 22100000 22200000 22300000 22400000
position

rs4977574

ASAP MMed
54 AA // 78 AG // 19 GG
ASAP AMed
40 AA // 46 AG // 17 GG
ASAP AAdv
29 AA // 46 AG // 17 GG
bike plaque hgu133plus2
33 AA // 56 AG // 17 GG

MT AP
C9orf53
CDKN2A
CDKN2BAS
CDKN2B

Identifying GWAS: MI (NA, 3)
rs6511720 relation by 0–1–2 model

SNP located on chr chr19 at 11.2 MB. This SNP was measured on array.

Identifying GWAS: LDL (8)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- CARM1 (~169 kb)
- YIPF2 (~163 kb)
- C19orf52 (~161 kb)
- SMARCA4 (~29 kb)
- LDLR (0 kb)
- SPC24 (54 kb)
- KANK2 (73 kb)
- DOCK6 (108 kb)
rs13116494 relation by 0–1–2 model
SNP located on chr4 at 183.8 MB. The rs13116598 which is in LD 1 was used as proxy.

Identifying GWAS: Waist–circumference (10)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- ODZ3 (−104 kb)
- DCTD (0 kb)
- WWC2 (195 kb)
rs6756629 relation by 0–1–2 model

SNP located on chr 2 at 44,07 MB. This SNP was measured on array.

Identifying GWAS: TG (2), Total cholesterol (2)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- PLEKHH2 (−70 kb)
- DYNC2LI1 (−28 kb)
- ABCG5 (0 kb)
- ABCG8 (1 kb)
- LRPPRC (49 kb)

PLEKHH2
DYNC2LI1
ABCG5
ABCG8
LRPPRC

rs6756629

1st quartile
2nd quartile
3rd quartile
4th quartile
rs1746048 relation by 0−1−2 model
SNP located on chr chr10 at 44.78 MB. This SNP was measured on array.
Identifying GWAS: MI (11)

expression level
● 1st quartile
● 2nd quartile
● 3rd quartile
● 4th quartile

gene and distance to SNP
● CXCL12 (90 kb)
rs17228212 relation by 0−1−2 model

SNP located on chr chr15 at 67,46 MB. The rs731874 which is in LD 1 was used as proxy.

Identifying GWAS: MI (11, 14)

SNP located on chr chr15 at 67.46 MB. The rs731874 which is in LD 1 was used as proxy.
rs12526453 relation by 0–1–2 model

Identifying GWAS: MI (11)

SNP located on chr chr6 at 12.93 Mb. This SNP was imputed.

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- PHACTR1 (0 kb)
rs10483186 relation by 0–1–2 model

SNP located on chr chr22 at 35.34 MB. The rs5755440 which is in LD 1 was used as proxy.

Identifying GWAS: Left ventricular mass (1)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP

ISX (122 kb)
rs2228671 relation by 0–1–2 model
SNP located on chr chr19 at 11.21 MB. This SNP was measured on array.

Identifying GWAS: Total cholesterol (2)
rs4737325 relation by 0–1–2 model

SNP located on chr chr8 at 72.62 MB. The rs10283242 which is in LD 1 was used as proxy.

Identifying GWAS: Waist-circumference (10)

MSC

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP

MSC (136 kb)
rs1078985 relation by 0–1–2 model

SNP located on chr chr3 at 30.69 MB. This SNP was measured on array.

Identifying GWAS: Abdominal Aortic Aneurysm (6)

TGFBR2 (0 kb)
GADL1 (77 kb)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP

TGFBR2
GADL1

Identifying GWAS: Abdominal Aortic Aneurysm (6)
rs4715215 relation by 0−1−2 model

SNP located on chr chr6 at 50.96 MB. The rs11759809 which is in LD 1 was used as proxy.

Identifying GWAS: Waist−hip−ratio (10)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- TFAP2B (−145 kb)
- RPS17P5 (−135 kb)
rs987237 relation by 0–1–2 model

Identifying GWAS: Waist-circumference (10), Waist-hip-ratio (10)

SNP located on chr chr6 at 50.8 MB. This SNP was measured on array.

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- TFAP2D (~62 kb)
- TFAP2B (0 kb)
- RPS17P5 (22 kb)
rs16998899 relation by 0–1–2 model

SNP located on chr chr20 at 17.26 MB. This SNP was measured on array.

Identifying GWAS: Waist–hip–ratio (10)
rs693 relation by 0−1−2 model

SNP located on chr chr2 at 21.23 MB. This SNP was measured on array.

Identifying GWAS: LDL (7, 2, 15)

APOB (0 kb)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP

APOB

Identifying GWAS: LDL (7, 2, 15)
rs12414558 relation by 0–1–2 model

SNP located on chr chr10 at 11.73 MB. The rs17150715 which is in LD 1 was used as proxy.

Identifying GWAS: Waist-circumference (10), Waist-hip-ratio (10)

SNP located on chr chr10 at 11.73 MB. The rs17150715 which is in LD 1 was used as proxy.

Identifying GWAS: Waist-circumference (10), Waist-hip-ratio (10)
rs12678919 relation by 0–1–2 model

SNP located on chr chr8 at 19.84 Mb. This SNP was measured on array.

Identifying GWAS: HDL (8), TG (8)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile
gene and distance to SNP
- INTS10 (~135 kb)
- LPL (~19 kb)
- SLC18A1 (~158 kb)

INTS10
LPL
SLC18A1
rs2059238 relation by 0–1–2 model

SNP located on chr chr16 at 78.26 MB. This SNP was imputed.
Identifying GWAS: Wall thickness (16)

- log10(P)

<table>
<thead>
<tr>
<th>Gene</th>
<th>ASAP_MMed</th>
<th>ASAP_L</th>
<th>ASAP_AMed</th>
<th>ASAP_AAdv</th>
</tr>
</thead>
</table>

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- CLEC3A (~193 kb)
- WWOX (0 kb)

Identifying GWAS: Wall thickness (16)

SNP located on chr chr16 at 78.26 MB. This SNP was imputed.
rs17321467 relation by 0−1−2 model

SNP located on chr10 at 7.038 MB. This SNP was imputed.
Identifying GWAS: Waist−hip−ratio (10)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- SFMBT2 (162 kb)
rs328 relation by 0–1–2 model

SNP located on chr chr8 at 19.82 MB. This SNP was imputed.

Identifying GWAS: HDL (7)
rs17482753 relation by 0–1–2 model
SNP located on chr chr8 at 19.83 MB. This SNP was imputed.

Identifying GWAS: TG (17)
rs202680 relation by 0−1−2 model

SNP located on chr chr11 at 49.22 MB. The rs202712 which is in LD 1 was used as proxy.

Identifying GWAS: Abdominal Aortic Aneurysm (5)

SNP located on chr chr11 at 49.22 MB. The rs202712 which is in LD 1 was used as proxy.
rs1800588 relation by 0–1–2 model

SNP located on chr 15 at 58,72 MB. This SNP was imputed.

Identifying GWAS: LDL (7)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- LIPC (0 kb)
- ADAM10 (164 kb)
rs2681472 relation by 0–1–2 model
SNP located on chr chr12 at 90.01 MB. This SNP was measured on array.

Identifying GWAS: Diastolic blood pressure (9)

expression level
- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP
- WDR51B (−89 kb)
- GALNT4 (−90 kb)
- ATP2B1 (0 kb)

Identifying GWAS: Diastolic blood pressure (9)
rs2681492 relation by 0−1−2 model

SNP located on chr chr12 at 90.01 MB. This SNP was measured on array.

Identifying GWAS: Systolic blood pressure (9, 12)

Identifying GWAS: Systolic blood pressure (9, 12)

expression level

- 1st quartile
- 2nd quartile
- 3rd quartile
- 4th quartile

gene and distance to SNP

- WDR51B (~93 kb)
- GALNT4 (~95 kb)
- ATP2B1 (0 kb)

WDR51B

GALNT4

ATP2B1

position

89800000 89900000 90000000 90100000 90200000

89800000 89900000 90000000 90100000 90200000

rs2681492

ASAP_MMed

67 AA // 21 AG

ASAP_L

118 AA // 33 AG

ASAP_AMed

85 AA // 18 AG

ASAP_AAdv

70 AA // 20 AG

bike_plaque_hgu133plus2

80 AA // 25 AG // 1 GG

89800000 89900000 90000000 90100000 90200000

WDR51B

GALNT4

ATP2B1

rs2681492

Identifying GWAS: Systolic blood pressure (9, 12)

SNP located on chr chr12 at 90.01 MB. This SNP was measured on array.

Identifying GWAS: Systolic blood pressure (9, 12)
rs515135 relation by 0–1–2 model

SNP located on chr chr2 at 21.29 MB. The rs541041 which is in LD 1 was used as proxy.

Identifying GWAS: LDL (8)

The gene expression and distance to SNP are shown below.

APOB (−19 kb)
References


