Network-Based Identification and Prioritization of Key Regulators of Coronary Artery Disease Loci

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Objective**—**Recent genome-wide association studies of coronary artery disease (CAD) have revealed 58 genome-wide significant and 148 suggestive genetic loci. However, the molecular mechanisms through which they contribute to CAD and the clinical implications of these findings remain largely unknown. We aim to retrieve gene subnetworks of the 206 CAD loci and identify and prioritize candidate regulators to better understand the biological mechanisms underlying the genetic associations.

Approach and Results**—**We devised a new integrative genomics approach that incorporated (1) candidate genes from the top CAD loci, (2) the complete genetic association results from the 1000 genomes-based CAD genome-wide association studies from the Coronary Artery Disease Genome Wide Replication and Meta-Analysis Plus the Coronary Artery Disease consortium, (3) tissue-specific gene regulatory networks that depict the potential relationship and interactions between genes, and (4) tissue-specific gene expression patterns between CAD patients and controls. The networks and top-ranked regulators according to these data-driven criteria were further queried against literature, experimental evidence, and drug information to evaluate their disease relevance and potential as drug targets. Our analysis uncovered several potential novel regulators of CAD such as *LUM* and *STAT3*, which possess properties suitable as drug targets. We also revealed molecular relations and potential mechanisms through which the top CAD loci operate. Furthermore, we found that multiple CAD-relevant biological processes such as extracellular matrix, inflammatory and immune pathways, complement and coagulation cascades, and lipid metabolism interact in the CAD networks.

Conclusions**—**Our data-driven integrative genomics framework unraveled tissue-specific relations among the candidate genes of the CAD genome-wide association studies loci and prioritized novel network regulatory genes orchestrating biological processes relevant to CAD. **(*Arterioscler Thromb Vasc Biol*. 2016;36:928-941. DOI: 10.1161/ATVBAHA.115.306725.)**

Key Words: coronary artery disease ■ gene expression ■ gene regulatory networks ■ genomics ■ genome-wide association study

Coronary artery disease (CAD) is a major cause of morbidity and mortality for both men and women in the Western world. Several clinical risk factors have long been associated with CAD, including high blood pressure, cigarette smoking, elevated low-density lipoprotein cholesterol, and diabetes mellitus, and randomized clinical studies have consistently shown a 30% to 40% reduction in CAD-related deaths by modifying these factors.[1–3] However, our ability to fully mitigate CAD remains limited because of the incomplete understanding of the molecular basis of CAD. CAD is highly heritable with genetic risk accounting for 40% to 60% of the susceptibility to CAD.[4] Empowered by the genomic technologies, a total of ≈206 CAD susceptibility loci (58 genome-wide significant and 148 suggestive) have been identified by human genome-wide association studies (GWAS).[5] The mechanisms of these loci/genes seem to be diverse. For example, genes involved in both lipid metabolism (*APOB*, *ABCG5-ABCG8*, *PCSK9*, *SORT1*, *ABO*, *LDLR*, *APOE*, and *LPA*) and blood pressure regulation (*CYP17A1-NT5C2*, *SH2B3*, *GUCY1A3*, *FES*, and *ZC3HC1*) are among the GWAS loci, providing molecular basis for the long-observed clinical importance of these intermediate clinical traits in CAD development.[5] However, for the majority of the remaining significant loci, there is a lack of understanding of their functional relevance and molecular mechanisms involved. In addition, together the 206 genetic loci explain ≈25% of the heritability, leaving a large proportion of the genetic heritability to be further explored.[6,7] These challenges make it difficult to translate the GWAS findings into clinical applications.

To address these challenges, various efforts have been made recently to decode CAD GWAS signals into pathways and gene networks through integrative systems

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Nonstandard Abbreviations and Acronyms

CAD	coronary artery disease
ECM	extracellular matrix
GWAS	genome-wide association studies
KD	key driver
KDA	key driver analysis

biology approaches.[8–11] The underlying concept emphasizes that instead of acting alone, disease genes interact through complex regulatory machinery that governs the overall genetic (and epigenetic) control of disease susceptibility.[12,13] Genetic variants of both strong and subtle effects (ie, loci reaching genome-wide significance and those that are well below the significance cutoff) can perturb parts of the regulatory network, termed subnetworks. Moreover, disease genes do not play equal roles in disease development, that is, some important genes tend to regulate more CAD genes than others do in the regulatory networks, as demonstrated in recent studies of CAD[8] and late-onset Alzheimer diseases.[14] These studies have unraveled many novel molecular pathways and gene subnetworks in addition to confirming previously known mechanisms, testifying to the power of utilizing context-specific (eg, tissues, drug treatments, and diet changes) regulatory networks in conjunction with genetic signals to retrieve the perturbed subnetworks. Subsequently, the key regulators in the networks can be captured based on the network topology.[8,9]

Despite the progress, none of these previous studies has focused on the top 206 CAD loci to more closely investigate their tissue-specific network properties and whether they coordinate their actions to affect specific biological functions. Furthermore, the fact that a majority of these top CAD loci only exhibit moderate effects on CAD points to a role of these loci as disease-modifying genes, rather than strong disease-determining genes.[6] From the point of view of clinical and therapeutic applications, it is perhaps more productive to identify potential central regulators that coordinate the actions of multiple genes affected by the top CAD loci. These central regulators, when perturbed, may elicit stronger effects on CAD, but can be missed by GWAS because of evolutionary constraints that eliminate common variants affecting the functions of the key regulators in the population.[8,9,15]

In this study, we device an integrative network approach that combines multiple types of CAD-related genomic data sets to examine the potential relationship and interactions between the candidate genes at these top CAD loci to better understand the molecular pathways involved in CAD pathogenesis, as well as to identify and prioritize key regulators in tissue-specific networks for CAD. By focusing on the top CAD candidate genes, we aim to (1) delineate the tissue-specific characteristics of CAD gene regulatory networks affected by the top loci, (2) highlight candidate key regulators for CAD, and (3) provide insights into the causal mechanisms of CAD loci/genes.

Materials and Methods

Materials and Methods are available in the online-only Data Supplement.

Results

Overview of the Analytic Pipeline

We designed and implemented an integrative genomics pipeline to pinpoint the gene networks of the top GWAS loci and potential regulators by integrating diverse genomic data sets and tools. The framework can be divided into 4 steps (Figure 1).

First, we retrieve 7 CAD candidate gene lists from GWAS based on different curation and gene mapping criteria (Figure 1A; full list in Table I in the online-only Data Supplement). Comprehensive curation of CAD candidate genes is important because mapping disease-associated loci to candidate genes is not straightforward.[16] The 7 gene lists include

CAD GWAS Gene List (n=145)

We downloaded the NHGRI GWAS catalog (https://www.genome.gov/26525384) and extracted candidate GWAS genes for phenotypes relevant to CAD including coronary heart disease, myocardial infarction, and coronary artery calcification with association $P<1e-5$.

CAD+C4D Gene List (n=239)

The above CAD GWAS list based on GWAS catalog was supplemented with additional candidate genes identified through the Coronary Artery Disease Genome Wide Replication and Meta-Analysis Plus the Coronary Artery Disease (CARDIoGRAM-C4D) study,[5] which was based on Metabochip data and therefore was not included in the GWAS catalog.

CAD GWAS No-Lipid Gene List (n=124)

Lipid metabolism genes were removed from the CAD GWAS gene list to prevent the lipid genes from overshadowing and diluting other novel mechanisms.[17]

CAD+C4D No-Lipid Gene List (n=149)

Similarly, lipid metabolism genes were removed from the CAD+C4D gene list to enable better exploration of novel mechanisms.

CAD+C4D Extend Gene List (n=559)

The above 4 CAD candidate lists were primarily based on chromosomal distance-based locus to gene mapping. As suggested by previous studies, disease loci may not affect their most adjacent genes but may function through long-range regulation of distant genes.[16,18] To address this concern, we used an alternative locus-gene mapping that is based on empirical evidence provided by expression quantitative trait loci from CAD-relevant tissues, as described by Braenne et al.[16] The expression quantitative trait loci studies included were retrieved from Genome-Wide Repository of Associations between single nucleotide polymorphisms and Phenotypes database,[19] Stockholm Atherosclerosis Gene Expression (STAGE)[20] study, a liver/adipose study,[21] Cardiogenics consortium monocyte/macrophages study,[22] RNA-sequencing study in blood,[23,24] and aortic endothelial cells study.[25]

CAD 1000G Gene List (n=257)

The CAD+C4D list was supplemented with additional candidate genes from the recent 1000 genomes study.[7]

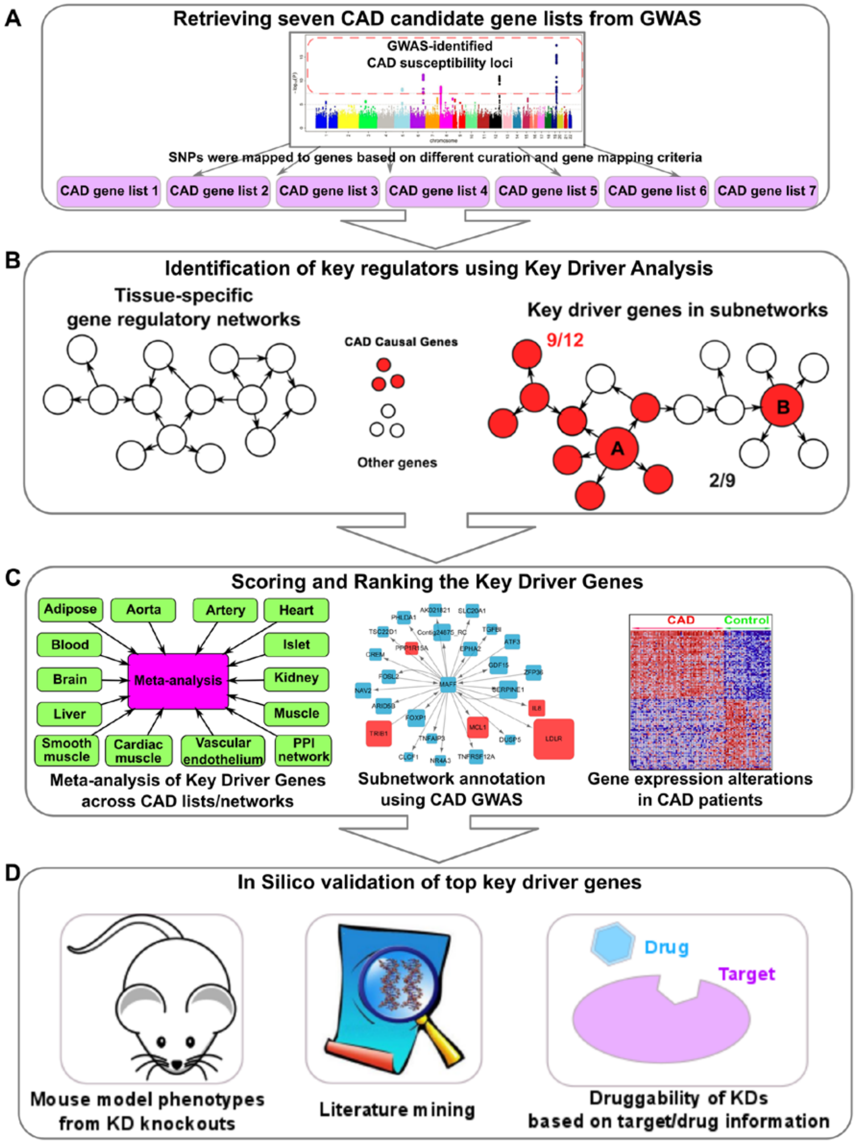

Figure 1. A framework for prioritizing coronary artery disease (CAD) genes using network-based approaches. The workflow contains 4 steps, including (**A**) retrieving CAD gene lists from genome-wide association studies (GWAS) and other functional studies, (**B**) key driver (KD) analysis, (**C**) scoring and ranking based on network consistency of KD analysis, GWAS gene annotation, and gene expression profiles between myocardial infarction and normal subjects, and (**D**) in silico validation.

CAD 1000G Extend Gene List (n=880)

We applied the same expression quantitative trait loci–based mapping to the CAD 1000G supplemented loci to map candidate genes as described for the CAD+C4D extended list.

Second, we perform the key driver analysis (KDA)[26–28] to identify potential network regulators, termed KDs of the CAD gene lists using 13 tissue-specific regulatory networks (adipose, aorta, artery, blood, brain, cardiac muscle, heart, islet, kidney, liver, skeletal muscle, smooth muscle, and vascular endothelium) and a protein–protein interaction network (Figure 1B; details of network construction in Supplemental Text in the online-only Data Supplement). We chose these tissues or network types because they are involved in CAD and related risk phenotypes. This step is essential for detecting the interactions and central orchestrators of the CAD genes.

Third, we evaluate the association strength between CAD and the predicted KDs as well as their direct partners in the gene subnetworks to confirm their relationship with CAD, based on 3 criteria: (1) the consistency of KDA performance for each KD across the 7 CAD gene lists and the 14 networks, (2) the CAD association strength of the KD subnetworks in CAD GWAS, and (3) tissue-specific gene expression pattern changes of the KD subnetworks between myocardial infarction and control subjects (Figure 1C). The KDs are scored and ranked based on these 3 data-driven criteria.

Finally, the associations between KDs and CAD are further validated using diverse bioinformatics databases and tools such as phenotypes from knockout mouse models, drug target databases, and literature mining (Figure 1D).

Identification of KD Genes in Tissue-Specific Networks

From the 98 sets of KDA (7 CAD lists × 14 networks), we detected a total of 287 KD genes at false discovery rate <0.05 (detailed KDs for each CAD gene set are listed in separate spreadsheets in Table II in the online-only Data Supplement), with 156 appearing in at least 2 KDA sets and 44 in at least 2 tissue-specific networks. Then, a meta-analysis, which considers both the consistency across the 98 sets of KDA analysis and the KDA statistics, was performed to derive meta P values for the KDs. This yielded 139 KDs with meta $P<0.01$(listed in the last spreadsheet in Table II in the online-only Data Supplement), among which 49 were captured by at least 3 networks and CAD gene lists and 22 were detected as multiple-tissue KDs (Table 1). Therefore, many of the KDs are less sensitive to the curation methods used to retrieve the top CAD GWAS candidate genes (ie, the 7 CAD gene lists) or the networks used in KDA.

We retrieved literature-based information about the KDs to assess their CAD relevance. Among the 139 KDs at meta $P<0.01$, 29 are within the 7 CAD candidate gene lists. These include *APOA1*, *GBP1*, *GBP2*, *PLG*, *VEGFA*, *COL4A2*, *KCNK13*, *CXCL12*, *ABCG5*, *APOC2*, *APOB*, *ADM*, *SLIT3*, *PHACTR1*, *OSM*, *LARGE*, *IRF1*, *APOA5*, *LDLR*, *KLF6*, *APOC4*, *FN1*, *HEMGN*, *APOC3*, *ABCG8*, *NME6*, *SHC1*, *THADA*, and *PTPN11*. There are 12 KDs satisfying GWAS significance of $P<5.0e{-}08$, including *PHACTR1*, *APOA1*, *APOA5*, *APOC3*, *LDLR*, *COL4A2*, *PTPN11*, *PLG*, *APOC2*, *APOC4*, *APOB*, and *CXCL12* in CARDIoGRAM or CAD 1000 genomes GWAS. Notably, many of these KDs are lipid genes, confirming the importance of lipid metabolism in CAD. We found that 61 of the 139 KDs, when genetically perturbed in knockout mouse models, showed phenotypes directly related to CAD or CAD risk phenotypes such as lipid level changes, hypertension, and obesity based on the Mouse Genome Informatics database (http://www.informatics.jax.org/), representing a significant enrichment for genes linked to CAD phenotypes (Fisher exact test $P=6.31e{-}16$, fold change=5.09). In addition, 23 of the 139 KDs were included in the CADgene V2.0 database,[29] which contains 583 CAD-related genes and detailed CAD association information from ≈5000 publications (Fisher exact test, $P=44.36e{-}13$; fold enrichment, 7.67). These lines of literature-based evidence support the relevance of the KDs to CAD.

Data-Driven Assessment of the Relevance of KDs and KD Subnetworks to CAD

To more objectively evaluate the CAD relevance of the KDs and their subnetworks, we used multiple data-driven approaches. The KD subnetworks are relatively independent (Figure I in the online-only Data Supplement). First, we utilized the 1000 Genomes–based CAD GWAS to assess the

Table 1. Top Multitissue KD Genes in Gene Regulatory and Protein–Protein Interaction Networks Ranked by KD Analysis Meta *P* Value Across CAD Gene Lists and Networks

KD	Ad	Ao	Ar	Bl	Br	CM	Ht	Is	Kd	Li	Mu	PP	SM	VE	Tissue Consist	List Consist	Meta *P* Values	KD *P* Values in 1000G CAD GWAS
DUSP6	0	2	2	0	0	3	0	0	0	0	0	0	6	2	5	15	1.35e–34	1.47e–03
DUSP1	0	1	6	0	0	0	0	0	0	0	0	0	4	0	3	11	2.77e–26	2.07e–03
KNG1	0	0	0	0	5	0	0	0	0	0	4	0	0	0	2	9	8.60e–15	2.65e–03
F2	5	0	0	0	0	0	0	0	0	0	4	0	0	0	2	9	4.22e–13	2.62e–04
APOA1	4	0	0	0	5	0	0	0	0	0	2	0	0	0	3	11	1.93e–09	5.60e–05
HGD	0	0	0	0	4	0	0	0	0	0	5	0	0	0	2	9	1.05e–08	4.15e–03
GBP1	2	0	0	2	0	0	0	0	0	0	0	0	0	2	3	6	3.41e–08	6.76e–04
GBP2	0	0	0	2	0	0	0	0	2	0	0	0	2	0	3	6	1.60e–07	6.76e–04
ANXA1	0	0	3	0	0	0	0	0	0	0	0	0	1	0	2	4	9.70e–07	9.12e–03
PLG	4	0	0	0	0	0	0	0	0	1	0	0	0	0	2	5	3.13e–06	2.88e–34
COL4A2	0	0	0	0	0	0	0	0	0	0	4	3	0	0	2	7	4.04e–06	1.83e–10
MSN	0	0	0	0	0	0	0	0	0	2	0	0	0	1	2	3	7.30e–06	1.00e+00
ANXA2	0	0	0	0	0	2	0	0	0	0	0	2	0	0	2	4	1.47e–05	3.43e–03
CXCL12	1	0	0	0	0	1	0	0	0	3	1	0	0	0	4	6	2.28e–05	2.95e–10
ABCG5	1	0	0	0	0	0	0	0	0	2	0	0	0	0	2	3	3.70e–05	1.35e–07
APOB	2	0	0	0	0	0	0	0	0	0	0	3	0	0	2	5	6.48e–05	3.09e–08
ADM	0	0	1	0	0	0	0	0	0	0	0	0	1	0	2	2	7.95e–05	2.77e–04
RDH16	0	0	0	0	2	0	0	0	0	0	2	0	0	0	2	4	0.000115	3.17e–03
PAPSS2	0	0	0	0	0	1	0	0	0	0	0	0	2	0	2	3	0.000136	4.68e–03
APOA5	0	0	0	0	1	0	0	0	0	2	0	0	0	0	2	3	0.0005	5.60e–05
FN1	0	0	0	0	0	0	0	0	1	0	0	3	0	0	2	4	0.000759	5.14e–07
IRF7	1	0	0	0	0	0	0	0	0	0	0	0	0	1	2	2	0.000912	8.68e–03

The numbers in each cell represent how many of the 7 CAD gene lists yielded the KD using the specific tissue network. Ad indicates adipose; Ao, aorta; Ar, artery; Bl, blood; Br, brain; CAD, coronary artery disease; CM, cardiac muscle; GWAS, genome-wide association studies; Ht, heart; Is, islet; Kd, kidney; KD, key driver; Li, liver; Mu, muscle; PP, protein–protein interaction; SM, smooth muscle; and VE, vascular endothelium networks.

overall enrichment of the KD subnetwork genes for stronger CAD association, as compared to subnetworks derived from random genes or those derived from the CAD top genes in our initial CAD lists (detailed in Materials and Methods in the online-only Data Supplement). Our results indicate that KD subnetworks tend to include stronger CAD GWAS signals than the subnetworks of random genes (Table III in the online-only Data Supplement) or those of the CAD top genes (Table 2; Table III in the online-only Data Supplement), supporting that KDs and their subnetworks may play more important roles in CAD development than the candidate genes of the top CAD loci. For example, 26.7% (12 of 45) of the member genes in the brain subnetwork of *LUM* had CAD GWAS $P<0.001$ in 1000 genome-based CAD GWAS. In contrast, the average percentages of genes showing CAD association at the same GWAS *P* value cutoff were much lower in the subnetworks of randomly selected genes (1.9%). The GWAS *P* value distribution of the *LUM* subnetwork genes was significantly different from random networks ($P<1.0e-16$ in 1-sided 2-sample Kolmogorov–Smirnov test) and those of the CAD top GWAS genes ($P=1.14e-3$). Similarly, for another KD example *KNG1*, 44.8% of the members in the KNG1 subnetwork in muscle had CAD GWAS $P<0.001$, in contrast to the much lower percentages for random genes (1.9%; $P<1.0e-16$ by Kolmogorov–Smirnov test) and CAD top GWAS genes (23.9%; $P=3.4e-3$). These results support that our data-driven systems biology approach that focuses on the aggregate behavior and properties of CAD genes in gene networks derives potentially stronger candidate genes than standard, individual locus-based methods.

Second, we hypothesize that if the KD subnetworks are important for CAD, the expression levels of the genes in the subnetworks are more likely to be perturbed in patients with CAD. To this end, we analyzed the expression profile alterations of the KD subnetworks between non-CAD subjects and patients with acute myocardial Infarction, in 10 CAD-relevant cell types or tissues, namely, endothelial cells, $CD34^+$ stem cells, $CD4^+$ T cells, resting $CD14^+$ monocytes, stimulated monocytes, peripheral blood mononuclear cells, whole blood, epicardial adipose tissue and subcutaneous adipose tissue, and macrophages. Among the 170 KD subnetworks of the 139 KDs (some KDs have subnetworks from multiple tissues), 58 and 81 showed significant up- or downregulation patterns in CAD versus controls in at least 1 cell type at false discovery rate <1% and false discovery rate <5%, respectively (Table IV in the online-only Data Supplement). Furthermore, 12 KD subnetworks were detected to be significantly perturbed in >2 cell types at false discovery rate <5%. For example, the *LUM* subnetwork was upregulated in CAD endothelial cells ($P<1.0e-16$; normalized enrichment score = 1.95), whereas down-regulated in resting $CD14^+$ monocytes ($P<1.0e-16$; normalized enrichment score = −1.68) and T cells ($P=1.92e-3$; normalized enrichment score = −1.18), with a meta *P* value of 1.38e−13 (Figure 2).

Scoring and Ranking of the KDs

We assigned a summary score to each KD according to the scores from measurements of KDA strength and consistency, subnetwork enrichment for 1000 genome-based CAD GWAS signals, and gene expression alterations between CAD and controls (top 20 genes are shown in Table 3). Based on the summary scores, the 10 top-ranked KDs are *LUM*, *COL1A1*, *DUSP6*, *HGD*, *MSN*, *CXCL12*, *DUSP1*, *GBP2*, *MTMR11*, and *CCL18*. It is reassuring that the ranking of most of these genes is consistent across the 3 scoring methods. For example, *LUM*, *COL1A1*, *HGD*, *MSN*, *CXCL12*, and *GBP2* are all within the top 40% in each of the 3 scoring schemes. Notably, none of the top 20 KDs was lipid-related genes although many lipid genes were among the 139 KDs.

In Silico Validation of the Top KD Genes

We conducted comprehensive bioinformatics mining of the 20 top-ranked KDs using various databases and tools. As summarized in Table 4, 8 of the top 20 genes have been linked to CAD or risk factors (eg, hypertension and diabetes) using at least one of the literature mining tools including PolySearch (http://www.wishart.biology.ualberta.ca/polysearch/), COREMINE (http://www.coremine.com/medical/), and Linguamatics (http://www.linguamatics.com/). *F2*, *SHC1*, and *CXCL12* have also been considered as CAD targets in drug development. The other genes including *LUM*, *LOXL2*, *ANXA3*, *SLC2A3*, *MSN*, *GBP2*, *CCL18*, *SLIT3*, *HGD*, and *STAT3* represent novel CAD genes uncovered from a data-driven approach, with *LUM*, *LOXL2*, *ANXA3*, *SLC2A3*, and *STAT3* suggested as potentially promising druggable targets based on drug databases DrugBank and Pharmaprojects as well as literature[30,31] (detailed in Materials and Methods in the online-only Data Supplement).

Biological Pathways and Networks of the Top KDs

We conducted pathway-enrichment analysis for the CAD subnetworks of the top 20 KDs using pathways curated in MSigDB to explore the potential biological mechanisms (details in Materials and Methods in the online-only Data Supplement). The top over-represented pathways for the subnetworks of the top KDs are shown in Table 5 and those for all the KD subnetworks are in Table V in the online-only Data Supplement. We found that the subnetworks of the top KDs are enriched in cardiovascular processes, including immune and inflammatory responses, coagulation, cell activation, and lipid metabolism (all Bonferroni-corrected $P<0.01$ in Fisher exact test), consistent with findings from another recent integrative genomic study that focused on the overall CAD GWAS instead of the top loci.[8] Notably, the subnetworks of 8 KDs, including *LUM*, *COL1A1*, *DUSP1*, *SLIT3*, *COL4A2*, *ANXA3*, and *SLC2A3*, were enriched for extracellular matrix (ECM) genes. ECM has been highlighted in recent integrative studies of both CVD and type 2 diabetes mellitus.[9,32]

We further explored the potential relationships between the top KDs and the CAD GWAS genes in gene regulatory networks. As shown in Figure 3, the top KDs and their subnetworks are closely connected, forming a large network linking multiple processes including complement and coagulation cascades, lipid metabolism, ECM, interferon signaling, focal adhesion, and JAK–STAT signaling. Importantly, the ECM genes constitute the center of the network and

Table 2. Top KDs Based on CAD GWAS Enrichment in the KD Subnetworks

KD	Subnetwork Size	No. of Genes With CAD 1000 Genomes GWAS *P*<0.001 in KD Subnetworks	Genes With CAD 1000 Genomes GWAS *P*<0.001 in KD Subnetworks	*P* Values Compared With GWAS Genes
SLIT3	28	11	*APOE, SLIT3, EPB41L2, NID1, FN1, TGFBR3, DOCK1, ADM, SCARA5, PROCR, THBS3*	<0.00114
AZGP1	23	8	*PLG, SLC22A1, UPB1, APOA5, AZGP1, ABCG5, CYP2A13, FBP1*	<0.00114
APOF	45	17	*PLG, APOC4, ITIH3, GLS2, APOB, APOA5, ARG1, APOF, AGXT, LIPC, ITIH4, MAT1A, PAH, PON1, CFI, APOC2, CYP2A13*	<0.00114
LDLR	11	7	*APOE, APOB, LRPAP1, LDLR, PCSK9, DAB1, AP1M2*	<0.00114
ACCN1	13	4	*LARGE, ACCN1, ITGA2, CYP17A1*	<0.00114
RIF1	11	2	*MALAT1, NBEAL1*	<0.00114
STAT3	102	35	*CDKN1A, PDGFRA, JUN, FGFR3, FLT1, CXCR4, RPS6KA5, BRCA1, HDAC3, STMN1, NLK, STAT5B, STAT3, ZNF467, MAP3K7, MTOR, NMI, RAC1, PML, KAT5, EIF2AK2, PRKCD, PTPN11, JAK3, FOXM1, PDGFRB, HNF1A, SUMO4, FES, IL2RA, IL6R, IGF1R, RELA, FER, ZNF148*	<0.00114
OAS2	12	4	*IFIT1, APOA4, OAS1, MMP12*	<0.00114
F2	Adipose (49); muscle (47)	Adipose (12); muscle (19)	Adipose (*PLG, SERPIND1, SEC14L2, APOC3, APOA5, APOA4, APOF, LIPC, PAH, AKR1C1, APOA1, F2*); Muscle (*PLG, SERPIND1, HPX, APOC3, ATP2A2, KLKB1, UPB1, TNNT1, APOA5, MYL2, ARG1, ASGR1, GNMT, MAT1A, PAH, AKR1C1, CFI, APOA1, F2*)	Adipose (0.0182); muscle (0.00114)
HGD	Brain (40); muscle (48)	Brain (8); muscle (12)	Brain (*PLG, APOC4, HPX, APOA5, APOF, PAH, AKR1D1, APOA1*); Muscle (*PLG, APOC4, CA5A, UROC1, APOC3, UPB1, APOB, APOA5, AGXT, MAT1A, CYP2A13, FBP1*)	Brain (0.00114); muscle (0.0136)
LUM	45	12	*CXCL12, COL3A1, TGFBR3, BMP6, FIBIN, TFPI, GBP1, ANXA4, SMOC2, SPOCK3, PCOLCE, ZFPM2*	0.00114
MTMR11	80	25	*DUSP8, ARHGAP22, ARL2BP, VCL, NRG1, SORBS2, TAGLN2, NID1, COL3A1, COL4A1, SMOX, SH2B3, ABCG5, MYO9B, FST, ARF5, HELLS, NUDT18, WFDC3, PDGFRB, SCD, SLC20A1, ST6GALNAC4, SGSM1, OTUD7B*	0.00114
COL1A1	73	23	*COL4A2, NCAM1, FBLN2, COL6A3, GINS2, TMSB10, ITGBL1, COL3A1, GAS6, COL4A1, LOXL4, WT1, SERPINH1, IGFBP2, CD163, PDGFRB, EFEMP2, MMP12, CCDC3, TREM2, EGR2, PCOLCE, LOXL1*	0.00114
CXCL12	Adipose (47); cardiac muscle (170); liver (30); muscle (36)	Adipose (10); cardiac muscle (54); liver (9); muscle (11)	Adipose (*PODXL, MMP3, CXCL12, TRERF1, KDR, SLC6A6, MRVI1, KLK10, SLC22A3, RAB19*); Cardiac_muscle (*CAV2, PYGL, HLA-DRA, COL4A2, ZCCHC24, CTGF, CXCL12, PPAP2B, ST5, GRK5, AXL, LRP1, NID1, ZCCHC14, PECAM1, SNED1, FGFR1, EPS8, WIPF1, VPS13D, PTRF, HLA-B, CRISPLD2, TMEM176A, NR2F2, COL4A1, LIPA, ZHX3, NPR1, CXCL1, SLC24A3, SFRP2, RHOQ, LPAR1, MYLK, RAB13, SGK1, CD302, FTO, PRCP, USP25, TRIB2, ZBTB20, PSD3, TIMP3, WIPI1, PCOLCE, LTBP1, LAMB2, GUCY1A3, LAMC1, ANGPT1, NFIB, KLC1*); Liver (*PLEKHA1, CXCL12, COL6A3, SLC2A1, RERG, SLC6A6, CUX2, HSD17B12, SFTPB*); Muscle (*COL4A2, AHR, PODXL, CXCL12, S100Z, SCUBE3, BRPF1, RNF213, ARHGDIB, CNIH3, OR4X2*)	Adipose (0.0534); cardiac muscle (0.0182); liver (0.00341); muscle (0.00114)
CFB	20	10	*PLG, APOC1, C3, APOA5, C4B, APOF, HP, CFI, APOC2, APOA1*	0.00114
APOC2	27	10	*APOC1, SLC22A1, APOC3, APOA5, AGT, CYP4F12, ARG1, ABCG5, APOF, APOC2*	0.00114
RDH16	Brain (43); muscle (36)	Brain (10); muscle (11)	Brain (*APOC4, SLC22A1, APOC3, KLKB1, MBL1P, APOA5, APOF, PON1, AKR1C1, CFI*); Muscle (*PLG, SEC14L2, APOC3, HAAO, APOB, ABCG5, C8G, APOA4, GNMT, CYP2A13, F2*)	Brain (0.0273); muscle (0.00114)
NGRN	32	10	*HDDC3, TRIM68, FURIN, KLHL25, RCCD1, SPC24, SLC22A3, MESDC1, APOC2, AKAP13*	0.00114
FN1	Kidney (16); PPI (75)	Kidney (3); PPI (21)	Kidney (*ERBB4, ADAM12, FN1*); PPI (*COL4A2, FBLN2, COL4A3, ITGB6, CXCL12, FSTL3, MMP9, GALNT6, FN1, COL7A1, COL4A1, SDC2, FST, LPA, FASLG, COL4A4, SMAD9, MEP1B, LTBP1, IGFBP5, FBLN1*)	Kidney (0.00114); PPI (0.0477)
NCOR2	12	7	*NCOR2, ACAD10, UBC, AACS, CUX2, PTPN11, VPS33A*	0.00114

The detailed information for all the KD genes is available in Table III in the online-only Data Supplement. CAD indicates coronary artery disease; GWAS, genome-wide association studies; KD, key driver; and PPI, protein–protein interaction.

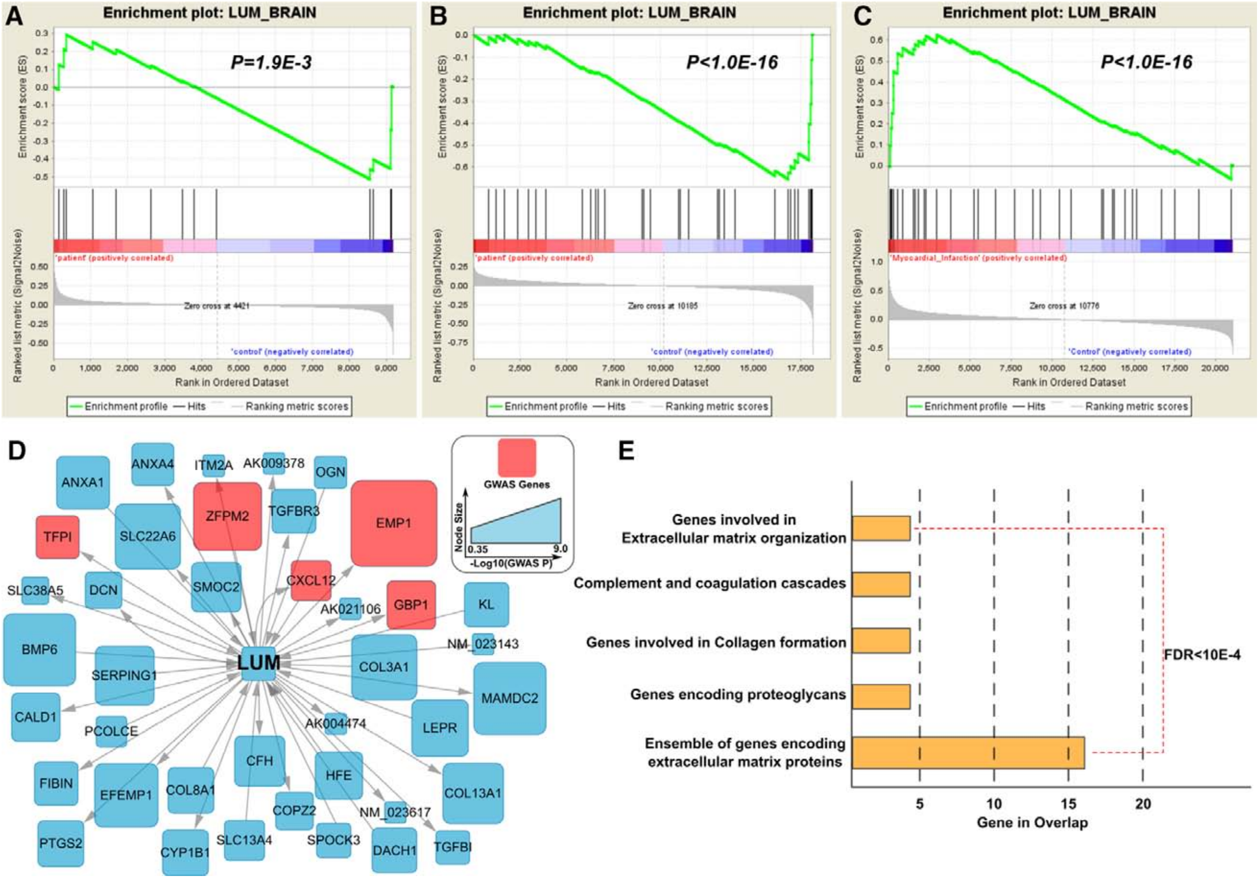

Figure 2. Gene expression perturbations of LUM subnetwork in brain tissue in myocardial infarction (MI) patients. The gene set enrichment analysis revealed significant gene expression perturbation in the LUM subnetwork in T cells (**A**), resting monocytes (**B**), and endothelial cells (**C**) in MI cases. Plots for the 7 nonsignificant cell or tissue types are not shown, but results are available in Table IV in the online-only Data Supplement. The red nodes in the LUM subnetwork (**D**) are coronary artery disease (CAD) genes from CAD extend list. Pathway analysis for the LUM subnetwork was performed using the Database for Annotation, Visualization and Integrated Discovery (DAVID), with all the pathways satisfying false discovery rate (FDR) <10e−4 (**E**).

connect with the other biological processes through tissue-specific interactions. In addition, although some KDs such as *COL4A2*, *CXCL12*, *SHC1*, *GBP2*, *GBP1*, and *SLIT3* are also top CAD GWAS genes, the majority of the CAD GWAS genes are not KDs but peripheral nodes interacting with one another through KDs in the network. This finding is consistent with our previous observations on the relationship between KDs and GWAS genes.[8,9] Furthermore, the KDs also bring together many additional CAD candidate genes curated in the CADgene database, which are not necessarily among the top CAD GWAS genes we have focused on but nevertheless provide additional support for the relevance of the KD subnetworks to CAD.

The convergence of our data-driven ranking and literature-based evidence supports the robustness of the top KDs, pathways, and networks revealed from our study. The data-driven summary scores provide an objective means to prioritize CAD genes for future studies, whereas the literature information can be used in flexible ways to further prioritize genes for different purposes. For instance, the data-driven score highlights *LUM* as the top-ranked CAD KD. In conjunction with information that it (1) has not been previously reported for CAD, (2) is druggable, (3) is a part of the ECM process that is supported by multiple KDs and also has known connection to CAD, and (4) is a part of a CAD subnetwork connecting with other CAD-relevant pathways, the potential novel role of Lum in CAD warrants further examination. If literature support for CAD involvement is considered important in prioritization, KDs *CXCL12* and *F2* can be ranked at the top because (1) extensive literature supports their connection to CAD and (2) they are known CAD drug target.

Discussion

The recent explosion in GWAS studies has contributed significantly to the identification of disease-associated genetic loci. However, the improved efficiency and accuracy in GWAS have not been translated into better biological insights and more effective therapeutic targets. As a result, incorporating other sources of evidence (such as gene regulation information and literature mining) is necessary to narrow down the candidate search space.[16,33] As summarized recently,[33] candidate disease genes can be prioritized through various computational methods, many of which carry the bias toward better characterized known genes for a given disease. In this study, we applied a data-driven approach by utilizing diverse tissue-specific regulatory networks and protein–protein interaction

Table 3. Top 20 KDs Based on an Overall Ranking Score Derived From 3 Data-Driven Criteria

KD	Meta *P* Value for KDA	*P* Value for GWAS Enrichment	Meta *P* Value for Differential Expression	Score 1 (KDA Strength and Consistency)	Score 2 (Subnetwork Enrichment for CARDIoGRAM-C4D GWAS Signals)	Score 3 (Gene Expression Alterations Between CAD and Controls)	Summary Score
LUM	5.74e–08	1.14e–03	1.38e–13	0.935	0.923	0.978	2.836
COL1A1	4.13e–06	1.14e–03	1.55e–05	0.848	0.923	0.819	2.590
DUSP6	1.35e–34	6.82e–03	1.00e–16	1.000	0.538	1.000	2.538
HGD	1.05e–08	1.14e–03	3.76e–02	0.957	0.923	0.616	2.496
MSN	7.30e–06	4.55e–03	4.44e–16	0.826	0.619	0.993	2.438
CXCL12	2.28e–05	1.14e–03	1.62e–02	0.797	0.923	0.652	2.372
DUSP1	2.77e–26	1.02e–02	2.46e–08	0.993	0.427	0.928	2.348
GBP2	1.60e–07	3.41e–03	9.42e–04	0.920	0.698	0.725	2.343
MTMR11	8.93e–07	1.14e–03	3.61e–01	0.913	0.923	0.486	2.322
CCL18	1.39e–06	9.09e–03	8.61e–11	0.877	0.474	0.949	2.300
SLIT3	2.04e–04	1.00e–03	2.44e–01	0.717	1.000	0.507	2.225
GBP1	3.41e–08	1.82e–02	1.05e–11	0.942	0.226	0.964	2.132
F2	4.22e–13	1.14e–03	9.53e–01	0.971	0.923	0.232	2.126
COL4A2	4.04e–06	5.68e–03	1.94e–03	0.855	0.582	0.688	2.126
LOXL2	1.68e–04	3.41e–03	2.96e–02	0.725	0.698	0.638	2.061
CXCL10	2.74e–04	1.02e–02	3.37e–12	0.659	0.427	0.971	2.058
ANXA3	3.06e–03	1.14e–03	7.02e–07	0.246	0.923	0.877	2.046
SLC2A3	2.74e–04	7.95e–03	4.76e–07	0.652	0.500	0.884	2.036
SHC1	4.26e–03	1.14e–03	1.32e–09	0.167	0.923	0.942	2.032
STAT3	3.50e–03	1.00e–03	3.27e–05	0.210	1.000	0.812	2.022

CAD indicates coronary artery disease; CARDIoGRAM-C4D, Coronary Artery Disease Genome Wide Replication and Meta-Analysis Plus the Coronary Artery Disease Consortium; KDA, key driver analysis; and GWAS, genome-wide association studies.

networks, which do not solely rely on previous knowledge about gene and protein functions. We found gene subnetworks that are concentrated with top CAD GWAS genes and identified potential key regulators or KDs of the CAD networks. We further ranked the KDs based on additional layers of data-rich analyses to provide high-confidence candidate genes for CAD. Our analyses not only detected well-implicated CAD disease genes such as lipid genes, *COL4A2*, and *CXCL12*[34–36] but also unraveled novel key regulators for CAD such as *LUM*, *HGD*, *F2*, *ANXA3*, and *STAT3*.

Among the novel KDs, *LUM* is ranked on the top. This gene has been previously associated with posterior amorphous corneal dystrophy and high myopia,[37] and there is little prior evidence for the link between CAD and *LUM*. *LUM* encodes lumican and belongs to a small leucine-rich proteoglycan protein family. SLRPs include lumican, decorin, biglycan, fibromodulin, keratocan, epiphycan, and osteoglycin. These proteins bind collagen fibrils and the highly charged hydrophilic glycosaminoglycans to regulate interfibrillar spacing.[38] We speculate that *LUM* might regulate the downstream collagen genes that are important for CAD development. This notion is supported by the literature evidence on the role of *LUM* in collagen fibrillogenesis in CAD[39,40] and the enrichment of collagen genes such as *COL3A1* and *COL8A1* in the *LUM* subnetworks found in our analysis. Interestingly, the *LUM* subnetworks are also enriched for genes important for complement and coagulation cascades, such as *SERPING1*, *CFH*, and *TFPI*, which have been implicated in CAD development.[41,42] We also found that the *LUM* subnetwork from the brain tissue contains estrogen signaling-related genes such as *EMP1*, *ANXA1*, *DCN*, *TGFBI*, and *PCOLCE*. Within the brain, estrogen signaling pathway regulates glucose transport, aerobic glycolysis, and mitochondrial function to generate ATP; estrogen signaling also coordinates the brain and peripheral on metabolic homeostasis.[43] The role of estrogen in angiogenesis, cellular regrowth, and downstream collagen formation has been well documented for cardiovascular diseases,[44,45] and the connection between the small leucine-rich proteoglycan *LUM* with estrogen signaling revealed by our network analysis is intriguing and warrants further investigation. Notably, although our network selection included mostly peripheral and vascular tissues and cell types, *LUM* was identified as the no. 1 KD and the *LUM* brain subnetwork stood out as a key component of the CAD network. Based on the data, we feel that *LUM* and brain ECM perhaps play a previously underappreciated role in CAD. Encouragingly, a recent independent data-driven study provides strong evidence that

Table 4. In Silico Validation of the Top 20 Key Driver Genes Using Text-Mining and Drug Information

KD	PolySearch (Z Score >0.5)	COREMINE (Significance <10e−4)	Top Associated Diseases in Linguamatics (PubMed >5)*	Drug Development†	Druggability‡
LUM	No	No	Melanoma, myopia, breast neoplasms	N/A	Yes
COL1A1	No	Yes	Osteogenesis imperfecta, otosclerosis, osteoporosis	Cancer, solid, unspecified; macular degeneration, age; scleroderma	Yes
DUSP6	No	No	Malignant neoplasm pancreas, carcinogenesis, obesity	N/A	N/A
HGD	No	No	Alkaptonuria, metabolic diseases, Barrett esophagus	N/A	N/A
MSN	No	No	Neoplasm metastasis, pseudohermaphroditism female	N/A	N/A
CXCL12	Yes	Yes	Diabetes mellitus, ischemia, myocardial infarction	Infection, HIV/AIDS; cancer, unspecified; infarction, myocardial	Yes
DUSP1	No	No	Malignant neoplasm, diabetes mellitus	N/A	N/A
GBP2	No	No	Breast neoplasms, neoplasm metastasis, vesicular stomatitis	N/A	N/A
MTMR11	No	No	Obesity, prostatic neoplasms, atherosclerosis	N/A	N/A
CCL18	No	No	Breast carcinoma	N/A	N/A
SLIT3	No	No	Breast neoplasms, rheumatoid, brain ischemia	N/A	N/A
GBP1	No	No	Inflammatory bowel diseases, vascular diseases	Anticancer, other; Gene therapy	Yes
F2	Yes	Yes	Thrombosis, myocardial infarction, stroke	Thrombosis; cardiovascular disease, unspecified; atherosclerosis	Yes
COL4A2	No	Yes	Anoxia, cerebral hemorrhage, edema	N/A	N/A
LOXL2	No	No	Tumor progression	Anticancer, other; hepatoprotective; respiratory; vulnerary	Yes
CXCL10	No	Yes	Communicable diseases, infection, inflammation	Traumatic brain injury; Crohn's disease; arthritis, rheumatoid	Yes
ANXA3	No	No	Neoplasm metastasis, ovarian neoplasms, prostatic neoplasms	N/A	Yes
SLC2A3	No	No	Carcinoma, squamous cell; lipidoses	N/A	Yes
SHC1	Yes	No	Breast neoplasms, carcinogenesis, diabetes mellitus	Neurological disease, unspecified; cardiovascular disease, unspecified	N/A
STAT3	No	No	Breast neoplasms, carcinogenesis, inflammation	Inflammatory disease, unspecified; cancer, unspecified; Alzheimer disease	Yes

N/A indicates not applicable.

*The key driver genes were searched against all the disease PubMed databases using Linguamatics.

†The drug target information was collected from DrugBank and Pharmaprojects databases. The listed diseases were the most targeted ones in the drug development.

‡The druggability information of the key drivers was retrieved from.[30,31]

brain may be one of the key tissues for CAD.[46] However, it is possible that the brain ECM network derived from our analysis reflects the role of ECM in atherosclerotic plaque caused by homology in network organization between tissues. Without plaque data to assess this possibility in the current study, caution is required in the interpretation of the role of brain and brain ECM in CAD pathogenesis.

In addition to *LUM*, several other ECM genes including *COL1A1* and *COL4A2* were also ranked as top KDs. Even KDs that are not direct ECM components, such as *DUSP1*, *SLIT3*, *ANXA3*, and *SLC2A3*, are highly connected to ECM genes in their respective gene subnetworks, highlighting the importance of ECM. In the tissue-specific regulatory networks, the key regulators tend to bridge ECM with many other molecular mechanisms involved in CAD development,[47,48] such as inflammatory responses, complement and coagulation, adhesion, and lipid metabolism (Table 5; Figure 3). These results suggest a central role of ECM in CAD, in agreement with the conclusion from a recent multiethnic genetic study,[9] where the top KDs for the shared genetic signals between CAD and type 2 diabetes mellitus either encode ECM or are involved in cell–matrix

Table 5. Functional Enrichment of Subnetworks of Top 20 KDs

KD	Subnetwork Sources	Subnetwork Size	Over-Represented Pathway Categories
LUM	Brain	45	ECM; proteoglycans
COL1A1	Liver	73	ECM; collagen formation
DUSP6	Aorta	253	FRA pathway
DUSP6	Artery	50	IL-6, IL-7 pathway; syndecan 4 pathway
DUSP6	Cardiac muscle	108	AP1 pathway; IL-6, IL-7 pathway
DUSP6	Smooth muscle	17	MAPK targets nuclear events mediated by map kinases; ERBB1 downstream pathway
DUSP6	Vascular endothelium	122	IL-6, IL-7 pathway
HGD	Brain	40	PPAR signaling pathway; synthesis of bile acids and bile salts via 7alpha hydroxycholesterol
HGD	Muscle	48	Complement and coagulation cascades
MSN	Liver	56	Fcγ R-mediated; CXCR4 pathway
MSN	Vascular endothelium	105	Focal adhesion; integrin1 pathway
CXCL12	Adipose	47	Adenylate cyclase activating and inhibitory pathway
CXCL12	Liver	30	Intestinal immune network for IGA production; amino acid and oligopeptide SLC transporters
DUSP1	Aorta	179	ECM
DUSP1	Artery	71	Integrin1 pathway
DUSP1	Smooth muscle	63	HIF1 pathway; FRA pathway
GBP2	Blood	20	Interferon signaling
GBP2	Kidney	12	Interferon signaling
MTMR11	Liver	80	Integrin3 pathway
CCL18	Aorta	214	Immune system
SLIT3	Muscle	28	ECM
GBP1	Adipose	25	Interferon signaling
GBP1	Blood	18	Interferon signaling
GBP1	Vascular endothelium	92	Interferon signaling
F2	Adipose	49	Complement and coagulation cascades; AMI pathway
F2	Muscle	47	Complement and coagulation cascades; intrinsic pathway
COL4A2	Muscle	28	Collagens
COL4A2	PPI	19	ECM; platelet amyloid precursor protein pathway
LOXL2	Liver	28	Collagen formation; NCAM1 interactions
CXCL10	Liver	46	Chemokine signaling pathway
ANXA3	Liver	49	Matrisome associated; ECM regulators
SLC2A3	Aorta	190	ECM; P53 downstream pathway
SHC1	PPI	118	ERBB signaling pathway; focal adhesion
STAT3	PPI	102	JAK-STAT signaling pathway; pathways in cancer

Fisher exact test was performed for the enrichment of the KD subnetworks in MSigDB canonical pathway database. Only the top 2 functional terms are shown based on the *P* values with Bonferroni corrections. All the pathways shown satisfy Bonferroni-corrected $P<0.01$. ECM indicates extracellular matrix; KD, key driver; PPAR, peroxisome proliferator-activated receptors; and PPI, protein–protein interaction.

interactions. It is postulated that the critical roles of ECM in cell integrity, cell adhesion, and cellular communication/signaling may underlie its connection with multiple CAD processes. Indeed, the importance of ECM in an array of complex diseases has been increasingly recognized.[49]

Besides the ECM genes, we detected other novel or less well-studied key regulators for CAD, such as *STAT3*, *HGD*, and *GBP2*. Although their direct roles in CAD development are poorly implicated, the biological processes involved in their subnetworks are biologically plausible. For example,

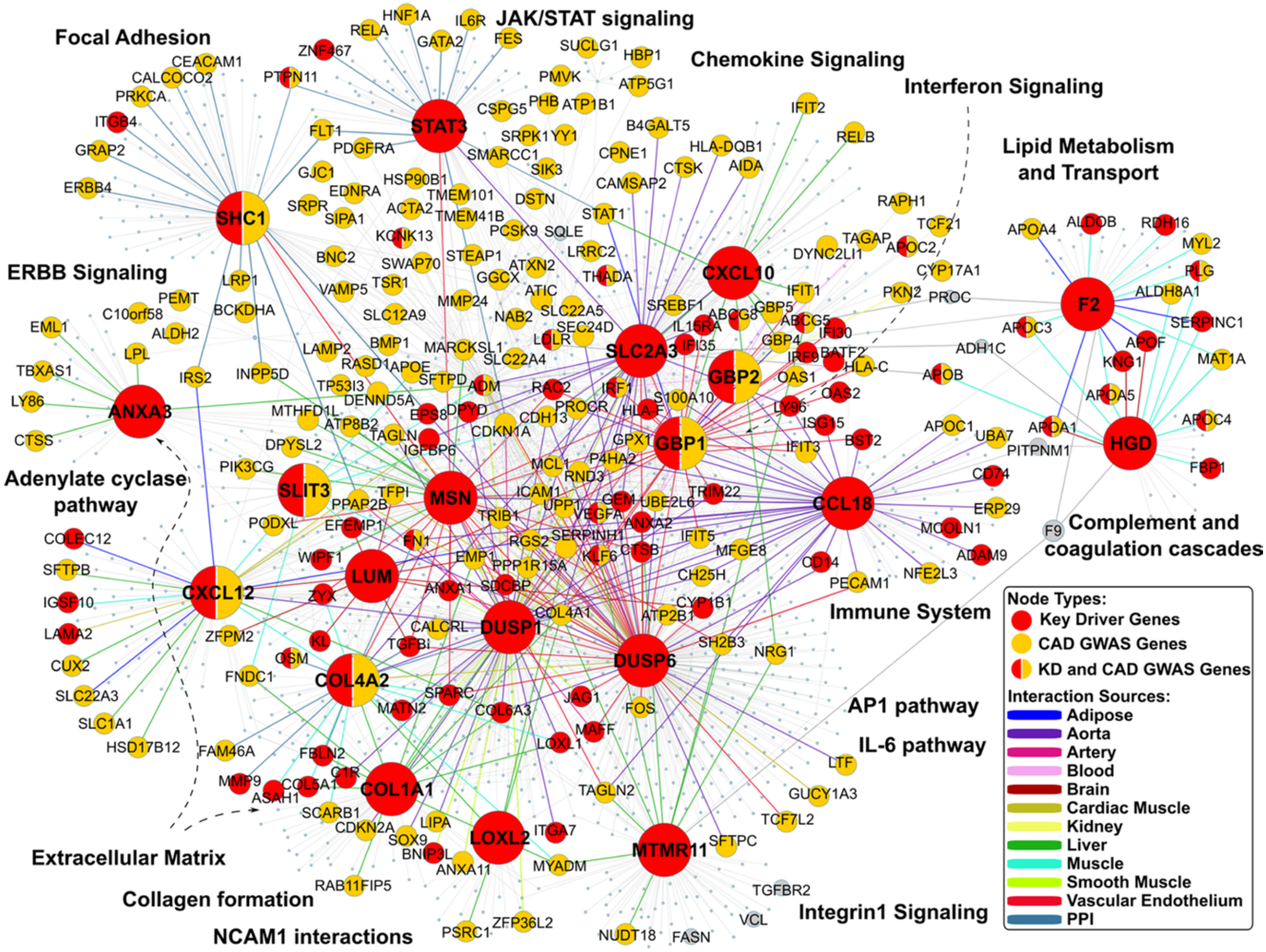

Figure 3. Top key driver (KD) subnetworks in tissue-specific gene regulatory and protein–protein interaction (PPI) networks. The largest nodes are the top 20 KDs. The nodes highlighted in red are KDs, whereas the yellow nodes are the coronary artery disease (CAD) genome-wide association studie (GWAS) genes. KDs that are also CAD GWAS genes are labeled half red and half yellow. The edge colors between genes denote the tissue or network sources of gene–gene interactions. JAK-STAT indicates Janus kinase-signal transducers and activators of transcription.

STAT3 is a member of JAK–STAT signaling pathway, the principal signaling mechanism for a wide array of cytokines and growth factors and a critical pathway for many physiological activities such as immune development, hematopoiesis, and adipogenesis.[50] The activation of JAK–STAT signaling has been implicated as a significant contributing factor to the pathogenesis of CAD,[51] and the interactions between *STAT3* and interleukin-6 signaling may play a role.[52] In support of the interleukin-6 path, *STAT3* is connected to the CAD GWAS gene *IL6R* in the CAD network derived through our analysis (Figure 3). Moreover, *STAT3* is a hub linking multiple additional CAD GWAS genes such as *PTPN11*, *HNF1A*, and *PDGFRA* in the network. Another KD gene *HGD* encodes the enzyme homogentisate 1 to 2 dioxygenase, which is involved in the catabolism of the amino acids tyrosine and phenylalanine. Defects in *HGD* are responsible for alkaptonuria, a genetic disease with Mendelian autosomal recessive inheritance, by causing accumulation of a proinflammatory and prooxidative stress intermediate, 2,5-dihydroxyphenylacetic acid in connective tissues. Patients with alkaptonuria often have cardiovascular disease, kidney disease, and damages to other organs. In our data-driven networks (Figure 3), *HGD* is a KD connected with multiple apolipoproteins (eg, *APOA1*, *APOA5*, *APOC3*, and *APOC4*) and coagulation factors (eg, *PLG*, *SERPINC1*, *F13B*, and *F9*), supporting an intimate interaction between this enzyme and known CAD processes and implying an underappreciated role of this gene in CAD. Another novel KD, *GBP2*, has been identified as a possible control factor for tumor development and a marker of efficient T-cell response.[53] In our analysis, *GBP2* subnetworks in both blood and kidney were enriched with interferon signaling genes and may contribute to CAD by modulating inflammatory responses.

In addition to identifying both well-known CAD driver genes such as lipid metabolism genes and novel KDs for the top CAD GWAS genes, our network-based method also unravels intimate connections among the top CAD GWAS genes and pathways (Figure 3), which has not been achieved by previous efforts. For example, many CAD GWAS genes involved in lipid metabolism and transport (eg, *APOA1, APOA4, APOA5, APOB,* and *APOC1-C4*) are joined with coagulation and complement genes (eg, *PLG*, *SERPINC1*) via KD genes *HGD* and *F2*. This lipid metabolism-coagulation subnetwork is further connected to several immune and inflammatory subnetworks, which are in turn connected to

ECM subnetworks. For other well-known lipid metabolism genes, such as *PCSK9*, *LDLR, LPL*, and *LIPA*, they tend to be spread around different subnetworks rather than strongly clustered (Figure 3), probably because of the limitations of gene regulatory networks in capturing biochemical and enzymatic reactions. These findings shed light on the complex interactions among CAD GWAS genes and between individual CAD processes via KDs, thus unraveling novel insights into the complex mechanisms of CAD development.

Recently, several pathway and network analysis of CAD utilizing CARDIoGRAM CAD GWAS have been conducted.[8,32,54] These studies use the full set of GWAS, which includes both strong and subtle genetic signals to identify CAD pathways and networks. In contrast to these existing studies, our current analysis specifically focuses on the smaller number of strong and significant CAD GWAS loci. Encouragingly, our current analysis based on the top CAD loci revealed highly consistent pathways and networks when compared with the previous studies utilizing full GWAS data set. Lipid metabolism, complement and coagulation, ECM, inflammatory pathways, focal adhesion, peroxisome proliferator-activated receptors signaling, and cell cycle are all replicated in our current analysis. In addition, the current study involves more comprehensive coverage of networks, a novel, vigorous, and streamlined gene ranking and prioritization scheme, and incorporation of multidimensional data and resources for validation. As a result, the current study provides a detailed illustration of the network architecture connecting the top CAD candidate genes and pinpoint potential regulators of these top loci. The prioritized KDs with full annotation of their tissue-specific subnetworks, biological pathways, literature evidence, and druggability information represent a step further toward a better understanding of the top GWAS loci as well as clinical and therapeutic application of the recent powerful genetic discoveries.

Similar to several previous studies, here we again demonstrate that the KDs identified are not necessarily significant GWAS signals although their neighbors in gene networks tend to be GWAS signals.[8,9,15] This phenomenon likely explains why GWAS hits have low selection pressure and commonality in the general population, and why each locus only explains a small fraction of heritability. These observations may argue against the importance of a majority of individual GWAS candidate genes as effective therapeutic targets because their subtle effects in disease modification. KDs, on the contrary, may serve as better drug targets because of their importance in regulating other GWAS genes. These hypotheses, however, need to be treated with caution. In fact, some of the GWAS genes such as *HMGCR* and *PCSK9* are proven, effective drug targets in CAD therapeutics, yet they were not detected as KDs in our study. Instead, genes *PMVK* and *LDLR* that functionally relate to the known targets were KDs in our analysis. One potential explanation is that the mostly transcription-based gene regulatory networks used in our analysis cannot capture the various types of regulation important for CAD and thus may miss additional KDs. Although it is appealing to suggest that KDs are more potent drug targets based on network properties, this hypothesis awaits future validation. The importance of KDs in regulating large numbers of genes may also imply more severe side effects accompanying stronger therapeutic impact. Therefore, selection of KDs with partners and functions specific to CAD is necessary to avoid potential adverse effects.

The lack of signals of KDs in GWAS may be a result of negative selection pressure because of their critical roles in biological networks, as hypothesized and discussed by multiple previous studies.[8,9,15] This negative pressure hypothesis is supported by the recent discovery of 3230 essential genes out of 31 345 human genes based on exome sequencing of 60 706 humans[55] (Exome Aggregation Consortium, http://www.exac.broadinstitute.org/). These essential genes demonstrate near-complete depletion of truncating variants and have no currently established human disease phenotypes because of the lack of functional variants. Among the top 20 KDs identified in our CAD study, 6 were among the essential genes, including *COL1A1, DUSP6, F2, MSN, SLIT3*, and *STAT3*, representing a significant enrichment of essential genes among the top KDs (fold change, 2.91; Fisher exact test, P=0.0028). Another recent study revealed that *BRD4* is essential for luminal cancer. However, there is lack of cancer GWAS signals in this gene.[56] Furthermore, in our previous comparison of KDs versus non-KDs for a set of inflammatory genes shared across >10 diseases,[26] we found 63.6% of KDs and 39.2% of non-KDs demonstrated observable phenotypes based on the Mouse Genome Informatics mouse phenome database. This represents a significantly higher percentage of genes with mutant phenotypes among KDs when targeted in mutant animals (P=0.001 by proportion test). Therefore, evidence from both humans and mice supports the essential role and stronger negative pressure of KDs. By focusing on gene networks connecting the top CAD GWAS genes and their KDs, our study offers a distinct angle to understand the complex CAD biology and detect more plausible therapeutic targets. In support of the therapeutic potential of the KDs, our study also provides evidence that many of the top KDs uncovered have been subject to drug development as druggable targets (Table 4) for multiple diseases, such as thrombosis, diabetes mellitus, and cancers. Based on their central locations in the network models, enrichment of CAD GWAS signals in their local subnetworks, and gene expression perturbations in myocardial infarction patients, these KDs are plausible potential targets for CAD.

Despite the advantages and novel discoveries discussed above, there are limitations in our study. First, the determination of candidate genes based on GWAS loci is not straightforward. Chromosomal location-based mapping lacks functional support, whereas functional data-supported mapping has incomplete coverage of tissue and lack of power in identifying weak *cis*-association and *trans*-regulation. Therefore, candidate gene mapping that was based on existing data can be far from comprehensive and may carry biases. To address these issues, we incorporated different CAD candidate gene lists according to different single nucleotide polymorphism-gene mapping approaches (ie, chromosomal location versus expression quantitative trait loci) and inclusion/exclusion criteria (eg, whether to consider or exclude genes in well-known lipid loci to avoid overshadowing novel genes and mechanisms by lipid genes). Interestingly, many top KDs do not seem to be sensitive to the

CAD gene curation parameters, supporting the robustness of the network structures and KDs. This carries important implications that the main biological pathways and networks of CAD are relatively stable despite that new genes are continuously discovered and inaccurate mapping of certain candidate genes by any particular mapping method may exist. Second, although we aim to conduct a comprehensive data-driven analysis, our investigation is limited by the availability of tissue-specific regulatory networks, which may introduce bias because networks from other critical cell or tissue types such as vascular smooth muscle cells are missed. Third, the gene networks used in our current analysis do not include other regulatory molecules or elements such as noncoding RNAs and enhances, which will miss essential key regulators that are not protein-coding genes, such as the noncoding ANRIL transcript for the 9p21 locus. Fourth, for the gene expression pattern analysis of the KD subnetworks between CAD and controls, we were not able to identify CAD transcriptomic data sets involving the tissue types perfectly matching those used for the gene networks. Refinement of our analysis is necessary when additional data sets become available in the future. Finally, our study represents a bioinformatics data mining effort and is exploratory in nature. Although we provide multiple lines of in silico evidence to support the importance of the KDs, experimental validation of the novel KDs for their roles in regulating the CAD GWAS genes, networks, and disease development is beyond the scope of the current study but warrant further investigation in future studies.

In summary, our study provides a novel integrative genomics framework to understand the relations among CAD GWAS genes and prioritize the genes impacted by genetic variations in CAD. Our findings offer novel mechanistic hypotheses about CAD pathogenesis and pinpoint potential drug targets to more effectively counteract CAD. Other complex diseases or phenotypes such as cancers, Alzheimer disease, and drug responses also involve multiple genetic determinants. Our analytic framework can be adapted for other disease areas to help generate new hypotheses and benefit drug target discovery.

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Disclosures

None.

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Significance

Genome-wide association studies have successfully identified hundreds of regions in the genome that harbor genetic variants that increase risks for coronary artery disease (CAD). However, it has been challenging to understand the molecular mechanisms through which these loci contribute to CAD, and the clinical implications and utilities of these findings remain largely unknown. In this work, we designed and implemented an integrative method that leverages the genetic association strength, tissue-specific gene regulations, and gene expression perturbations in patients with CAD, to understand the relations among the CAD loci and prioritize causal genes for CAD that are more suitable for drug development. Our approach revealed intimate interactions among the genes underlying the CAD loci and identified potential novel regulators, many of which druggable, that coordinate the actions of CAD genes and pathways to impact CAD pathogenesis.

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Network-Based Identification and Prioritization of Key Regulators of Coronary Artery Disease Loci

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Materials and Methods

Tissue-specific gene regulatory networks and protein-protein interaction networks

To retrieve gene-gene relations, we utilized two types of gene networks. The first type was tissue-specific Bayesian network models reconstructed from multiple previously published human and mouse studies (details and references in **Supplemental TEXT**), each involving genetics and gene expression data from hundreds of samples, using an established method[1, 2]. Mouse Bayesian networks were obtained from adipose tissue, brain, heart, islet cells, kidney, skeletal muscle, and liver while human networks were obtained from aorta, artery, adipose, blood, cardiac muscle, smooth muscle, vascular endothelium, and liver[3-9]. If there were more than one study for a given tissue, we took the union of the edges from multiple networks to derive a combined network for that tissue. In addition, we supplemented the gene regulatory networks which primarily reflect transcriptional regulation with human protein-protein interaction (PPI) network from Human protein reference database to capture functional relations between proteins[10]. In total, we compiled 14 network models: aorta, artery, adipose tissue, blood, brain, heart, islet, kidney, skeletal muscle, cardiac muscle, smooth muscle, vascular endothelium, liver, and PPI.

Key driver analysis (KDA) to pinpoint potential key regulators of CAD genes

We applied a previously developed KDA algorithm[11-13] that maps each of the five CAD candidate gene lists to the gene-gene interaction networks described above in order to identify the key regulatory genes. For a specific CAD gene list, we defined a key driver (KD) as a gene that is connected to a large number of CAD candidate genes, compared to the expected number for a randomly selected gene within a network [14]. Multiple testing correction was applied using the Benjamini-Hochberg false discovery rate (FDR) method.

KDA statistics and network consistency

We conducted 98 sets of KDA (seven CAD gene lists × 14 networks) and obtained 98 KD lists. To assess the overall performance of a KD across all the KDA analysis, we applied the Stouffer method for meta-analysis [15] to the KDA results to derive a meta p value for each KD:

$$Z_i = \Phi^{-1}(1-P_i) \qquad (1)$$

$$Z = \frac{\sum_{i=1}^{k} Z_i}{\sqrt{k}} \qquad (2)$$

Where Φ is the standard normal cumulative distribution function and Pi is the P value for a KD in the ith analysis among the 98 sets of KDA.

Functional enrichment analysis

The canonical pathways were downloaded from Molecular Signatures Database (MSigDB v 5.0, http://www.broadinstitute.org/gsea/msigdb/). Fisher's exact test with Bonferroni correction was used to assess the enrichment of the KD subnetworks in the canonical pathways.

CAD GWAS signal enrichment in KD subnetworks

To confirm that the KDs identified were relevant to CAD, we retrieved their associated subnetworks from the corresponding tissue-specific networks and assessed the overall CAD association strength of each KD subnetwork using the 1000 Genome-based CAD GWAS involving ~185,000 CAD cases and controls, interrogating 6.7 million common (minor allele frequency (MAF) > 0.05) and 2.7 million low-frequency ($0.005 < \text{MAF} < 0.05$) variants[17]. The GWAS index SNPs were mapped to genes according to chromosome distance (50 kb up- and downstream) and eQTL datasets described in the main text. Each unique gene was annotated with its CAD association strength based on the most significant SNP (i.e., the largest -log10 CAD GWAS P value) among all SNPs mapped to a gene based on distance or eQTLs. If a gene has no SNP mapped to it or no CAD GWAS p values could be retrieved, we assigned 0 as the CAD association strength.

To assess the overall CAD association strength of a subnetwork of a given KD, we compared the distribution of the GWAS p values of the member genes within the KD subnetwork with that of randomly selected genes using one-sided two-sample Kolmogorov-Smirnov (KS) test. For each KD, 100 random subnetworks of matching size were generated. The average KS test p values from the 100 KS tests was used for each KD. A significant KS test p value would indicate significant over-representation of SNPs with stronger CAD association among the KD subnetwork genes compared to the subnetworks of random genes in the same network.

As the KDs were detected based on their local enrichment of the CAD candidate genes derived from the top CAD GWAS loci (defined as GWAS top genes), the more central positions of the KDs in the networks suggest that they play more important regulatory roles in CAD pathogenesis than the individual top CAD genes. To assess the importance of KDs relative to the CAD top genes they appear to regulate, we compared the KD subnetworks with those of the CAD top genes in the *CAD extended gene list* as it contains the largest number of CAD candidate genes (C_N=880). Because KDs by definition have larger subnetworks than CAD top genes, which would bias the statistics, we used a different strategy to assess the CAD association strength between KDs and CAD top genes. As each KD needed be compared with the 880 CAD candidate genes to derive an overall CAD association strength estimate for the given KD against the CAD genes, we first generated a background association strength distribution for the CAD candidate genes. Here we used the percentage of subnetwork member genes whose representative SNPs reaching $p<0.001$ in CAD GWAS to represent the CAD association strength. The 880 percentage values of the CAD gene subnetworks were used to form the background distribution of CAD association strength, and the percentage value for each of the KD subnetworks was compared against this background to derive a p value. P values were calculated as (number of percentage values in the background that are higher than the percentage value of a given KD)/880.

Expression profile perturbations of KD subnetworks

To test whether the KD subnetworks are perturbed in disease conditions, we retrieved the expression profiles from patients experiencing coronary artery disease and from healthy cohorts in Gene Expression Omnibus (GEO) database (http://www.ncbi.nlm.nih.gov/geo/) using "cardiovascular disease" or "myocardial infarction" or "coronary artery disease". The data sets should satisfy the following criteria: 1) the expression profiles come from human study; 2) the data sets contain more than ten samples for CAD patients and healthy controls separately.

The circulating endothelial cells isolated from patients experiencing acute myocardial infarction (n=49) and from healthy cohorts (n=50), were retrieved with accession number GSE66360. In addition, we retrieved from GEO the transcriptome profiles of CD34+ stem cells, CD4+ T-cells, resting CD14+ monocytes, stimulated monocytes and macrophages, from patient with severe coronary atherosclerosis (n=18) and controls that had no coronary atherosclerosis as determined angiographically (n=13) using accession number GSE9820[18]. Expression profiling of peripheral blood mononuclear cells (PBMCs) isolated from CAD patients (n=27) with ≥70% stenosis in >1 major vessel or ≥50% stenosis in >2 arteries, and healthy controls (n=14) have luminal stenosis of 0% with accession number GSE10195 [19]. The blood samples isolated from 110 patients with CAD (CAD index > 23) and from 112 partially matched controls without CAD (CAD index = 0) using accession number GSE12288 [20]. Gene expression profiles of human epicardial adipose tissue and subcutaneous adipose tissue in CAD patients (n=13) and controls (n=10) with accession number GSE64554. The five datasets were processed using the RMA normalization method, including background correction, log2 transformation and quantile normalization in limma package[21].

The transcriptomic patterns of the KD subnetworks in each of these cell--specific CAD gene expression datasets were assessed using the Gene Set Enrichment Analysis (GSEA, the latest version gsea2-2.2.0.jar)[22] to identify KD subnetworks demonstrating significant differential expression patterns between the CAD subjects and the controls. For each KD subnetwork, we obtained 10 sets of GSEA results using data from the circulating endothelial cells, CD34+ stem cells, CD4+ T-cells, resting CD14+ monocytes, stimulated monocytes, macrophages, peripheral blood mononuclear cells (PBMCs), whole blood, epicardial adipose tissue, and subcutaneous adipose tissue. GSEA has default maximum and minimum gene numbers set to 500 and 15, respectively, and KD subnetworks exceeding the limits were not included in the analysis. Then we performed meta-analysis using formula (1) and (2) to represent the significance of differential expression for each KD subnetwork.

Summary scores for the key drivers

We took into consideration the performance of each KD in the three different types of data-driven analyses: KDA statistics and network consistency, CAD relevance of KD subnetworks in terms of CAD GWAS signal enrichment and differential expression of KD subnetworks in CAD vs controls. For each analysis i, we ranked the p values assigned to each KD and transformed the p values into a score using the following formula:

$$\text{Score}(i)= 1- \text{PercentileRank}(Pi) \qquad (3)$$

Where PercentileRank provides percentile rank scores that tell what percentage of same-grade peers have lower p values than the tested gene on a norm-referenced or standardized assessment. Finally, the three scores were summed to represent the summary score of each KD.

Literature-based assessment of the KDs in relation to CAD

To further investigate the relevance of the identified KDs to CAD based on previous literature evidence, we assessed all relevant information from different resources: 1) Mouse Phenotypes from the Mouse Genome Database (MGD)[23]; (2) the Gene Ontology (GO) annotations[24], 3) literature support for disease implication using Linguamatics[25], Polysearch[26], and COREMINE (http://www.coremine.com/medical).

Drug-target information for KDs

To evaluate the druggability of the identified KDs and to determine potential drug repurposing opportunities, we compared the list of KD genes against a list of genes targeted by pharma R&D pipeline projects derived from the Pharmaprojects database (Informa UK Ltd, https://citeline.com/products/pharmaprojects/), which tracks drugs under development from preclinical to clinical phases, as well as marketed drugs and discontinued projects. In addition, we collected drug targets from the DrugBank database[27] in version 4.3 updated on July 7th, 2015.

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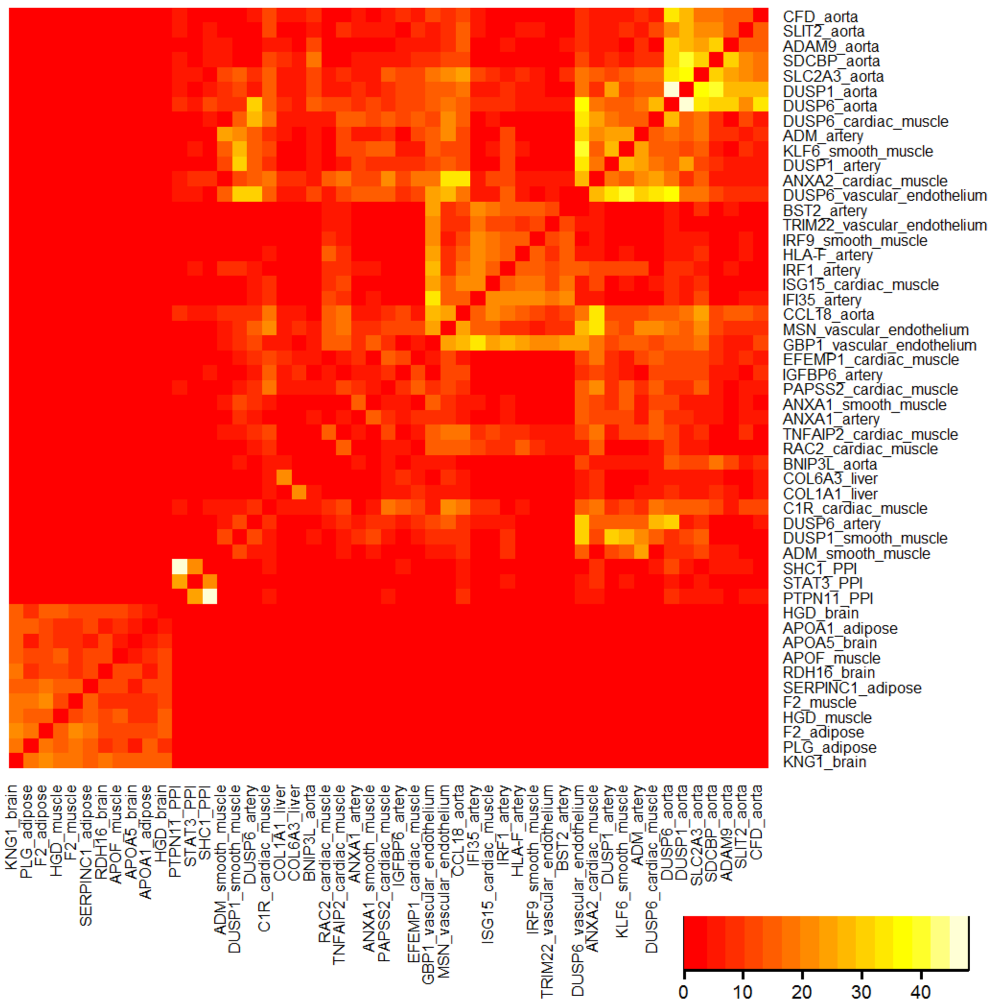
Supplement Material

Supplemental Text

Tissue-specific gene regulatory networks and protein-protein interaction networks

To retrieve gene-gene relations, we utilized two types of gene networks. The first type was Bayesian regulatory networks, which are directed acyclic graphs with the edges of the graph defined by conditional probabilities that characterize the distribution of states of each gene given the state of its parents (1, 2). The tissue-specific Bayesian network models adopted in our analysis were reconstructed from multiple previously published human and mouse studies (**Supplementary Table VI**), each involving genetics and gene expression data from hundreds of samples, using an established method (3, 4). Mouse Bayesian networks were obtained from adipose tissue, brain, heart, islet cells, kidney, skeletal muscle, and liver while human networks were obtained from aorta, artery, adipose, blood, cardiac muscle, smooth muscle, vascular endothelium, and liver (5-11). If there were more than one study for a given tissue, we took the union of the edges from multiple networks to derive a combined network for that tissue. In addition, we supplemented the gene regulatory networks which primarily reflect transcriptional regulation with human protein-protein interaction (PPI) network from Human protein reference database (http://www.hprd.org/) to capture functional relations between proteins (12). In total, we compiled 14 network models: aorta, artery, adipose tissue, blood, brain, heart, islet, kidney, skeletal muscle, cardiac muscle, smooth muscle, vascular endothelium, liver, and PPI.



Supplemental Figure I. The overlap architecture between KD subnetworks with >15 overlapping genes.

Supplemental Table I. CAD gene lists from CAD GWAS and other functional studies.

CAD Gene Lists	**Member Genes**
CAD GWAS	ABO; ACAD10; ADAMTS7; AGBL1; ALDH2; ALDH8A1; ANKS1A; APOA1; APOA4; APOA5; APOC3; ASIC2; ATP2B1; ATP5G1; ATXN3; BSND; BTNL2; C10orf76; C12orf43; C12orf51; C2orf85; C6orf10; CACNA1E; CACNA2D3; CALCRL; CAPS2; CCDC157; CDH13; CDH9; CDKN2A; CDKN2B; CELSR2; CNNM2; COL4A1; COL4A2; CUX2; CXCL12; CYP17A1; DNAH6; EEF1E1; EMP1; ERBB4; FBXO15; FBXO3; FHL5; FLJ43860; FLT1; FMN2; FN1; FNDC1; GIP; GRIN3A; GUCY1A3; HCG27; HECTD4; HEMGN; HFE2; HHIPL1; HLA-C; HLA-DQB1; HNF1A; HSP90B1; IFT88; IL6R; INPP5D; IPMK; KCNE2; KCNK13; KCNQ3; KIAA1462; KLF6; LARGE; LDLR; LIPA; LOC646730; LPA; LPAL2; LRP6; LYSMD4; MCART2; MIA3; MIR4499; MIR548AV; MIR548G; MORF4L1; MRAS; MRPS6; MSI2; MTAP; MTHFD1L; MUTED; MYL2; NRG1; NT5C2; NUMB; PCSK9; PDGFD; PECAM1; PEMT; PHACTR1; PLD5; PPAP2B; PRICKLE2; PRICKLE2-AS3; PRKCA; PSRC1; RAI1; RASD1; RGS2; RIT2; SEMA6D; SF3A1; SH2B3; SLC1A1; SLC22A3; SLC2A13; SLC5A3; SMAD3; SMARCA4; SMCR3; SMG6; SNF8; SORCS2; SORT1; SOX9; SPATA7; SRR; ST3GAL4; ST8SIA1; STEAP1; STK32B; SUCLG1; TCF21; TFPI; TTC32; UBE2Z; VEGFA; WDR12; WDR33; WDR35; WDR86-AS1; ZC3HC1; ZFPM2; ZNF259; ZNF383
CAD C4D	ABCG5; ABCG8; ABO; ACAD10; ACSS2; ADAMTS7; AGBL1; AKAP13; ALDH2; ALDH8A1; ALS2CR16; ANKS1A; ANXA11; APOA1; APOA4; APOA5; APOB; APOC1; APOC2; APOC3; APOC4; APOE; ARHGAP26; ARVCF; ASIC2; ATP2B1; ATP5G1; ATP5SL; ATPAF2; ATXN2; ATXN3; BMP1; BMPR1A; BNC2; BSND; BTNL2; C10orf76; C12orf43; C12orf51; C2orf85; C6orf10; CA10; CACNA1E; CACNA2D3; CALCRL; CAMSAP1L1; CAPS2; CCDC157; CDH13; CDH9; CDKN1A; CDKN2A; CDKN2B; CDKN2B-AS1; CELSR2; CKM; CNNM2; COG5; COL4A1; COL4A2; COL4A4; CTAGE1; CUX2; CXCL12; CYP17A1; CYP46A1; DCPS; DDX59; DNAH6; DYNC2LI1; EDNRA; EEF1E1; EMP1; ERBB4; FBXO15; FBXO3; FES; FHL5; FLJ43860; FLT1; FMN2; FN1; FNDC1; FURIN; GGCX; GIP; GNPDA2; GRIN3A; GUCY1A3; HCG27; HDAC9; HECTD4; HEMGN; HFE2; HHIPL1; HIP1; HLA-C; HLA-DQB1; HNF1A; HSD17B12; HSP90B1; IFT88; IL6R; INPP5D; IPMK; JAZF1; KCNE2; KCNK13; KCNK5; KCNQ3; KIAA1462; KLF6; LARGE; LDLR; LIPA; LMOD1; LOC646730; LPA; LPAL2; LPL; LRP6; LRRC2; LRRC48; LY86; LYSMD4; MAP3K4; MAP4; MAP9; MARK4; MCART2; MCL1; MIA3; MIR4499; MIR548AV; MIR548G; MORF4L1; MRAS; MRG15; MRPS6; MSI2; MTAP; MTHFD1L; MUTED; MYBPHL; MYL2; NGF; NME7; NRG1; NT5C2; NUMB; OBFC1; OSM; PARP12; PCNXL3; PCSK9; PDE3A; PDGFD; PDGFRA; PECAM1; PEMT; PHACTR1; PKN2; PLD5;

	PLEKHG1; PLG; PODXL; PPAP2B; PPP2R3A; PRICKLE2; PRICKLE2-AS3; PRKCA; PROCR; PSRC1; RAI1; RASD1; RBPMS2; RGS2; RIT2; RND3; RPEL; RPH3A; SARS; SCARB1; SEMA6D; SERPINH1; SF3A1; SH2B3; SKI; SLC1A1; SLC22A3; SLC22A4; SLC22A5; SLC2A13; SLC5A3; SLCO1B1; SMAD3; SMARCA4; SMCR3; SMG6; SNF8; SNX10; SORCS2; SORT1; SOX9; SPATA7; SPC24; SRR; ST3GAL4; ST8SIA1; STEAP1; STK32B; SUCLG1; SWAP70; TCF21; TERT; TFPI; TMEM161B; TNS1; TOM1L2; TOMM40; TRAFD1; TRIB1; TSC22D2; TTC32; UBE2Z; UBTF; USP53; VAMP8; VEGFA; WDR12; WDR33; WDR35; WDR86-AS1; ZC3HC1; ZEB2; ZFPM2; ZNF259; ZNF383; ZNF652
CAD C4D no Lipid	ACAD10; ACSS2; ADAMTS7; AKAP13; ANKS1A; ANXA11; ARHGAP26; ARVCF; ATP2B1; ATP5G1; ATP5SL; ATPAF2; ATXN2; BMPR1A; BNC2; BTNL2; C12ORF43; C3ORF38; C6ORF10; CA10; CAMSAP1L1; CDKN1A; CDKN2A; CDKN2B; CKM; CNNM2; COG5; COL4A1; COL4A2; COL4A4; CTAGE1; CUX2; CXCL12; CYP17A1; CYP46A1; DCPS; DDX59; DQ582071; DYNC2LI1; EDNRA; FES; FHL5; FLT1; FNDC1; FURIN; GGCX; GIP; GNPDA2; GUCY1A3; HCG27; HDAC9; HECTD4; HFE2; HHIPL1; HIP1; HSD17B12; HSP90B1; IGSF5; IL6R; JAZF1; KCNE2; KCNK5; KIAA1462; KLHL29; LIPA; LMOD1; LPAL2; LRRC2; LRRC48; LY86; MAP3K4; MAP4; MAP9; MARK4; MCL1; MFSD2B; MIA3; MORF4L1; MRAS; MRPS6; MTAP; MTHFD1L; MYBPHL; NGF; NME7; NT5C2; NUGGC; OBFC1; OPRM1; OSM; PARP12; PCNXL3; PDGFRA; PECAM1; PEMT; PHACTR1; PKN2; PLEKHG1; PLG; PODXL; PPAP2B; PPP2R3A; PROCR; PTPN11; RAI1; RASD1; RBPMS2; RND3; RPH3A; RPL6; SARS; SERPINH1; SH2B3; SKI; SLC12A9; SLC22A3; SLC22A4; SLC22A5; SLC30A1; SLC5A3; SLCO1B1; SMAD3; SMCR3; SMG6; SNF8; SNX10; SRR; STK32B; SWAP70; TCF21; TCF7L2; TERT; TEX41; TMEM161B; TNS1; TOM1L2; TRAFD1; TSC22D2; TTC32; UBE2Z; UBTF; USP53; VAMP5; VAMP8; WDR12; WDR35; ZC3HC1; ZEB2; ZNF652
CAD GWAS no lipid	ACAD10; ADAMTS7; AGBL1; ALDH8A1; ANKS1A; ASIC2; ATP2B1; ATP5G1; ATXN3; BSND; BTNL2; C10orf76; C12orf43; C2orf85; C6orf10; CACNA1E; CACNA2D3; CALCRL; CAPS2; CCDC157; CDH13; CDH9; CDKN2A; CDKN2B; CNNM2; COL4A1; COL4A2; CUX2; CXCL12; CYP17A1; DNAH6; EEF1E1; EMP1; ERBB4; FBXO15; FBXO3; FHL5; FLJ43860; FLT1; FMN2; FNDC1; GIP; GRIN3A; GUCY1A3; HCG27; HECTD4; HEMGN; HFE2; HHIPL1; HLA-C; HLA-DQB1; HSP90B1; IFT88; IL6R; INPP5D; IPMK; KCNE2; KCNK13; KCNQ3; KIAA1462; KLF6; LARGE; LIPA; LOC646730; LPAL2; LRP6; LYSMD4; MCART2; MIA3; MIR4499; MIR548AV; MIR548G; MORF4L1; MRAS; MRPS6; MSI2; MTAP; MTHFD1L; MUTED; NRG1; NT5C2; NUMB; PECAM1; PEMT; PHACTR1; PLD5; PPAP2B; PRICKLE2; PRICKLE2-AS3; PRKCA; RAI1; RASD1; RGS2; RIT2; SEMA6D; SF3A1; SH2B3; SLC1A1; SLC22A3; SLC2A13; SLC5A3; SMAD3; SMCR3; SMG6; SNF8; SORCS2; SOX9; SPATA7; SRR; ST8SIA1; STEAP1; STK32B; SUCLG1; TCF21; TFPI; TTC32; UBE2Z; WDR12; WDR33; WDR35; WDR86-AS1; ZC3HC1; ZFPM2; ZNF383
CAD Extend	ABCG5; ABCG8; ABO; AC026250.16; AC087164.1; ACAD10; ACSS2; ACTA2; ACTR1A; ADAMTS7; ADM; AF075116; AF085859; AF124731.2; AGBL1; AIDA; AK023781; AK023818; AK054569; AK095583; AK098707; AKAP13; AL049919; AL049980; AL591069.5; ALDH2; ALDH8A1; ALS2CR13; ALS2CR16; ALS2CR8; ANKDD1A; ANKRD10; ANKRD25; ANKS1A; ANXA11; APOA1; APOA4; APOA5; APOB; APOC1; APOC2; APOC3; APOC4; APOE; ARHGAP26; ARL3; ARVCF; ASB16; ASIC2; ATP1B1; ATP2B1; ATP5G1; ATP5SL; ATP8B2; ATPAF2; ATRIP; ATXN2; ATXN3; B3GNT8; BCKDHA; BLZF1; BMP1; BMPR1A; BNC2; BRAP; BSND; BTNL2; C10orf26; C10orf32; C10orf57; C10orf58; C10orf76; C12ORF24; C12orf30; C12orf43; C12orf47; C12orf51; C17orf39; C17orf53; C17orf65; C19orf52; C1orf58; C1ORF86; C21ORF7; C22ORF25; C2ORF44; C2orf84; C2orf85; C3orf38; C3ORF75; C6orf10; C6ORF64; CA10; CACNA1E; CACNA2D3; CACNG5; CALCOCO2; CALCRL; CAMP; CAMSAP1L1; CAPS2; CCBL2; CCDC157; CCDC181; CCDC85C; CCL25; CCT8; CD82; CDC25A; CDH13; CDH9; CDKN1A; CDKN2A; CDKN2B; CDKN2B-AS1; CEACAM1; CECR6; CELSR2; CEP70; CHRNA5; CKM; CLEC10A; CMTM2; CNNM2; COG5; COG6; COL4A1; COL4A2; COL4A4; COMT; Contig21679_RC; Contig46411_RC; CPNE1; CSNK1G1; CSPG5; CTAGE1; CTSH; CTSK; CTSS; CUX2; CXCL12; CYP17A1; CYP46A1; DCPS; DDX59; DEF6; DGCR8; DHX30; DKFZp434K191; DKFZP564C152; DKFZP761E198; DLX4; DNAH6; DOCK5; DPEP3; DRG2; DYNC2LI1; DYNLRB1; EDEM2; EDNRA; EEF1E1; EIF2A; EIF6; EML1; EMP1; ENSG00000047849.17; ENSG00000107798.11; ENSG00000111252.5; ENSG00000115486.6; ENSG00000135213.8; ENSG00000136378.8; ENSG00000138380.11; ENSG00000140395.3; ENSG00000154305.11; ENSG00000159202.11; ENSG00000160679.8; ENSG00000182511.7; ENST00000238803; ENST00000296496; ENST00000300223; ERBB4; ERCC2; ERGIC3; ERP29; EXOSC5; FAM117B; FAM118B; FAM177B; FAM46A; FARS2; FBF1; FBXO15; FBXO3; FBXO46; FBXW5; FES; FHL5; FIP1L1; FLCN; FLJ12334; FLJ21127; FLJ30092; FLJ39616; FLJ42875; FLJ43860; FLT1; FMN2; FN1; FNDC1; FOS; FOXRED1; FURIN; G6PC3; GALNT4; GATA2; GBP1; GBP2; GBP4; GBP5; GCDH; GDPD5; GGCX; GGT7; GGTL3; GIP; GJC1; GNAI3; GNGT2; GNLY; GNPDA2; GPN3; GPR22; GRAP2; GRIN3A; GSTM4; GTF2B; GUCY1A3; HBP1; HCG27; hCT1652322.2; HDAC9; HDC; HECTD4; HEMGN; HFE2; HHIPL1; HIP1; HIST1H2BD; HIVEP1; HLA-C; HLA-DQB1; HNF1A; HORMAD1; HS.443185; Hs.494277; HS.539450; hsa-miR-185; HSD17B12; HSP90B1; HSS00142168; ICA1L; IDS; IFIT3; IFIT5; IFT88; IL6R; IL8; INPP5D; INTS10; IPMK; IPO9; IREB2; IRS2; ITCH; ITGA3; ITGB4BP; JAZF1; KANK2; KAT3; KCNE2; KCNJ5; KCNK13; KCNK5; KCNQ3; KIAA1143; KIAA1324; KIAA1462; KIF14; KLC3; KLF6; KLHDC10; KLHL35; LAMP2; LARGE; LDLR; LIMD1; LIPA; LMOD1; LOC100129828; LOC100131662; LOC283033; LOC338862; LOC340322; LOC401152; LOC402176; LOC407835; LOC646730; LOC653764; LOC729580; LPA; LPAL2; LPL; LRP6; LRRC2; LRRC48; LTF; LY86; LYSMD4; MAN2A2; MAP3K4; MAP4; MAP9; MAPKAPK5; MAPRE3; MARCKSL1; MARK4; MAT1A; MAT2A; MCART2; MCL1; MEF2C; MIA3; MIR1297; MIR4499; MIR4693; MIR548AV; MIR548G; MMP24; MORF4L1; MRAS; MRG15; MRPS6; MSI2; MSL2; MSL2L1; MT1P3; MTAP; MTHFD1L; MTP18; MUTED; MYADM; MYBPHL; MYH7B; MYL2; MYO15A; NA; NALP12; NBEAL1; NCLN; NCRNA00173; NFE2L3; NGF; NME6; NME7; NRG1; NT5C2; NUDT18; NUGGC; NUMB; OAS1; OASL; OAZ2; OBFC1; OPLAH; OSM; OVOL1; P4HA2; PARP12; PCCB; PCNXL3; PCSK7; PCSK9; PDE3A; PDGFD; PDGFRA; PECAM1; PEMT; PFN4; PHACTR1; PHB; PHOSPHO1; PIK3CG; PKN2; PLD5; PLEKHG1; PLEKHH2; PLG; PMS2L3; PMS2P3; PODXL; POLG2; PPAP2B; PPP1R15A; PPP2R3A; PRICKLE2; PRICKLE2-AS3; PRKAB2; PRKCA; PROCR; PSME3; PSRC1; PTPN23; PVRL2; RAI1; RALY; RANBP9; RAPH1; RASD1; RBL1; RBPMS2; RELA; REST; RGS2; RHBDD1; RIT2; RND3; ROMO1; RP11-541N10.2; RPEL; RPH3A; RUNDC3A; S100A10; SARS; SCARB1; SEC24D; SEMA6D; SERPINH1; SF3A1; SFTPC; SFXN2; SH2B3; SH3PXD2A; SHE; SHISA4; SIDT2; SIPA1; SKAP1; SKI; SLC1A1; SLC22A3; SLC22A4; SLC22A5; SLC25A39; SLC2A13; SLC4A1; SLC5A3; SLCO1B1; SLIT3; SMAD3; SMARCA4; SMARCC1; SMCR3; SMG6; SNF8; SNX1; SNX10; SORCS2; SORT1; SOX9; SPAG9; SPATA7; SPC24; SPC25; SPG21; SREBF1; SRPK1; SRPR; SRR; SSU72; ST3GAL4; ST8SIA1; STAG3L3; STAT1; STEAP1; STK32B; STMN3; SUCLG1; SURF1; SURF6; SWAP70; SYP; T40707; TAF1A; TAGAP; TAGLN; TBXAS1; TCF21; TCP11; TCTN1; TERT; TEX2; TFPI; TGM3; TIRAP; TMEM101; TMEM116; TMEM161B; TMEM180; TMEM91; TMUB2; TNS1; TOM1L2; TOMM40; TP53I3; TRAFD1; TRIB1; TRIM73; TRIP4; TRPC4AP; TSC22D2; TSPAN14; TSR1; TTC32; UBAP2L; UBE2L6; UBE2Z; UBTF; UBXD4; UBXN2A; UNC45A; UNQ9391; UPP1; UQCC; USMG5; USP39; USP53; UVRAG; VAMP5; VAMP8; VASP; VEGFA; VPS33B; WBSCR16; WDR12; WDR33; WDR35; WDR51B; WDR86-AS1; XRRA1; YY1; Z85996.1-1; ZC3HC1; ZEB2; ZFPM2; ZFYVE20; ZNF259; ZNF383; ZNF589; ZNF652
CAD 1000G	ABCG5; ABCG8; ABHD2; ABO; ACAD10; ACO74093.1; ACSS2; ADAMTS7; ADORA2A; ADTRP; AGBL1; AK097927; AKAP13; ALDH2; ALDH8A1; ALS2CR16; ANKS1A; ANXA11; APOA1; APOA4; APOA5; APOB; APOC1; APOC2; APOC3; APOC4; APOE; ARHGAP26; ARVCF; ASIC2; ATP2B1; ATP5G1; ATP5SL; ATPAF2; ATXN2; ATXN3; BCAS3; BMP1; BMPR1A; BNC2; BSND; BTNL2; C10orf76; C12orf43; C12orf51; C2orf85; C6orf10; C6orf105; CA10; CACNA1E; CACNA2D3; CALCRL; CAMSAP1L1; CAPS2; CCDC157; CDH13; CDH9; CDKN1A; CDKN2A; CDKN2B; CDKN2B-AS1; CELSR2; CKM; CNNM2; COG5; COL4A1; COL4A2; COL4A4; CTAGE1; CUX2; CXCL12; CYP17A1; CYP46A1; DCPS; DDX59; DNAH6; DYNC2LI1; EDNRA; EEF1E1; EMP1; ERBB4; FBXO15; FBXO3; FES; FHL5; FLJ43860; FLT1; FMN2; FN1; FNDC1; FURIN; GGCX; GIP; GNPDA2; GRIN3A; GUCY1A3; HCG27; HDAC9; HECTD4; HEMGN; HFE2; HHIPL1; HIP1; HLA-C; HLA-DQB1; HNF1A; HSD17B12; HSP90B1; IFT88; IL6R; INPP5D; IPMK; JAZF1; KCNE2; KCNK13; KCNK5; KCNQ3; KIAA1462; KLF6; KSR2; LARGE; LDLR; LIPA; LMOD1; LOC400684; LOC646730; LPA; LPAL2; LPL; LRP6; LRRC2; LRRC48; LY86; LYSMD4; MAP3K4; MAP4; MAP9; MARK4; MC4R; MCART2; MCL1; MFGE8; MIA3; MIR4499; MIR548AV; MIR548G; MORF4L1;

	MRAS; MRG15; MRPS6; MSI2; MTAP; MTHFD1L; MUTED; MYBPHL; MYL2; NGF; NME7; NOA1; NOS3; NRG1; NT5C2; NUMB; OBFC1; OSM; PARP12; PCNXL3; PCSK9; PDE3A; PDGFD; PDGFRA; PECAM1; PEMT; PHACTR1; PKN2; PLD5; PLEKHG1; PLG; PMAIP1; PODXL; POM121L9P; PPAP2B; PPP2R3A; PRICKLE2; PRICKLE2-AS3; PRKCA; PROCR; PSRC1; RAI1; RASD1; RBPMS2; REST; RGS2; RIT2; RND3; RPEL; RPH3A; SARS; SCARB1; SEMA6D; SERPINH1; SF3A1; SH2B3; SKI; SLC1A1; SLC22A3; SLC22A4; SLC22A5; SLC2A13; SLC5A3; SLCO1B1; SMAD3; SMARCA4; SMCR3; SMG6; SNF8; SNX10; SORCS2; SORT1; SOX9; SPATA7; SPC24; SRR; ST3GAL4; ST8SIA1; STEAP1; STK32B; SUCLG1; SWAP70; TCF21; TERT; TFPI; TMEM161B; TNS1; TOM1L2; TOMM40; TRAFD1; TRIB1; TSC22D2; TTC32; UBE2Z; UBTF; USP53; VAMP5; VAMP8; VEGFA; WDR12; WDR33; WDR35; WDR86-AS1; ZC3HC1; ZEB2; ZFPM2; ZNF259; ZNF383; ZNF507; ZNF652
CAD 1000G Extend	A4GNT; ABCB8; ABCG5; ABCG8; ABO; AC026250.16; AC087164.1; ACAD10; ACOX1; ACSS2; ACTA2; ACTR1A; ADAM1A; ADAMTS7; ADAMTSL4; ADM; ADTRP; AF001540; AF075116; AF085859; AF124731.2; AF147302; AGAP3; AGBL1; AIDA; AJ276246; AK023781; AK023818; AK025221; AK054569; AK054837; AK055254; AK095583; AK095904; AK097622; AK098707; AK124806; AK296065; AKAP11; AKAP13; AL049353; AL049919; AL049980; AL512662.8-2; AL591069.5; AL713721; ALDH2; ALDH8A1; ALS2CR13; ALS2CR16; ALS2CR8; ANKDD1A; ANKRD10; ANKRD25; ANKRD52; ANKS1A; ANXA11; APOA1; APOA4; APOA5; APOB; APOC1; APOC1P1; APOC2; APOC3; APOC4; APOC4-APOC2; APOE; AQP10; ARHGAP26; ARHGEF26; ARHGEF26-AS1; ARL3; ARNT; ARNTL; ARVCF; AS3MT; ASB16; ASB16-AS1; ASIC2; ASIC3; ATG9B; ATIC; ATP1B1; ATP2B1; ATP5G1; ATP5SL; ATP8B2; ATPAF2; ATRIP; ATXN2; ATXN3; ATXN7L2; ATXN7L3; AX747860; B3GALT7; B3GNT8; B4GALT5; B9D2; BC038201; BC040833; BC040861; BC041459; BC042070; BC128410; BC150162; BCAP29; BCKDHA; BLM; BLZF1; BMP1; BMPR1A; BNC2; BRAP; BSND; BTNL2; BUD13; C10orf26; C10orf32; C10orf57; C10orf58; C10orf76; C12ORF24; C12orf30; C12orf43; C12orf47; C12orf51; C16orf52; C17orf39; C17orf53; C17orf65; C19orf52; C19orf69; C19orf80; C1orf138; C1orf58; C1orf80; C1ORF86; C21orf7; C22ORF25; C2CD4D; C2orf44; C2orf68; C2orf84; C2orf85; C3orf38; C3ORF75; C4orf3; C6orf10; C6orf106; C6orf64; C6orf72; C9orf96; CA10; CACNA1E; CACNA2D3; CACNG5; CALCOCO2; CALCRL; CAMP; CAMSAP1L1; CAMSAP2; CAPS2; CARF; CARM1; CARS2; CCBL2; CCDC157; CCDC181; CCDC19; CCDC85C; CCL25; CCT8; CD82; CDC25A; CDH13; CDH9; CDK5; CDKN1A; CDKN2A; CDKN2B; CDKN2B-AS1; CDKN2B_AS; CEACAM1; CECR6; CELSR2; CEP250; CEP70; CGGBP1; CH25H; CHRNA5; CHRNB4; CKM; CKS1B; CLASRP; CLEC10A; CLPTM1; CMTM2; CNNM2; CNPY2; COG5; COG6; COL4A1; COL4A2; COL4A2-AS1; COL4A4; COMT; Contig21679_RC; Contig2512_RC; Contig30461_RC; Contig37346; Contig46411_RC; Contig53460_RC; COQ10A; CPNE1; CRTC3; CS; CSNK1G1; CSPG5; CTAGE1; CTSH; CTSK; CTSS; CUX2; CXCL12; CYP17A1; CYP17A1-AS1; CYP26B1; CYP46A1; CYP4F11; CYP4F2; DAB2IP; DCPS; DCST1; DCST2; DDX59; DEF6; DENND5A; DGCR8; DHX30; DHX36; DKFZp434K191; DKFZP564C152; DKFZP761E198; DL490821; DLX4; DNAH6; DOCK5; DOCK6; DPEP3; DPF2; DPH1; DPYSL2; DQ601906; DRG2; DSTN; DYDC2; DYNC2LI1; DYNLRB1; EDEM2; EDNRA; EEF1E1; EIF2A; EIF6; EML1; EMP1; ENSA; ENSG00000047849.17; ENSG00000107798.11; ENSG00000111252.5; ENSG00000115486.6; ENSG00000135213.8; ENSG00000136378.8; ENSG00000138380.11; ENSG00000140395.3; ENSG00000154305.11; ENSG00000159202.11; ENSG00000160679.8; ENSG00000182511.7; ENST00000238803; ENST00000296496; ENST00000300223; ERBB4; ERCC2; ERGIC3; ERP29; ESYT3; EXOSC5; FABP2; FAIM; FAM100B; FAM102B; FAM109A; FAM117B; FAM118B; FAM177B; FAM212A; FAM213A; FAM228A; FAM228B; FAM46A; FARS2; FASTK; FBF1; FBXO15; FBXO3; FBXO46; FBXW5; FCF1P2; FCHO1; FES; FHL3; FHL5; FIP1L1; FKBP1B; FLAD1; FLCN; FLJ12334; FLJ20004; FLJ21127; FLJ30092; FLJ35700; FLJ39616; FLJ42875; FLJ43860; FLT1; FMN2; FN1; FNDC1; FOS; FOXRED1; FURIN; G6PC3; GALK1; GALNT4; GAPDHP14; GAST; GATA2; GBGT1; GBP1; GBP2; GBP4; GBP5; GCDH; GDPD5; GGCX; GGT7; GGTL3; GID4; GINM1; GIP; GJC1; GNAI3; GNGT2; GNLY; GNPDA2; GOLPH3L; GON4L; GPN3; GPR22; GPX1; GRAP2; GRIN3A; GSS; GSTM4; GTF2B; GUCY1A3; HBP1; HCG27; hCT1644816.3; hCT1652322.2; hCT1815537; hCT1970935; HDAC5; HDAC9; HDC; HDDC3; HECTD4; HEMGN; HFE2; HHIPL1; HIP1; HIST1H2BD; HIVEP1; HLA-C; HLA-DQB1; HNF1A; HORMAD1; HS.443185; Hs.494277; HS.539450; hsa-miR-185; HSD17B12; HSP90B1; HSS00142168; ICA1L; ICAM1; IDS; IFIT1; IFIT2; IFIT3; IFIT5; IFT88; IGF2BP1; IGSF9; IL20RB; IL23A; IL6R; IL8; INPP5B; INPP5D; INTS10; IP6K2; IPMK; IPO7; IPO9; IREB2; IRF1; IRS2; ITCH; ITGA3; ITGB4BP; JAZF1; JB074994; KANK2; KAT3; KATNA1; KCNE2; KCNH2; KCNJ5; KCNK13; KCNK5; KCNN3; KCNQ3; KIAA1143; KIAA1324; KIAA1462; KIF14; KLC3; KLF6; KLHDC10; KLHL18; KLHL35; LAMP2; LARGE; LATS1; LDLR; LENEP; LIMD1; LINC00189; LINC00310; LINC00857; LINGO4; LIPA; LMOD1; LOC100129828; LOC100131662; LOC283033; LOC338862; LOC340322; LOC401152; LOC402176; LOC407835; LOC646730; LOC653764; LOC729580; LPA; LPAL2; LPIN3; LPL; LRP1; LRP11; LRP6; LRRC16A; LRRC2; LRRC48; LTF; LY86; LYSMD4; MALAT1; MAN2A2; MAP1LC3A; MAP1S; MAP3K11; MAP3K4; MAP3K7CL; MAP4; MAP6; MAP9; MAPKAPK5; MAPKAPK5-AS1; MAPRE3; MARCKSL1; MARCKSL1P1; MARK4; MAT1A; MAT2A; MCART2; MCL1; MED22; MEF2C; METTL14; MFGE8; MFSD2B; MGC34034; MIA3; MIR1228; MIR1297; MIR1306; MIR1307; MIR185; MIR324; MIR3618; MIR384; MIR4257; MIR4258; MIR4499; MIR4693; MIR4761; MIR5188; MIR5193; MIR548AV; MIR548G; MLEC; MMP24; MMP24-AS1; MORF4L1; MORN1; MRAS; MRG15; MRPL18; MRPL38; MRPL9; MRPS18AP1; MRPS6; MSI2; MSL2; MSL2L1; MSTO2P; MT1P3; MTAP; MTHFD1L; MTP18; MUTED; MYADM; MYBPHL; MYH7B; MYL2; MYO15A; N4BP2L2; NA; NAB2; NABP2; NAE1; NALP12; NBEAL1; NCLN; NCOA6; NCRNA00173; NDUFA4L2; NFE2L3; NGF; NICN1; NICN1-AS1; NME6; NME7; NM_015055; NM_018035; NOS3; NRG1; NT5C2; NUDT13; NUDT18; NUGGC; NUMB; NUP43; NXPH4; OAS1; OASL; OAZ2; OAZ3; OBFC1; OIT3; OPLAH; OR10H4; OSM; OVOL1; P4HA2; PAN2; PARP12; PBXIP1; PCCB; PCMT1; PCNXL3; PCSK7; PCSK9; PDE3A; PDE5A; PDGFD; PDGFRA; PDLIM4; PECAM1; PEMT; PEX10; PFAAP5; PFN4; PHACTR1; PHB; PHOSPHO1; PIK3CG; PKN2; PLAC9; PLD5; PLEKHG1; PLEKHH2; PLG; PMS2L3; PMS2P10; PMS2P3; PMVK; POC1B; PODXL; POLG2; POM121C; PPAP2B; PPHLN1; PPP1R15A; PPP2R3A; PRICKLE2; PRICKLE2-AS3; PRKAB2; PRKCA; PRKCZ; PRO1185; PROCR; PRPSAP1; PSMA4; PSMA5; PSME3; PSRC1; PTPN23; PVRL2; PYGO2; QRICH2; RAB11FIP5; RAB20; RAET1E-AS1; RAET1G; RAI1; RALY; RANBP9; RAPH1; RASD1; RBL1; RBM6; RBPMS2; RCCD1; RELA; RELB; RER1; REST; RGS2; RHBDD1; RIT2; RNASEH2C; RND3; RNF157; RNF157-AS1; RNF181; RNF184; RNF41; ROMO1; RORC; RP11-541N10.2; RPEL; RPH3A; RPL7A; RRBP1; RUNDC3A; S100A10; SARS; SCARB1; SCGN; SEC24D; SEMA6D; SERPINH1; SF3A1; SF3A3; SF3B14; SFTPB; SFTPC; SFTPD; SFXN2; SGSM2; SH2B3; SH2D4B; SH3PXD2A; SHC1; SHE; SHISA4; SHMT2; SIDT2; SIK3; SIPA1; SKAP1; SKI; SLAMF9; SLC1A1; SLC22A1; SLC22A3; SLC22A4; SLC22A5; SLC25A39; SLC2A12; SLC2A13; SLC39A5; SLC4A1; SLC4A2; SLC5A3; SLCO1B1; SLIT3; SMAD3; SMARCA4; SMARCC1; SMCR3; SMG6; SNF8; SNORA16; SNORD24; SNORD36A; SNORD36B; SNORD36C; SNRPC; SNRPD2; SNX1; SNX10; SORCS2; SORT1; SOX9; SPAG9; SPATA7; SPC24; SPC25; SPG21; SPINK8; SPPL3; SPRYD4; SREBF1; SRPK1; SRPR; SRR; SSU72; ST3GAL4; ST8SIA1; STAG3L1; STAG3L3; STAT1; STAT2; STAT6; STEAP1; STK32B; STMN3; SUCLG1; SURF1; SURF2; SURF4; SURF6; SWAP70; SYP; SYPL2; SYT11; T40707; TAF1A; TAGAP; TAGLN; TAGLN2; TANGO2; TBPL1; TBX2; TBXAS1; TCF21; TCP11; TCTN1; TDGF1; TDRD10; TDRKH; TEAD3; TERT; TEX2; TEX41; TFPI; TGM3; THADA; THEM4; THEM5; TIRAP; TMA7; TMEM101; TMEM116; TMEM150A; TMEM161B; TMEM180; TMEM194A; TMEM41B; TMEM91; TMUB1; TMUB2; TNS1; TOM1L2; TOMM40; TP53I3; TP53INP2; TRAFD1; TRIB1; TRIM47; TRIM65; TRIM73; TRIP4; TRPC4AP; TSC22D2; TSPAN14; TSR1; TTC32; TTLL6; U6; U80770; UBA7; UBALD2; UBAP2L; UBC; UBE2L6; UBE2Z; UBTF; UBXD4; UBXN2A; UCA1; UFL1; UHRF1BP1; UNC13D; UNC45A; UNQ599; UNQ9391; UPP1; UQCC; USMG5; USP39; USP48; USP53; UTP11L; UVRAG; VAMP5; VAMP8; VASP; VEGFA; VPS33B; WBP1L; WBP2; WBSCR16; WDR12; WDR33; WDR35; WDR51B; WDR86-AS1; XRRA1; YY1; YY1AP1; Z85996.1-1; ZBTB7B; ZC3HC1; ZCRB1; ZEB2; ZEB2-AS1; ZFP36L2; ZFPM2; ZFYVE20; ZNF226; ZNF259; ZNF383; ZNF589; ZNF652

The spreadsheets in Supplemental Table II are listed in the order:

Supplemental Table II a. Key driver genes in CAD_GWAS gene list;

Supplemental Table II b. Key driver genes in CAD_GWAS_lipid gene list;

Supplemental Table II c. Key driver genes in CAD_C4D gene list;

Supplemental Table II d. Key driver genes in CAD_C4D_lipid gene list;

Supplemental Table II e. Key driver genes in CAD_Extend gene list;

Supplemental Table II f. Key driver genes in CAD_1000G gene list;

Supplemental Table II g. Key driver genes in CAD_1000G_Extend gene list.

Supplemental Table II h. Meta-analysis of KDA results based on seven gene lists in 14 networks (13 tissue-specific gene regulatory networks and 1 PPI network).

Supplemental Table II a. Key driver genes in CAD_GWAS gene list. Key driver genes with red highlight are detected in at least network.

CAD Gene List	Key Drivers	P Values	FDR	Belonging to CAD Genes	Network Sources
CAD_GWAS	COL6A3	3.90E-10	3.90E-09	FALSE	Liver
CAD_GWAS	KNG1	1.25E-08	1.25E-07	FALSE	Brain
CAD_GWAS	NM_009245	4.09E-07	2.05E-06	FALSE	Brain
CAD_GWAS	DUSP1	3.78E-07	3.78E-06	FALSE	Artery
CAD_GWAS	CAV1	4.57E-06	1.57E-05	FALSE	Artery
CAD_GWAS	MGLL	4.73E-06	1.60E-05	FALSE	Artery
CAD_GWAS	SERPINE1	9.67E-06	2.42E-05	FALSE	Artery
CAD_GWAS	LUM	7.32E-06	2.44E-05	FALSE	Brain
CAD_GWAS	VEGFC	1.27E-05	2.54E-05	FALSE	Artery
CAD_GWAS	ZFP36L2	4.00E-06	2.68E-05	FALSE	Vascular_endothelium
CAD_GWAS	SH2B3	5.54E-06	2.94E-05	TRUE	Vascular_endothelium
CAD_GWAS	CCL2	1.11E-05	3.69E-05	FALSE	Vascular_endothelium
CAD_GWAS	DUSP6	2.66E-05	3.89E-05	FALSE	Artery
CAD_GWAS	CAST	2.74E-05	3.91E-05	FALSE	Artery
CAD_GWAS	TRIB1	3.16E-05	3.95E-05	FALSE	Artery
CAD_GWAS	CCL2	3.85E-05	4.28E-05	FALSE	Artery
CAD_GWAS	DUSP5	4.50E-05	4.50E-05	FALSE	Artery
CAD_GWAS	HMOX1	4.87E-05	7.43E-05	FALSE	Vascular_endothelium
CAD_GWAS	JAG1	5.02E-05	7.50E-05	FALSE	Vascular_endothelium
CAD_GWAS	SAT1	9.98E-06	7.67E-05	FALSE	Aorta
CAD_GWAS	PLAUR	5.16E-05	7.67E-05	FALSE	Vascular_endothelium
CAD_GWAS	EMP1	5.27E-05	7.84E-05	TRUE	Vascular_endothelium
CAD_GWAS	MAF	1.09E-05	8.74E-05	FALSE	Smooth_muscle
CAD_GWAS	ACTN1	1.62E-05	8.85E-05	FALSE	Aorta
CAD_GWAS	KCNK13	1.87E-05	9.36E-05	TRUE	Liver
CAD_GWAS	PDCD4	3.38E-05	0.000112647	FALSE	Aorta
CAD_GWAS	SDCBP	4.52E-05	0.000112974	FALSE	Aorta
CAD_GWAS	DUSP6	1.85E-05	0.000119978	FALSE	Smooth_muscle
CAD_GWAS	HMOX1	1.37E-05	0.000136611	FALSE	Cardiac_muscle
CAD_GWAS	C3	0.000113123	0.000141404	FALSE	Vascular_endothelium
CAD_GWAS	SORL1	0.000143964	0.00014446	FALSE	Vascular_endothelium
CAD_GWAS	TCF7L2	8.17E-05	0.000161643	FALSE	Aorta
CAD_GWAS	CTGF	3.37E-05	0.000168706	FALSE	Cardiac_muscle
CAD_GWAS	SFRP1	7.10E-05	0.00023676	FALSE	Cardiac_muscle
CAD_GWAS	ITGB5	8.71E-05	0.000290261	FALSE	Smooth_muscle
CAD_GWAS	TRIB2	0.000208724	0.000521809	FALSE	Cardiac_muscle
CAD_GWAS	F2	8.61E-05	0.000860973	FALSE	Muscle
CAD_GWAS	COL1A1	0.000262743	0.00087581	FALSE	Liver
CAD_GWAS	ADAMTS1	0.000402993	0.001007483	FALSE	Smooth_muscle

CAD_GWAS	LY96	0.00014446	0.00103343	FALSE	Vascular_endothelium
CAD_GWAS	MTMR11	0.000451541	0.001128853	FALSE	Liver
CAD_GWAS	CXCL12	0.000811656	0.001425988	TRUE	Cardiac_muscle
CAD_GWAS	CCND1	0.000870283	0.001496343	FALSE	Cardiac_muscle
CAD_GWAS	DUSP1	0.000789195	0.001578389	FALSE	Smooth_muscle
CAD_GWAS	APOC3	0.00066515	0.001662875	TRUE	Brain
CAD_GWAS	LHFPL2	0.001357161	0.002261935	FALSE	Smooth_muscle
CAD_GWAS	LARGE	0.001363821	0.002273034	TRUE	Liver
CAD_GWAS	WIPF1	0.001363821	0.002273034	FALSE	Liver
CAD_GWAS	EPS8	0.001806033	0.002580047	FALSE	Liver
CAD_GWAS	APOA5	0.002064846	0.002581058	TRUE	Liver
CAD_GWAS	RBPMS	0.002515072	0.002961547	FALSE	Cardiac_muscle
CAD_GWAS	RND3	0.002607603	0.003013951	FALSE	Cardiac_muscle
CAD_GWAS	EFEMP1	0.002714358	0.003122763	FALSE	Cardiac_muscle
CAD_GWAS	CKLF	0.003016213	0.003351348	FALSE	Liver
CAD_GWAS	LOXL2	0.003818081	0.003818081	FALSE	Liver
CAD_GWAS	KCTD12	0.003164751	0.003830979	FALSE	Smooth_muscle
CAD_GWAS	F2	0.000435926	0.004359255	FALSE	Adipose
CAD_GWAS	EMP1	0.004651287	0.004651287	TRUE	Cardiac_muscle
CAD_GWAS	APOA1	0.003219456	0.006438912	TRUE	Brain
CAD_GWAS	APOA1	0.00132646	0.006632299	TRUE	Muscle
CAD_GWAS	PHACTR1	0.004587929	0.007646549	TRUE	Brain
CAD_GWAS	VEGFA	0.002337765	0.008109102	TRUE	Adipose
CAD_GWAS	MCOLN1	0.005731326	0.008187608	FALSE	Brain
CAD_GWAS	MMT00019644	0.00244958	0.008477713	FALSE	Adipose
CAD_GWAS	HGD	0.0095898	0.01198725	FALSE	Brain
CAD_GWAS	KL	0.011608888	0.012735789	FALSE	Brain
CAD_GWAS	COL4A2	0.006927095	0.013758662	TRUE	Muscle
CAD_GWAS	KNG1	0.007753219	0.014291424	FALSE	Muscle
CAD_GWAS	ALDOB	0.008652748	0.014656671	FALSE	Muscle
CAD_GWAS	SCARA3	0.008652748	0.014656671	FALSE	Muscle
CAD_GWAS	HELZ	0.010689486	0.015270695	FALSE	Muscle
CAD_GWAS	SPARC	0.013073267	0.016341584	FALSE	Muscle
CAD_GWAS	TNFAIP3	0.003300456	0.0168216	FALSE	Smooth_muscle
CAD_GWAS	MMP9	0.004125589	0.025561743	FALSE	PPI
CAD_GWAS	FN1	0.005338642	0.02701645	TRUE	PPI
CAD_GWAS	CTNNB1	0.008466229	0.028220762	FALSE	PPI
CAD_GWAS	TGFBI	0.012124266	0.030310666	FALSE	PPI
CAD_GWAS	CD74	0.013368713	0.033421783	FALSE	Adipose
CAD_GWAS	SLC4A7	0.003506459	0.035651774	FALSE	Smooth_muscle
CAD_GWAS	IGSF10	0.034113846	0.037904273	FALSE	Muscle
CAD_GWAS	MATN2	0.019282765	0.038565529	FALSE	PPI
CAD_GWAS	RRAD	0.022443991	0.040388568	FALSE	Adipose
CAD_GWAS	HGD	0.042742486	0.042742486	FALSE	Muscle
CAD_GWAS	ADCY5	0.026677325	0.042745594	FALSE	Adipose
CAD_GWAS	COL4A1	0.029787573	0.043829884	TRUE	Adipose
CAD_GWAS	SERPINC1	0.036765977	0.045957472	FALSE	Adipose
CAD_GWAS	RDH16	0.012735789	0.046726945	FALSE	Brain
CAD_GWAS	ERBB4	0.032370318	0.046774284	TRUE	Kidney
CAD_GWAS	TMEM169	0.032370318	0.046774284	FALSE	Kidney
CAD_GWAS	BC042789	0.033208996	0.047309976	FALSE	Kidney
CAD_GWAS	ITGA7	0.042725397	0.047472663	FALSE	Adipose
CAD_GWAS	NCOR2	0.034037802	0.047828522	FALSE	Kidney
CAD_GWAS	AK003941	0.037297337	0.055406219	FALSE	Kidney
CAD_GWAS	FN1	0.037297337	0.055406219	TRUE	Kidney
CAD_GWAS	APOB	0.036424793	0.056519349	FALSE	PPI
CAD_GWAS	COLEC12	0.038106203	0.058167113	FALSE	Kidney
CAD_GWAS	COL4A2	0.040743713	0.058840922	TRUE	PPI
CAD_GWAS	MCM6	0.059403499	0.059403499	FALSE	Adipose
CAD_GWAS	GEM	0.038915074	0.060880629	FALSE	Kidney
CAD_GWAS	SHC1	0.049934402	0.061219145	FALSE	PPI
CAD_GWAS	SGK1	0.003830979	0.063390471	FALSE	Smooth_muscle
CAD_GWAS	FBLN2	0.055689348	0.065392812	FALSE	PPI
CAD_GWAS	PRKACB	0.000122299	0.086877956	FALSE	Aorta

Supplemental Table II b. Key driver genes in CAD_GWAS_lipid gene list. Key driver genes with red highlight are detected in at least network.

CAD Gene List	Key Drivers	P Values	FDR	Belonging to CAD Genes	Network Sources
CAD_GWAS_lipid	COL6A3	4.38E-08	4.38E-07	FALSE	Liver
CAD_GWAS_lipid	LUM	1.11E-06	1.11E-05	FALSE	Brain

CAD_GWAS_lipid	KCNK13	6.61E-06	3.31E-05	TRUE	Liver
CAD_GWAS_lipid	CCL2	6.11E-06	6.11E-05	FALSE	Vascular_endothelium
CAD_GWAS_lipid	SH2B3	3.76E-05	0.000187889	TRUE	Vascular_endothelium
CAD_GWAS_lipid	DUSP1	1.98E-05	0.000197696	FALSE	Artery
CAD_GWAS_lipid	MLLT11	6.66E-05	0.000220575	FALSE	Aorta
CAD_GWAS_lipid	CNIH1	7.15E-05	0.000224462	FALSE	Aorta
CAD_GWAS_lipid	PNRC1	9.12E-05	0.000237847	FALSE	Aorta
CAD_GWAS_lipid	TCF7L2	0.000121288	0.000248226	FALSE	Aorta
CAD_GWAS_lipid	SLIT2	0.000129435	0.000249993	FALSE	Aorta
CAD_GWAS_lipid	PRKACB	0.000145838	0.000253256	FALSE	Aorta
CAD_GWAS_lipid	ACTN1	0.000194659	0.000261255	FALSE	Aorta
CAD_GWAS_lipid	PDCD4	0.000209847	0.000265792	FALSE	Aorta
CAD_GWAS_lipid	BNIP3L	0.000287527	0.000295381	FALSE	Aorta
CAD_GWAS_lipid	COL1A1	8.92E-05	0.000297309	FALSE	Liver
CAD_GWAS_lipid	PLAUR	0.000157011	0.000355172	FALSE	Vascular_endothelium
CAD_GWAS_lipid	MTMR11	0.00015168	0.0003792	FALSE	Liver
CAD_GWAS_lipid	JAG1	0.000200786	0.000385818	FALSE	Vascular_endothelium
CAD_GWAS_lipid	LY96	0.000218498	0.000403158	FALSE	Vascular_endothelium
CAD_GWAS_lipid	RND3	0.000230917	0.000414549	FALSE	Vascular_endothelium
CAD_GWAS_lipid	IGFBP6	8.86E-05	0.00044295	FALSE	Artery
CAD_GWAS_lipid	CAV1	0.000155947	0.000473888	FALSE	Artery
CAD_GWAS_lipid	SERPINE1	0.000191879	0.00048489	FALSE	Artery
CAD_GWAS_lipid	AKT3	0.000249078	0.000498156	FALSE	Artery
CAD_GWAS_lipid	COL5A2	0.000387735	0.00052346	FALSE	Vascular_endothelium
CAD_GWAS_lipid	ZFP36L2	0.000427066	0.000539836	FALSE	Vascular_endothelium
CAD_GWAS_lipid	FAS	0.000568724	0.000575933	FALSE	Vascular_endothelium
CAD_GWAS_lipid	MGLL	0.000438943	0.000649184	FALSE	Artery
CAD_GWAS_lipid	CNN3	0.000570899	0.000721254	FALSE	Artery
CAD_GWAS_lipid	ANXA1	0.000632175	0.000748232	FALSE	Artery
CAD_GWAS_lipid	SERPINH1	0.000647242	0.000754494	FALSE	Artery
CAD_GWAS_lipid	KCTD12	0.000817066	0.000817066	FALSE	Artery
CAD_GWAS_lipid	MAF	9.15E-05	0.000914589	FALSE	Smooth_muscle
CAD_GWAS_lipid	DUSP6	0.000309948	0.001328244	FALSE	Smooth_muscle
CAD_GWAS_lipid	LARGE	0.00084687	0.00141145	TRUE	Liver
CAD_GWAS_lipid	WIPF1	0.00084687	0.00141145	FALSE	Liver
CAD_GWAS_lipid	EPS8	0.001105451	0.001579216	FALSE	Liver
CAD_GWAS_lipid	ADAMTS1	0.00041394	0.002166074	FALSE	Smooth_muscle
CAD_GWAS_lipid	CKLF	0.001797606	0.002247007	FALSE	Liver
CAD_GWAS_lipid	CXCL12	0.002778417	0.00308713	TRUE	Liver
CAD_GWAS_lipid	SRPX	0.000575933	0.004140986	FALSE	Vascular_endothelium
CAD_GWAS_lipid	MMT00002956	0.004956035	0.004956035	FALSE	Liver
CAD_GWAS_lipid	SLC2A3	0.000295381	0.007534392	FALSE	Aorta
CAD_GWAS_lipid	SFRP1	0.001091951	0.008618538	FALSE	Cardiac_muscle
CAD_GWAS_lipid	HMOX1	0.001864935	0.009493368	FALSE	Cardiac_muscle
CAD_GWAS_lipid	TRIB2	0.002937893	0.009792976	FALSE	Cardiac_muscle
CAD_GWAS_lipid	PHACTR1	0.002435576	0.00996116	TRUE	Brain
CAD_GWAS_lipid	CD74	0.001166917	0.011669173	FALSE	Adipose
CAD_GWAS_lipid	CTGF	0.004749154	0.011872886	FALSE	Cardiac_muscle
CAD_GWAS_lipid	MCOLN1	0.003044786	0.016049166	FALSE	Brain
CAD_GWAS_lipid	LHFPL2	0.011128221	0.023092513	FALSE	Smooth_muscle
CAD_GWAS_lipid	DUSP1	0.0137867	0.024499619	FALSE	Smooth_muscle
CAD_GWAS_lipid	KCTD12	0.014598953	0.024688138	FALSE	Smooth_muscle
CAD_GWAS_lipid	VEGFA	0.009533491	0.025538385	FALSE	Adipose
CAD_GWAS_lipid	SLC4A7	0.019843577	0.025725582	FALSE	Smooth_muscle
CAD_GWAS_lipid	ITGA7	0.010384847	0.026415883	FALSE	Adipose
CAD_GWAS_lipid	MMT00019644	0.010384847	0.026415883	FALSE	Adipose
CAD_GWAS_lipid	ACKR3	0.02096515	0.038963809	FALSE	Cardiac_muscle
CAD_GWAS_lipid	CXCL12	0.022396979	0.039384685	TRUE	Adipose
CAD_GWAS_lipid	CD14	0.024003626	0.040712501	FALSE	Adipose
CAD_GWAS_lipid	RBPMS	0.024274449	0.042786554	FALSE	Cardiac_muscle
CAD_GWAS_lipid	LYVE1	0.033349729	0.047642469	FALSE	Adipose
CAD_GWAS_lipid	SGK1	0.021540162	0.055639894	FALSE	Smooth_muscle
CAD_GWAS_lipid	HAVCR2	0.045120329	0.056400412	FALSE	Adipose
CAD_GWAS_lipid	TBC1D9	0.044090304	0.062986149	FALSE	Cardiac_muscle
CAD_GWAS_lipid	KANK1	0.058553976	0.063558804	FALSE	Cardiac_muscle
CAD_GWAS_lipid	ACCN1	0.006494572	0.064945716	FALSE	Islet
CAD_GWAS_lipid	COL4A2	0.007204289	0.072042887	TRUE	Muscle
CAD_GWAS_lipid	NCOR2	0.014867707	0.08386397	FALSE	Kidney
CAD_GWAS_lipid	GEM	0.017276253	0.09320353	FALSE	Kidney
CAD_GWAS_lipid	TNFAIP3	0.023905956	0.094191343	FALSE	Smooth_muscle
CAD_GWAS_lipid	MPRIP	0.062867871	0.095832082	FALSE	Cardiac_muscle

Supplemental Table II c. Key driver genes in CAD_C4D gene list. Key driver genes with red highlight are detected in at least network.

CAD Gene List	Key Drivers	P Values	FDR	Belonging to CAD Genes	Network Sources
CAD_C4D	F2	6.86E-11	6.86E-10	FALSE	Adipose
CAD_C4D	CD93	8.15E-09	8.15E-08	FALSE	Aorta
CAD_C4D	C3	1.06E-08	8.80E-08	FALSE	Vascular_endothelium
CAD_C4D	CCL2	1.84E-08	1.09E-07	FALSE	Vascular_endothelium
CAD_C4D	EMP1	5.24E-08	1.75E-07	TRUE	Vascular_endothelium
CAD_C4D	SAT1	4.13E-08	2.07E-07	FALSE	Aorta
CAD_C4D	TMX4	6.34E-08	2.10E-07	FALSE	Aorta
CAD_C4D	RGS2	8.42E-08	2.21E-07	TRUE	Aorta
CAD_C4D	C8orf4	1.24E-07	2.48E-07	FALSE	Aorta
CAD_C4D	PDCD4	2.00E-07	3.33E-07	FALSE	Aorta
CAD_C4D	PNRC1	4.36E-07	6.23E-07	FALSE	Aorta
CAD_C4D	LYN	5.07E-07	6.34E-07	FALSE	Aorta
CAD_C4D	ZFP36L2	2.77E-07	6.93E-07	FALSE	Vascular_endothelium
CAD_C4D	JAG1	3.51E-07	7.03E-07	FALSE	Vascular_endothelium
CAD_C4D	DUSP1	1.16E-07	8.26E-07	FALSE	Artery
CAD_C4D	JUN	5.18E-07	8.63E-07	FALSE	Vascular_endothelium
CAD_C4D	CCL2	1.71E-07	9.48E-07	FALSE	Artery
CAD_C4D	SH2B3	7.00E-07	1.00E-06	TRUE	Vascular_endothelium
CAD_C4D	ACTN1	9.11E-07	1.01E-06	FALSE	Aorta
CAD_C4D	ELL2	1.14E-06	1.14E-06	FALSE	Aorta
CAD_C4D	PODXL	9.76E-07	1.22E-06	TRUE	Vascular_endothelium
CAD_C4D	VEGFA	3.27E-07	1.51E-06	TRUE	Adipose
CAD_C4D	HLA-F	6.02E-07	1.57E-06	FALSE	Artery
CAD_C4D	ANXA1	6.98E-07	1.65E-06	FALSE	Artery
CAD_C4D	RCAN1	8.25E-07	1.74E-06	FALSE	Artery
CAD_C4D	DUSP5	1.16E-06	1.93E-06	FALSE	Artery
CAD_C4D	G0S2	1.88E-06	2.32E-06	FALSE	Artery
CAD_C4D	ADM	2.01E-06	2.38E-06	FALSE	Artery
CAD_C4D	MMT00019644	4.63E-07	2.43E-06	FALSE	Adipose
CAD_C4D	RFTN1	2.14E-06	2.45E-06	FALSE	Artery
CAD_C4D	KLF10	2.76E-06	2.76E-06	FALSE	Artery
CAD_C4D	SRPX	2.49E-06	2.77E-06	FALSE	Vascular_endothelium
CAD_C4D	F3	3.05E-06	3.05E-06	FALSE	Vascular_endothelium
CAD_C4D	CTGF	5.69E-07	3.88E-06	FALSE	Cardiac_muscle
CAD_C4D	CCND1	8.02E-07	6.17E-06	FALSE	Cardiac_muscle
CAD_C4D	PLG	6.81E-06	1.70E-05	TRUE	Adipose
CAD_C4D	DUSP6	1.32E-05	4.40E-05	FALSE	Cardiac_muscle
CAD_C4D	MAF	5.30E-06	5.30E-05	FALSE	Smooth_muscle
CAD_C4D	TNFAIP8	2.54E-05	6.34E-05	FALSE	Cardiac_muscle
CAD_C4D	EFEMP1	5.13E-05	9.16E-05	FALSE	Cardiac_muscle
CAD_C4D	PAPSS2	5.60E-05	9.78E-05	FALSE	Cardiac_muscle
CAD_C4D	ABCG5	4.99E-05	9.97E-05	TRUE	Adipose
CAD_C4D	ADAMTS1	2.24E-05	0.00011199	FALSE	Smooth_muscle
CAD_C4D	EMP1	0.000129002	0.000184288	TRUE	Cardiac_muscle
CAD_C4D	KCTD12	5.58E-05	0.000186159	FALSE	Smooth_muscle
CAD_C4D	C1R	0.000175679	0.000219599	FALSE	Cardiac_muscle
CAD_C4D	DPYD	0.000262958	0.000292176	FALSE	Cardiac_muscle
CAD_C4D	DUSP1	0.00015651	0.000326882	FALSE	Smooth_muscle
CAD_C4D	DUSP6	0.000165388	0.000333898	FALSE	Smooth_muscle
CAD_C4D	ITGB5	0.000267745	0.000389386	FALSE	Smooth_muscle
CAD_C4D	TRIB2	0.000436158	0.000436158	FALSE	Cardiac_muscle
CAD_C4D	AZGP1	0.000262549	0.000437581	FALSE	Adipose
CAD_C4D	APOB	0.000759449	0.001084927	TRUE	Adipose
CAD_C4D	MMP9	0.000111306	0.001113064	FALSE	PPI
CAD_C4D	COL5A1	0.001207701	0.001509626	FALSE	Adipose
CAD_C4D	APOA1	0.002260732	0.002511924	TRUE	Adipose
CAD_C4D	LAMA2	0.002741304	0.002741304	FALSE	Adipose
CAD_C4D	OSM	0.001779516	0.005644107	TRUE	PPI
CAD_C4D	TGFBI	0.001779516	0.005644107	FALSE	PPI
CAD_C4D	LDLR	0.002323124	0.006262867	TRUE	PPI
CAD_C4D	MATN2	0.003776347	0.007552693	FALSE	PPI
CAD_C4D	APOB	0.010384441	0.017307401	TRUE	PPI
CAD_C4D	COL6A3	0.003097879	0.017595283	FALSE	Liver
CAD_C4D	COL4A2	0.012379781	0.017685402	TRUE	PPI
CAD_C4D	KNG1	0.001788614	0.017886137	FALSE	Brain
CAD_C4D	HGD	0.006004892	0.019976877	FALSE	Muscle
CAD_C4D	FN1	0.018162221	0.021794539	TRUE	PPI
CAD_C4D	APOC2	0.00801654	0.022048381	TRUE	Muscle

CAD_C4D	KNG1	0.008542234	0.022513379	FALSE	Muscle
CAD_C4D	NGRN	0.007925296	0.023311984	FALSE	Liver
CAD_C4D	RDH16	0.010512081	0.023551715	FALSE	Muscle
CAD_C4D	APOF	0.013384436	0.023812025	FALSE	Muscle
CAD_C4D	F2	0.014081304	0.0238678	FALSE	Muscle
CAD_C4D	GC	0.018352302	0.024165468	FALSE	Muscle
CAD_C4D	FBLN2	0.020128679	0.024603885	FALSE	PPI
CAD_C4D	CFB	0.00656752	0.027102596	FALSE	Brain
CAD_C4D	IL15RA	0.017191994	0.028291738	FALSE	Liver
CAD_C4D	ZBTB44	0.020926679	0.028407456	FALSE	Liver
CAD_C4D	COL1A1	0.021999756	0.028437446	FALSE	Liver
CAD_C4D	LOXL2	0.023338719	0.028473182	FALSE	Liver
CAD_C4D	ABCG8	0.025024824	0.028515807	TRUE	Liver
CAD_C4D	CXCL12	0.025024824	0.028515807	TRUE	Liver
CAD_C4D	MTMR11	0.025443165	0.028526008	FALSE	Liver
CAD_C4D	SERPINE1	0.028598742	0.028598742	FALSE	Liver
CAD_C4D	ACVR1C	0.011107056	0.031355151	FALSE	Brain
CAD_C4D	HGD	0.012024532	0.032077425	FALSE	Brain
CAD_C4D	APOC4	0.023020999	0.038298337	TRUE	Brain
CAD_C4D	NM_009245	0.023845301	0.038652854	FALSE	Brain
CAD_C4D	APOA1	0.027296504	0.039808695	TRUE	Brain
CAD_C4D	KL	0.039376058	0.042868938	FALSE	Brain
CAD_C4D	RDH16	0.040517104	0.055073056	FALSE	Brain
CAD_C4D	FBP1	0.020114077	0.057116353	FALSE	Muscle
CAD_C4D	TNFRSF1A	0.0003497	0.06617493	FALSE	Smooth_muscle
CAD_C4D	PAPSS2	0.000362714	0.075272243	FALSE	Smooth_muscle
CAD_C4D	ADM	0.000362727	0.075281126	FALSE	Smooth_muscle
CAD_C4D	LUM	0.042868938	0.079372558	FALSE	Brain

Supplemental Table II d. Key driver genes in CAD_C4D_lipid gene list. Key driver genes with red highlight are detected in at least network.

CAD Gene List	Key Drivers	P Values	FDR	Belonging to CAD Genes	Network Sources
CAD_C4D_lipid	CD93	2.22E-07	2.22E-06	FALSE	Aorta
CAD_C4D_lipid	MGP	1.61E-06	8.03E-06	FALSE	Aorta
CAD_C4D_lipid	IL15RA	1.14E-06	1.14E-05	FALSE	Liver
CAD_C4D_lipid	BMPR2	5.25E-06	1.75E-05	FALSE	Aorta
CAD_C4D_lipid	KLF10	8.84E-06	1.84E-05	FALSE	Aorta
CAD_C4D_lipid	COL18A1	9.24E-06	1.87E-05	FALSE	Aorta
CAD_C4D_lipid	NR2F1	1.41E-05	2.35E-05	FALSE	Aorta
CAD_C4D_lipid	ACVR1C	2.84E-06	2.84E-05	FALSE	Brain
CAD_C4D_lipid	DUSP6	2.12E-05	3.03E-05	FALSE	Aorta
CAD_C4D_lipid	WWC2	2.97E-05	3.71E-05	FALSE	Aorta
CAD_C4D_lipid	KCTD12	3.79E-05	4.22E-05	FALSE	Aorta
CAD_C4D_lipid	ADAM9	4.36E-05	4.36E-05	FALSE	Aorta
CAD_C4D_lipid	PODXL	7.38E-06	6.36E-05	TRUE	Vascular_endothelium
CAD_C4D_lipid	ZNF496	1.77E-05	8.87E-05	FALSE	Liver
CAD_C4D_lipid	KCTD12	1.36E-05	0.000109815	FALSE	Vascular_endothelium
CAD_C4D_lipid	JAG1	0.000135207	0.000450692	FALSE	Vascular_endothelium
CAD_C4D_lipid	LTBP1	4.95E-05	0.000495089	FALSE	Cardiac_muscle
CAD_C4D_lipid	CCL2	5.17E-05	0.000517193	FALSE	Artery
CAD_C4D_lipid	PTRF	0.000105934	0.000529671	FALSE	Cardiac_muscle
CAD_C4D_lipid	KLF10	0.00023449	0.000988435	FALSE	Artery
CAD_C4D_lipid	COL6A3	0.000319467	0.001064891	FALSE	Liver
CAD_C4D_lipid	COL1A1	0.000436603	0.001091508	FALSE	Liver
CAD_C4D_lipid	AXL	0.000379624	0.001174878	FALSE	Artery
CAD_C4D_lipid	KCTD12	0.000445301	0.001269598	FALSE	Artery
CAD_C4D_lipid	CCL2	0.000849798	0.001318288	FALSE	Vascular_endothelium
CAD_C4D_lipid	SRPX	0.000850024	0.001387237	FALSE	Vascular_endothelium
CAD_C4D_lipid	CTGF	0.000628784	0.001635742	FALSE	Cardiac_muscle
CAD_C4D_lipid	ZCCHC24	0.000941009	0.001729202	FALSE	Artery
CAD_C4D_lipid	DUSP6	0.000740389	0.001744439	FALSE	Cardiac_muscle
CAD_C4D_lipid	ANXA1	0.001060275	0.001782707	FALSE	Artery
CAD_C4D_lipid	SERPINE1	0.001312613	0.001839237	FALSE	Artery
CAD_C4D_lipid	HHEX	0.001484621	0.001897308	FALSE	Artery
CAD_C4D_lipid	S100A10	0.00087255	0.001915582	FALSE	Cardiac_muscle
CAD_C4D_lipid	M93275	0.000420832	0.002104162	FALSE	Brain
CAD_C4D_lipid	SMAD3	0.002012781	0.002106534	TRUE	Artery
CAD_C4D_lipid	OSM	0.000230067	0.002300675	TRUE	PPI
CAD_C4D_lipid	CDC42EP3	0.002026903	0.002833676	FALSE	Cardiac_muscle
CAD_C4D_lipid	ZNF467	0.002603144	0.005206288	FALSE	Liver

CAD_C4D_lipid	AK007927	0.001040834	0.006955244	FALSE	Muscle
CAD_C4D_lipid	BTNL9	0.004248225	0.007080375	FALSE	Liver
CAD_C4D_lipid	KCTD12	0.000911447	0.007445112	FALSE	Smooth_muscle
CAD_C4D_lipid	LOXL2	0.005320233	0.007600332	FALSE	Liver
CAD_C4D_lipid	CXCL12	0.006587188	0.008072175	TRUE	Liver
CAD_C4D_lipid	COL3A1	0.00161804	0.008110665	FALSE	Smooth_muscle
CAD_C4D_lipid	ASAH1	0.001462569	0.008130552	FALSE	Muscle
CAD_C4D_lipid	TRIM8	0.00263142	0.008147015	FALSE	Smooth_muscle
CAD_C4D_lipid	BMPR2	0.003262127	0.008730997	FALSE	Smooth_muscle
CAD_C4D_lipid	DENND5A	0.006132861	0.012265722	FALSE	Smooth_muscle
CAD_C4D_lipid	STAT3	0.003065905	0.012736125	FALSE	PPI
CAD_C4D_lipid	TNFRSF1A	0.008184721	0.013641202	FALSE	Smooth_muscle
CAD_C4D_lipid	COL5A1	0.001388926	0.013889256	FALSE	Adipose
CAD_C4D_lipid	COASY	0.004602257	0.01403315	FALSE	Muscle
CAD_C4D_lipid	COL4A2	0.00588487	0.014761635	TRUE	Muscle
CAD_C4D_lipid	LOXL1	0.007428981	0.014857962	FALSE	Muscle
CAD_C4D_lipid	SMAD1	0.005222298	0.015998114	FALSE	PPI
CAD_C4D_lipid	KCNMA1	0.002106534	0.016272135	FALSE	Artery
CAD_C4D_lipid	SPARC	0.011445185	0.016978191	FALSE	Muscle
CAD_C4D_lipid	MMP9	0.005820336	0.017156894	FALSE	PPI
CAD_C4D_lipid	POR	0.012670442	0.01749615	FALSE	Muscle
CAD_C4D_lipid	CXCL12	0.013994209	0.018544087	TRUE	Muscle
CAD_C4D_lipid	PHACTR1	0.005951423	0.019838078	TRUE	Brain
CAD_C4D_lipid	MMT00005552	0.020379601	0.022644001	FALSE	Muscle
CAD_C4D_lipid	GABRA4	0.009457379	0.023643448	FALSE	Brain
CAD_C4D_lipid	TRIM22	0.000933139	0.02562145	FALSE	Vascular_endothelium
CAD_C4D_lipid	TGFBI	0.015036785	0.027972826	FALSE	PPI
CAD_C4D_lipid	CDK4	0.017297963	0.029215203	FALSE	PPI
CAD_C4D_lipid	MATN2	0.025068258	0.031335323	FALSE	PPI
CAD_C4D_lipid	PDZD3	0.025068258	0.031335323	FALSE	PPI
CAD_C4D_lipid	PTPRB	0.013349378	0.033111294	FALSE	Adipose
CAD_C4D_lipid	SLC4A3	0.016027838	0.034900553	FALSE	Adipose
CAD_C4D_lipid	ATP6V0A1	0.025508769	0.036166218	FALSE	Brain
CAD_C4D_lipid	DCT	0.020128046	0.037196154	FALSE	Adipose
CAD_C4D_lipid	VPS33A	0.020128046	0.037196154	FALSE	Adipose
CAD_C4D_lipid	TCF3	0.026578644	0.039473495	FALSE	Adipose
CAD_C4D_lipid	CYP1B1	0.030376184	0.039878758	FALSE	Brain
CAD_C4D_lipid	VAV3	0.030376184	0.039878758	FALSE	Brain
CAD_C4D_lipid	ZEB2	0.030376184	0.039878758	TRUE	Brain
CAD_C4D_lipid	OSBPL11	0.028382534	0.039983216	FALSE	Adipose
CAD_C4D_lipid	TNXB	0.030267779	0.040487885	FALSE	Adipose
CAD_C4D_lipid	PLCG1	0.036440817	0.040489796	FALSE	PPI
CAD_C4D_lipid	QKI	0.029476609	0.042109442	FALSE	Smooth_muscle
CAD_C4D_lipid	AK013470	0.043430526	0.043430526	FALSE	Adipose
CAD_C4D_lipid	LAMA2	0.043430526	0.043430526	FALSE	Adipose
CAD_C4D_lipid	PXDC1	0.002415641	0.053138196	FALSE	Cardiac_muscle
CAD_C4D_lipid	CD93	0.056607274	0.056607274	FALSE	PPI
CAD_C4D_lipid	F3	0.002453576	0.057646029	FALSE	Cardiac_muscle
CAD_C4D_lipid	COL6A1	0.001072662	0.062164777	FALSE	Vascular_endothelium
CAD_C4D_lipid	PAPSS2	0.056260768	0.064676865	FALSE	Smooth_muscle
CAD_C4D_lipid	NCOR2	0.018593487	0.070087843	FALSE	Kidney
CAD_C4D_lipid	NGRN	0.008072175	0.075887794	FALSE	Liver
CAD_C4D_lipid	PCOLCE2	0.008072175	0.075887794	FALSE	Liver
CAD_C4D_lipid	ZDHHC17	0.075728996	0.084143329	FALSE	Brain
CAD_C4D_lipid	TNFAIP8	0.002693741	0.084803523	FALSE	Cardiac_muscle
CAD_C4D_lipid	KIF1B	0.060722019	0.098076661	FALSE	Smooth_muscle
CAD_C4D_lipid	ENG	0.001233888	0.099315847	FALSE	Vascular_endothelium
CAD_C4D_lipid	CCND1	0.002833676	0.099634522	FALSE	Cardiac_muscle

Supplemental Table II e. Key driver genes in CAD_Extend gene list. Key driver genes with red highlight are detected in at least networks.

CAD Gene List	Key Drivers	P Values	FDR	Belonging to CAD Genes	Network Sources
CAD_Extend	C8orf4	7.46E-10	7.46E-09	FALSE	Aorta
CAD_Extend	MFGE8	1.74E-09	8.70E-09	FALSE	Aorta
CAD_Extend	JUN	1.57E-09	1.20E-08	FALSE	Artery
CAD_Extend	DUSP5	2.48E-09	1.33E-08	FALSE	Artery
CAD_Extend	DUSP1	4.79E-09	1.60E-08	FALSE	Artery
CAD_Extend	HLA-DPB1	1.51E-08	3.86E-08	FALSE	Aorta
CAD_Extend	AXL	2.45E-08	4.62E-08	FALSE	Aorta
CAD_Extend	CCL18	2.53E-08	4.68E-08	FALSE	Aorta

CAD_Extend	LRP1	2.65E-08	4.78E-08	FALSE	Aorta
CAD_Extend	BGN	3.94E-08	5.63E-08	FALSE	Aorta
CAD_Extend	TAGLN2	5.75E-08	7.18E-08	FALSE	Aorta
CAD_Extend	ITGB4	7.18E-08	7.98E-08	FALSE	Aorta
CAD_Extend	DUSP6	9.01E-08	9.01E-08	FALSE	Aorta
CAD_Extend	DUSP6	1.23E-08	1.23E-07	FALSE	Vascular_endothelium
CAD_Extend	IFI44	6.71E-08	1.39E-07	FALSE	Artery
CAD_Extend	IFI35	6.99E-08	1.41E-07	FALSE	Artery
CAD_Extend	ICAM1	5.01E-08	1.45E-07	FALSE	Vascular_endothelium
CAD_Extend	TIMP3	8.88E-08	1.48E-07	FALSE	Artery
CAD_Extend	C3	5.48E-08	1.48E-07	FALSE	Vascular_endothelium
CAD_Extend	KLF4	5.84E-08	1.63E-07	FALSE	Vascular_endothelium
CAD_Extend	HLA-F	1.19E-07	1.71E-07	FALSE	Artery
CAD_Extend	CDKN1A	1.88E-07	2.35E-07	TRUE	Artery
CAD_Extend	CCL2	2.85E-07	2.89E-07	FALSE	Artery
CAD_Extend	GRN	3.32E-07	5.83E-07	FALSE	Vascular_endothelium
CAD_Extend	IFI27	3.54E-07	6.06E-07	FALSE	Vascular_endothelium
CAD_Extend	SH2B3	5.91E-07	8.44E-07	TRUE	Vascular_endothelium
CAD_Extend	GBP1	7.88E-07	9.85E-07	TRUE	Vascular_endothelium
CAD_Extend	PLAUR	1.13E-07	1.13E-06	FALSE	Cardiac_muscle
CAD_Extend	F3	1.84E-06	2.04E-06	FALSE	Vascular_endothelium
CAD_Extend	MSN	2.75E-06	2.75E-06	FALSE	Vascular_endothelium
CAD_Extend	KNG1	2.98E-07	2.98E-06	FALSE	Brain
CAD_Extend	CCND1	7.37E-07	3.39E-06	FALSE	Cardiac_muscle
CAD_Extend	AKAP12	1.09E-06	4.13E-06	FALSE	Cardiac_muscle
CAD_Extend	ATF3	4.29E-07	4.29E-06	FALSE	Smooth_muscle
CAD_Extend	KCTD12	2.24E-06	5.53E-06	FALSE	Smooth_muscle
CAD_Extend	KLF6	2.26E-06	5.54E-06	TRUE	Smooth_muscle
CAD_Extend	DUSP6	2.74E-06	6.06E-06	FALSE	Smooth_muscle
CAD_Extend	PLAU	2.81E-06	6.17E-06	FALSE	Smooth_muscle
CAD_Extend	LMNA	2.53E-06	6.33E-06	FALSE	Cardiac_muscle
CAD_Extend	RAC2	3.17E-06	6.33E-06	FALSE	Cardiac_muscle
CAD_Extend	TNFAIP2	4.43E-06	6.86E-06	FALSE	Cardiac_muscle
CAD_Extend	IFI27	4.85E-06	7.30E-06	FALSE	Cardiac_muscle
CAD_Extend	GBP2	5.80E-06	9.67E-06	TRUE	Smooth_muscle
CAD_Extend	TRIM8	7.58E-06	1.08E-05	FALSE	Smooth_muscle
CAD_Extend	SAT1	1.17E-05	1.46E-05	FALSE	Cardiac_muscle
CAD_Extend	TIMP3	1.49E-05	1.87E-05	FALSE	Smooth_muscle
CAD_Extend	SAT1	1.87E-05	1.88E-05	FALSE	Smooth_muscle
CAD_Extend	GBP1	1.13E-05	0.000113391	TRUE	Blood
CAD_Extend	ANXA2	0.000123905	0.000127462	FALSE	Cardiac_muscle
CAD_Extend	COL6A3	1.75E-05	0.000174586	FALSE	Liver
CAD_Extend	MSN	7.48E-05	0.000305038	FALSE	Liver
CAD_Extend	ABCG5	9.49E-05	0.000366301	TRUE	Liver
CAD_Extend	HGD	7.46E-05	0.000437596	FALSE	Muscle
CAD_Extend	SLIT3	8.95E-05	0.000491909	TRUE	Muscle
CAD_Extend	MMT00021022	5.42E-05	0.000541582	FALSE	Heart
CAD_Extend	DENND5A	1.88E-05	0.001033	FALSE	Smooth_muscle
CAD_Extend	CXCL10	0.000510374	0.00111934	FALSE	Liver
CAD_Extend	ANXA3	0.000719928	0.001238177	FALSE	Liver
CAD_Extend	MTMR11	0.000740434	0.001239294	FALSE	Liver
CAD_Extend	ZBTB44	0.000872093	0.001245848	FALSE	Liver
CAD_Extend	MMT00081256	0.000597658	0.00147602	FALSE	Muscle
CAD_Extend	MAFF	0.001196123	0.001495153	FALSE	Liver
CAD_Extend	CFB	0.00030824	0.001541199	FALSE	Brain
CAD_Extend	LOXL2	0.001393018	0.001547798	FALSE	Liver
CAD_Extend	HEMGN	0.000719204	0.001579235	TRUE	Muscle
CAD_Extend	APOF	0.000931824	0.001751151	FALSE	Muscle
CAD_Extend	FBP1	0.001024962	0.001839238	FALSE	Muscle
CAD_Extend	ABCG8	0.001870204	0.001870204	TRUE	Liver
CAD_Extend	F2	0.001179508	0.001970369	FALSE	Muscle
CAD_Extend	APOC4	0.000759403	0.002180799	TRUE	Brain
CAD_Extend	NM_009245	0.000896906	0.002305717	FALSE	Brain
CAD_Extend	TNFSF10	2.89E-07	0.002400977	FALSE	Artery
CAD_Extend	APOC2	0.001970669	0.002463336	TRUE	Muscle
CAD_Extend	COL4A2	0.002297695	0.002552995	TRUE	Muscle
CAD_Extend	KNG1	0.002669536	0.002669536	FALSE	Muscle
CAD_Extend	APOA1	0.001680306	0.00280051	TRUE	Brain
CAD_Extend	AW475929	0.001680306	0.00280051	FALSE	Brain
CAD_Extend	NOTCH1	0.000386613	0.003866126	FALSE	PPI
CAD_Extend	BATF2	0.000977451	0.004887256	FALSE	Blood
CAD_Extend	ACVR1C	0.00447158	0.006387971	FALSE	Brain
CAD_Extend	HGD	0.006547637	0.007275152	FALSE	Brain
CAD_Extend	TRAPPC3	0.006547637	0.007275152	FALSE	Brain

CAD_Extend	CTGF	0.000127462	0.007325627	FALSE	Cardiac_muscle
CAD_Extend	NME6	0.001305695	0.007955052	TRUE	Kidney
CAD_Extend	AK021074	0.00188318	0.008883334	FALSE	Kidney
CAD_Extend	MMP9	0.002028751	0.010143756	FALSE	PPI
CAD_Extend	LUM	0.01184934	0.01184934	FALSE	Brain
CAD_Extend	ANXA2	0.003654997	0.012183324	FALSE	PPI
CAD_Extend	GBP2	0.002653287	0.012300169	TRUE	Kidney
CAD_Extend	RPUSD4	0.001845898	0.018458977	FALSE	Islet
CAD_Extend	PTCHD1	0.006812441	0.020870973	FALSE	Adipose
CAD_Extend	PLG	0.006974387	0.021046794	TRUE	Adipose
CAD_Extend	GBP1	0.008498788	0.022576627	TRUE	Adipose
CAD_Extend	F2	0.008720739	0.022782993	FALSE	Adipose
CAD_Extend	NM_021792	0.011246591	0.028116478	FALSE	Kidney
CAD_Extend	APOA1	0.017007364	0.028377564	TRUE	Adipose
CAD_Extend	ATP8B2	0.014382099	0.028764197	TRUE	Kidney
CAD_Extend	ACAD10	0.018655946	0.029193682	TRUE	Adipose
CAD_Extend	SERPINC1	0.020435531	0.02931283	FALSE	Adipose
CAD_Extend	VEGFA	0.024422814	0.02955081	TRUE	Adipose
CAD_Extend	MMT00019644	0.026649264	0.030291004	FALSE	Adipose
CAD_Extend	JUNB	0.034383023	0.034383023	FALSE	Adipose
CAD_Extend	COL4A2	0.022387772	0.05596943	TRUE	PPI
CAD_Extend	SLC34A3	0.034467535	0.057445892	FALSE	Kidney
CAD_Extend	OSM	0.039363188	0.060874908	TRUE	PPI
CAD_Extend	TGFBI	0.039363188	0.060874908	FALSE	PPI
CAD_Extend	PTPN11	0.042791769	0.061786171	FALSE	PPI
CAD_Extend	LDLR	0.051151933	0.063939916	TRUE	PPI
CAD_Extend	JUN	0.072576936	0.08064104	FALSE	PPI
CAD_Extend	HSPA5	0.081739862	0.081739862	FALSE	PPI
CAD_Extend	GBP2	0.028959053	0.096530177	TRUE	Blood

Supplemental Table II f. Key driver genes in CAD_1000G gene list. Key driver genes with red highlight are detected in at least networks.

CAD Gene List	Key Drivers	P Values	FDR	Belonging to CAD Genes	Network Sources
CAD_1000G	SAT1	4.39E-09	4.39E-08	FALSE	Aorta
CAD_1000G	RGS2	1.96E-08	9.81E-08	TRUE	Aorta
CAD_1000G	CD93	3.62E-08	1.21E-07	FALSE	Aorta
CAD_1000G	LYN	2.17E-07	5.43E-07	FALSE	Aorta
CAD_1000G	DUSP1	9.24E-08	9.24E-07	FALSE	Artery
CAD_1000G	PDCD4	5.11E-07	1.02E-06	FALSE	Aorta
CAD_1000G	CFD	1.05E-06	1.75E-06	FALSE	Aorta
CAD_1000G	SERPINE1	7.36E-07	2.37E-06	FALSE	Artery
CAD_1000G	CCL2	1.17E-06	2.71E-06	FALSE	Artery
CAD_1000G	DUSP5	1.27E-06	2.77E-06	FALSE	Artery
CAD_1000G	ACTN1	2.13E-06	3.05E-06	FALSE	Aorta
CAD_1000G	DUSP6	1.92E-06	3.28E-06	FALSE	Artery
CAD_1000G	MGLL	1.95E-06	3.30E-06	FALSE	Artery
CAD_1000G	CAV1	2.00E-06	3.33E-06	FALSE	Artery
CAD_1000G	MPZL1	2.94E-06	3.67E-06	FALSE	Aorta
CAD_1000G	TRIB1	3.20E-06	4.00E-06	TRUE	Artery
CAD_1000G	SRPX	3.61E-06	4.01E-06	FALSE	Artery
CAD_1000G	PPP1R15A	3.84E-06	4.27E-06	FALSE	Aorta
CAD_1000G	SAT1	8.94E-07	5.02E-06	FALSE	Vascular_endothelium
CAD_1000G	CCL2	1.02E-06	5.34E-06	FALSE	Vascular_endothelium
CAD_1000G	DUSP1	5.57E-06	5.57E-06	FALSE	Aorta
CAD_1000G	CAST	6.59E-06	6.59E-06	FALSE	Artery
CAD_1000G	SORL1	2.92E-06	9.73E-06	FALSE	Vascular_endothelium
CAD_1000G	HMOX1	4.01E-06	1.00E-05	FALSE	Vascular_endothelium
CAD_1000G	F3	9.92E-06	1.38E-05	FALSE	Vascular_endothelium
CAD_1000G	IGFBP7	1.05E-05	1.40E-05	FALSE	Vascular_endothelium
CAD_1000G	C3	1.09E-05	1.43E-05	FALSE	Vascular_endothelium
CAD_1000G	ZFP36L2	1.13E-05	1.46E-05	FALSE	Vascular_endothelium
CAD_1000G	FAS	1.65E-05	1.83E-05	FALSE	Vascular_endothelium
CAD_1000G	DUSP6	2.30E-06	2.30E-05	FALSE	Smooth_muscle
CAD_1000G	DSE	3.03E-05	3.03E-05	FALSE	Vascular_endothelium
CAD_1000G	MAF	1.33E-05	4.67E-05	FALSE	Smooth_muscle
CAD_1000G	KCTD12	1.41E-05	4.75E-05	FALSE	Smooth_muscle
CAD_1000G	PLAU	2.15E-05	5.37E-05	FALSE	Smooth_muscle
CAD_1000G	ITGB5	3.02E-05	6.04E-05	FALSE	Smooth_muscle
CAD_1000G	SRPX	4.27E-05	7.12E-05	FALSE	Smooth_muscle
CAD_1000G	ADAMTS1	7.17E-05	0.000102372	FALSE	Smooth_muscle

CAD_1000G	AKAP12	1.03E-05	0.000102806	FALSE	Cardiac_muscle
CAD_1000G	CTSB	9.46E-05	0.000118242	FALSE	Smooth_muscle
CAD_1000G	CCND1	3.14E-05	0.000156961	FALSE	Cardiac_muscle
CAD_1000G	KNG1	2.14E-05	0.000168905	FALSE	Muscle
CAD_1000G	RDH16	3.58E-05	0.000182682	FALSE	Muscle
CAD_1000G	F2	7.28E-05	0.000192941	FALSE	Muscle
CAD_1000G	HGD	7.74E-05	0.000202957	FALSE	Muscle
CAD_1000G	DUSP1	0.000189518	0.000210575	FALSE	Smooth_muscle
CAD_1000G	CTGF	0.000112938	0.000312233	FALSE	Cardiac_muscle
CAD_1000G	SFRP1	0.000128072	0.000341967	FALSE	Cardiac_muscle
CAD_1000G	ANXA1	0.000420507	0.000420507	FALSE	Smooth_muscle
CAD_1000G	KNG1	6.19E-05	0.000618759	FALSE	Brain
CAD_1000G	APOC2	0.000358657	0.000717313	FALSE	Muscle
CAD_1000G	HMOX1	0.000494275	0.000833298	FALSE	Cardiac_muscle
CAD_1000G	CLU	0.000501681	0.000841348	FALSE	Cardiac_muscle
CAD_1000G	FGF2	0.000857907	0.001225582	FALSE	Cardiac_muscle
CAD_1000G	HSD17B13	0.000768274	0.001280457	FALSE	Muscle
CAD_1000G	SLC1A5	0.000945745	0.001351064	FALSE	Muscle
CAD_1000G	TRIB2	0.001736318	0.002170397	FALSE	Cardiac_muscle
CAD_1000G	DUSP6	0.002261048	0.002370437	FALSE	Cardiac_muscle
CAD_1000G	CFB	0.000581317	0.002627085	FALSE	Brain
CAD_1000G	COL6A3	0.000299159	0.002991594	FALSE	Liver
CAD_1000G	NM_009245	0.000842809	0.003116305	FALSE	Brain
CAD_1000G	GC	0.002881742	0.003602178	FALSE	Muscle
CAD_1000G	HGD	0.001753079	0.004382698	FALSE	Brain
CAD_1000G	LUM	0.002210866	0.004395889	FALSE	Brain
CAD_1000G	ALDH2	0.001449728	0.004914361	TRUE	Liver
CAD_1000G	VAV3	0.002640621	0.004951997	FALSE	Brain
CAD_1000G	APOA5	0.001818006	0.005204133	TRUE	Liver
CAD_1000G	MTMR11	0.002067706	0.005347234	FALSE	Liver
CAD_1000G	A1BG	0.00325398	0.005865502	FALSE	Liver
CAD_1000G	ITIH2	0.003549953	0.005948143	FALSE	Liver
CAD_1000G	APOA1	0.005395963	0.005995515	TRUE	Muscle
CAD_1000G	PLG	0.004553041	0.006131709	TRUE	Liver
CAD_1000G	KCNK13	0.0049292	0.006471743	TRUE	Liver
CAD_1000G	F2	0.000668135	0.006681348	FALSE	Adipose
CAD_1000G	ASAH1	0.006696374	0.006696374	FALSE	Muscle
CAD_1000G	MMP9	0.001180469	0.007182905	FALSE	PPI
CAD_1000G	LDLR	0.00148701	0.008042351	TRUE	PPI
CAD_1000G	APOC3	0.009433108	0.013475868	TRUE	Brain
CAD_1000G	APOB	0.00411444	0.013714799	TRUE	PPI
CAD_1000G	PLG	0.00282881	0.01414405	TRUE	Adipose
CAD_1000G	COL1A1	0.013203656	0.014670729	FALSE	Liver
CAD_1000G	AZGP1	0.006486893	0.015224034	FALSE	Adipose
CAD_1000G	APOB	0.007989151	0.015511047	TRUE	Adipose
CAD_1000G	APOA1	0.010145073	0.01596161	TRUE	Adipose
CAD_1000G	SERPINC1	0.011101688	0.016437514	FALSE	Adipose
CAD_1000G	VEGFA	0.012115963	0.016904623	TRUE	Adipose
CAD_1000G	MMT00019644	0.01264555	0.017135181	FALSE	Adipose
CAD_1000G	TUBB6	0.002370437	0.017218673	FALSE	Cardiac_muscle
CAD_1000G	LARGE	0.019200268	0.019200268	TRUE	Liver
CAD_1000G	CD14	0.019568328	0.019568328	FALSE	Adipose
CAD_1000G	MMT00078179	0.019568328	0.019568328	FALSE	Adipose
CAD_1000G	APOA1	0.019986725	0.02402097	TRUE	Brain
CAD_1000G	MAL	0.003247907	0.032479071	FALSE	Blood
CAD_1000G	FN1	0.028820454	0.058101858	TRUE	PPI
CAD_1000G	TGFBI	0.029601491	0.066428856	FALSE	PPI
CAD_1000G	APOA5	0.022610119	0.070619583	TRUE	Brain
CAD_1000G	PHACTR1	0.02402097	0.09382028	TRUE	Brain

Supplemental Table II g. Key driver genes in CAD_1000G_Extend gene list. Key driver genes with red highlight are detected in at least networks.

CAD Gene List	Key Drivers	P Values	FDR	Belonging to CAD Genes	Network Sources
CAD_1000G_Extend	ATF3	2.26E-08	2.26E-07	FALSE	Smooth_muscle
CAD_1000G_Extend	IFI35	7.88E-08	4.44E-07	FALSE	Artery
CAD_1000G_Extend	DUSP1	8.98E-08	4.68E-07	FALSE	Artery
CAD_1000G_Extend	HLA-F	2.50E-07	7.67E-07	FALSE	Artery
CAD_1000G_Extend	IRF1	3.22E-07	8.39E-07	TRUE	Artery
CAD_1000G_Extend	DUSP5	5.76E-07	9.99E-07	FALSE	Artery
CAD_1000G_Extend	JUN	6.03E-07	1.03E-06	FALSE	Artery

CAD_1000G_Extend	PLAUR	1.06E-07	1.06E-06	FALSE	Cardiac_muscle
CAD_1000G_Extend	JUN	3.06E-07	1.38E-06	FALSE	Smooth_muscle
CAD_1000G_Extend	GBP2	4.37E-07	1.48E-06	TRUE	Smooth_muscle
CAD_1000G_Extend	IRF9	7.44E-07	1.53E-06	FALSE	Smooth_muscle
CAD_1000G_Extend	SERPINE1	1.08E-06	1.55E-06	FALSE	Artery
CAD_1000G_Extend	PLAU	7.67E-07	1.56E-06	FALSE	Smooth_muscle
CAD_1000G_Extend	TAPBP	1.99E-07	1.99E-06	FALSE	Vascular_endothelium
CAD_1000G_Extend	LMNA	4.06E-07	2.03E-06	FALSE	Cardiac_muscle
CAD_1000G_Extend	CCL18	2.44E-07	2.44E-06	FALSE	Aorta
CAD_1000G_Extend	CDKN1A	2.23E-06	2.79E-06	TRUE	Artery
CAD_1000G_Extend	BGN	5.74E-07	2.87E-06	FALSE	Aorta
CAD_1000G_Extend	GRN	6.06E-07	3.03E-06	FALSE	Vascular_endothelium
CAD_1000G_Extend	ICAM1	9.15E-07	3.05E-06	TRUE	Vascular_endothelium
CAD_1000G_Extend	TAPBP	2.36E-06	3.49E-06	FALSE	Smooth_muscle
CAD_1000G_Extend	RELA	2.64E-06	3.69E-06	TRUE	Smooth_muscle
CAD_1000G_Extend	DUSP6	2.95E-06	3.86E-06	FALSE	Smooth_muscle
CAD_1000G_Extend	IFI30	3.85E-06	4.27E-06	FALSE	Smooth_muscle
CAD_1000G_Extend	OASL	4.12E-06	4.58E-06	TRUE	Artery
CAD_1000G_Extend	CTGF	1.77E-06	4.80E-06	FALSE	Aorta
CAD_1000G_Extend	BST2	5.07E-06	5.07E-06	FALSE	Artery
CAD_1000G_Extend	ITGB4	1.96E-06	5.18E-06	FALSE	Aorta
CAD_1000G_Extend	MPRIP	2.98E-06	8.19E-06	FALSE	Cardiac_muscle
CAD_1000G_Extend	TNFAIP2	3.35E-06	8.83E-06	FALSE	Cardiac_muscle
CAD_1000G_Extend	ZYX	1.10E-05	1.10E-05	FALSE	Smooth_muscle
CAD_1000G_Extend	GAA	5.78E-06	1.16E-05	FALSE	Aorta
CAD_1000G_Extend	RARRES3	5.07E-06	1.27E-05	FALSE	Vascular_endothelium
CAD_1000G_Extend	ELL2	7.60E-06	1.27E-05	FALSE	Aorta
CAD_1000G_Extend	IFNAR1	9.23E-06	1.32E-05	FALSE	Aorta
CAD_1000G_Extend	ITPKC	1.12E-05	1.40E-05	FALSE	Aorta
CAD_1000G_Extend	NOS3	1.49E-05	1.51E-05	TRUE	Aorta
CAD_1000G_Extend	GRK5	7.59E-06	1.52E-05	FALSE	Cardiac_muscle
CAD_1000G_Extend	PTRF	3.34E-05	4.55E-05	FALSE	Cardiac_muscle
CAD_1000G_Extend	CCND1	3.43E-05	4.61E-05	FALSE	Cardiac_muscle
CAD_1000G_Extend	ISG15	3.72E-05	4.80E-05	FALSE	Cardiac_muscle
CAD_1000G_Extend	IFI27	2.74E-05	5.47E-05	FALSE	Vascular_endothelium
CAD_1000G_Extend	ANXA2	4.94E-05	5.49E-05	FALSE	Cardiac_muscle
CAD_1000G_Extend	SH2B3	3.94E-05	6.56E-05	TRUE	Vascular_endothelium
CAD_1000G_Extend	DUSP6	4.64E-05	6.63E-05	FALSE	Vascular_endothelium
CAD_1000G_Extend	CTSS	6.64E-05	6.64E-05	TRUE	Cardiac_muscle
CAD_1000G_Extend	IRF7	0.000102682	0.000128352	FALSE	Vascular_endothelium
CAD_1000G_Extend	GBP1	0.00014387	0.000159856	TRUE	Vascular_endothelium
CAD_1000G_Extend	DENND5A	0.00016117	0.00016117	TRUE	Vascular_endothelium
CAD_1000G_Extend	PHLDB1	7.48E-05	0.000376455	FALSE	Liver
CAD_1000G_Extend	CXCL10	7.54E-05	0.000379027	FALSE	Liver
CAD_1000G_Extend	MMT00021022	0.000279155	0.001395777	FALSE	Heart
CAD_1000G_Extend	RIF1	0.000279155	0.001395777	FALSE	Heart
CAD_1000G_Extend	NGRN	0.000529759	0.001765864	FALSE	Liver
CAD_1000G_Extend	KNG1	0.000207241	0.002072412	FALSE	Brain
CAD_1000G_Extend	MSN	0.00085342	0.00213355	FALSE	Liver
CAD_1000G_Extend	APOA1	0.000253583	0.002535826	TRUE	Adipose
CAD_1000G_Extend	HLA-DPB1	1.51E-05	0.003307094	FALSE	Aorta
CAD_1000G_Extend	RTP4	0.00040671	0.004067102	FALSE	Muscle
CAD_1000G_Extend	COL6A3	0.002299741	0.004599482	FALSE	Liver
CAD_1000G_Extend	APOC2	0.001730135	0.005536128	TRUE	Muscle
CAD_1000G_Extend	SLIT3	0.001958738	0.005670547	TRUE	Muscle
CAD_1000G_Extend	HGD	0.002271992	0.006116079	FALSE	Muscle
CAD_1000G_Extend	ABCG5	0.004262699	0.006802628	TRUE	Liver
CAD_1000G_Extend	MTMR11	0.004958303	0.007299947	FALSE	Liver
CAD_1000G_Extend	PLG	0.00223865	0.007497996	TRUE	Adipose
CAD_1000G_Extend	AQP1	0.002251548	0.007532012	FALSE	Adipose
CAD_1000G_Extend	SPARC	0.00395128	0.00790256	FALSE	Muscle
CAD_1000G_Extend	NOLC1	0.006461142	0.008076427	FALSE	Liver
CAD_1000G_Extend	MMT00081256	0.006142554	0.00983798	FALSE	Muscle
CAD_1000G_Extend	HEMGN	0.00712113	0.010243765	TRUE	Muscle
CAD_1000G_Extend	FBP1	0.009471415	0.010523794	FALSE	Muscle
CAD_1000G_Extend	MYOG	0.009471415	0.010523794	FALSE	Muscle
CAD_1000G_Extend	APOA1	0.003226995	0.010756649	TRUE	Brain
CAD_1000G_Extend	AW475929	0.003226995	0.010756649	FALSE	Brain
CAD_1000G_Extend	CD274	0.010760451	0.011956056	FALSE	Liver
CAD_1000G_Extend	APOF	0.012403157	0.012403157	FALSE	Muscle
CAD_1000G_Extend	INSIG1	0.014306442	0.014306442	FALSE	Liver
CAD_1000G_Extend	THADA	0.007020688	0.015762868	TRUE	Brain
CAD_1000G_Extend	CFB	0.008130205	0.016432124	FALSE	Brain
CAD_1000G_Extend	HLA-DQA1	0.012575643	0.017490753	FALSE	Brain

CAD_1000G_Extend	CPD	0.013259961	0.017623506	FALSE	Brain
CAD_1000G_Extend	SP6	0.014105003	0.017697697	FALSE	Brain
CAD_1000G_Extend	APOC4	0.016062039	0.01784671	TRUE	Brain
CAD_1000G_Extend	NM_009245	0.018240549	0.018240549	FALSE	Brain
CAD_1000G_Extend	PC	0.008159988	0.020399971	FALSE	Adipose
CAD_1000G_Extend	GPX1	0.010775362	0.021550724	TRUE	Adipose
CAD_1000G_Extend	NOTCH1	0.002454922	0.024549225	FALSE	PPI
CAD_1000G_Extend	BATF2	0.002502504	0.025025037	FALSE	Blood
CAD_1000G_Extend	AZGP1	0.019199335	0.031998892	FALSE	Adipose
CAD_1000G_Extend	IRF7	0.022967076	0.032810109	FALSE	Adipose
CAD_1000G_Extend	IFIT1	0.006800762	0.034003812	TRUE	Blood
CAD_1000G_Extend	GBP1	0.027307883	0.034134854	TRUE	Adipose
CAD_1000G_Extend	GBP1	0.010586414	0.035288045	TRUE	Blood
CAD_1000G_Extend	GBP2	0.015994085	0.039985212	TRUE	Blood
CAD_1000G_Extend	GBP4	0.036443942	0.040493269	TRUE	Adipose
CAD_1000G_Extend	F2	0.046003727	0.046003727	FALSE	Adipose
CAD_1000G_Extend	PARP14	0.007992834	0.047907404	FALSE	Kidney
CAD_1000G_Extend	MMP9	0.011780649	0.049304089	FALSE	PPI
CAD_1000G_Extend	NM_021792	0.009973913	0.050140134	FALSE	Kidney
CAD_1000G_Extend	NME6	0.036353945	0.053658963	TRUE	Kidney
CAD_1000G_Extend	RTP4	0.036353945	0.053658963	FALSE	Kidney
CAD_1000G_Extend	AK021074	0.04208131	0.054229299	FALSE	Kidney
CAD_1000G_Extend	GBP2	0.048441339	0.054864573	TRUE	Kidney
CAD_1000G_Extend	NCOR2	0.048441339	0.054864573	FALSE	Kidney
CAD_1000G_Extend	OAS2	0.048441339	0.054864573	FALSE	Kidney
CAD_1000G_Extend	GBP4	0.055495403	0.055495403	TRUE	Kidney
CAD_1000G_Extend	ANXA2	0.01706091	0.056460411	FALSE	PPI
CAD_1000G_Extend	IL4R	0.02211516	0.066123281	FALSE	PPI
CAD_1000G_Extend	RPUSD4	0.008633996	0.086339962	FALSE	Islet
CAD_1000G_Extend	RELB	0.049423059	0.098846118	TRUE	PPI

Supplemental Table II h. Meta-analysis of KDA results based on seven gene lists in 14 networks (13 tissue-specific gene regulatory networks and 1 PPI network).

Part 1:

Key Drivers	Adipose	Aorta	Artery	Blood	Brain	Cardiac Muscle	Heart	Islet	Kidney	Liver	Muscle	PPI	Smooth Muscle	Vascular Endothelium
DUSP6	0	2	2	0	0	3	0	0	0	0	0	0	6	2
DUSP1	0	1	6	0	0	0	0	0	0	0	0	0	4	0
KNG1	0	0	0	0	5	0	0	0	0	0	4	0	0	0
COL6A3	0	0	0	0	0	0	0	0	0	7	0	0	0	0
F2	5	0	0	0	0	0	0	0	0	0	4	0	0	0
APOA1	4	0	0	0	5	0	0	0	0	0	2	0	0	0
HGD	0	0	0	0	4	0	0	0	0	0	5	0	0	0
HLA-F	0	0	3	0	0	0	0	0	0	0	0	0	0	0
GBP1	2	0	0	2	0	0	0	0	0	0	0	0	0	2
LUM	0	0	0	0	5	0	0	0	0	0	0	0	0	0
JAG1	0	0	0	0	0	0	0	0	0	0	0	0	0	4
GBP2	0	0	0	2	0	0	0	0	2	0	0	0	2	0
MTMR11	0	0	0	0	0	0	0	0	0	6	0	0	0	0
ANXA1	0	0	3	0	0	0	0	0	0	0	0	0	1	0
MMP9	0	0	0	0	0	0	0	0	0	0	0	6	0	0
NM_009245	0	0	0	0	5	0	0	0	0	0	0	0	0	0
IFI35	0	0	2	0	0	0	0	0	0	0	0	0	0	0
CCL18	0	2	0	0	0	0	0	0	0	0	0	0	0	0
PLG	4	0	0	0	0	0	0	0	0	1	0	0	0	0
VEGFA	5	0	0	0	0	0	0	0	0	0	0	0	0	0
COL4A2	0	0	0	0	0	0	0	0	0	0	4	3	0	0
COL1A1	0	0	0	0	0	0	0	0	0	5	0	0	0	0
ITGB4	0	2	0	0	0	0	0	0	0	0	0	0	0	0
MMT00019644	5	0	0	0	0	0	0	0	0	0	0	0	0	0
MSN	0	0	0	0	0	0	0	0	0	2	0	0	0	1
KCNK13	0	0	0	0	0	0	0	0	0	3	0	0	0	0
ANXA2	0	0	0	0	0	2	0	0	0	0	0	2	0	0
TNFAIP2	0	0	0	0	0	2	0	0	0	0	0	0	0	0
CXCL12	1	0	0	0	0	1	0	0	0	3	1	0	0	0
ABCG5	1	0	0	0	0	0	0	0	0	2	0	0	0	0
CFB	0	0	0	0	4	0	0	0	0	0	0	0	0	0
APOC2	0	0	0	0	0	0	0	0	0	0	4	0	0	0
APOB	2	0	0	0	0	0	0	0	0	0	0	3	0	0
SORL1	0	0	0	0	0	0	0	0	0	0	0	0	0	2
ACVR1C	0	0	0	0	3	0	0	0	0	0	0	0	0	0
ADM	0	0	1	0	0	0	0	0	0	0	0	0	1	0
RDH16	0	0	0	0	2	0	0	0	0	0	2	0	0	0
PAPSS2	0	0	0	0	0	1	0	0	0	0	0	0	2	0
LOXL2	0	0	0	0	0	0	0	0	0	4	0	0	0	0
SLIT3	0	0	0	0	0	0	0	0	0	0	2	0	0	0
MMT00021022	0	0	0	0	0	0	2	0	0	0	0	0	0	0
TGFBI	0	0	0	0	0	0	0	0	0	0	0	5	0	0
PHACTR1	0	0	0	0	4	0	0	0	0	0	0	0	0	0

IL15RA	0	0	0	0	0	0	0	0	0	2	0	0	0	0
TRIM8	0	0	0	0	0	0	0	0	0	0	0	0	2	0
OSM	0	0	0	0	0	0	0	0	0	0	0	3	0	0
LY96	0	0	0	0	0	0	0	0	0	0	0	0	0	2
CXCL10	0	0	0	0	0	0	0	0	0	2	0	0	0	0
SLC2A3	0	1	0	0	0	0	0	0	0	0	0	0	0	0
LARGE	0	0	0	0	0	0	0	0	0	3	0	0	0	0
IRF1	0	0	1	0	0	0	0	0	0	0	0	0	0	0
AZGP1	3	0	0	0	0	0	0	0	0	0	0	0	0	0
NGRN	0	0	0	0	0	0	0	0	0	3	0	0	0	0
EFEMP1	0	0	0	0	0	2	0	0	0	0	0	0	0	0
IRF9	0	0	0	0	0	0	0	0	0	0	0	0	1	0
APOA5	0	0	0	0	1	0	0	0	0	2	0	0	0	0
CFD	0	1	0	0	0	0	0	0	0	0	0	0	0	0
NOTCH1	0	0	0	0	0	0	0	0	0	0	0	2	0	0
APOF	0	0	0	0	0	0	0	0	0	0	3	0	0	0
LDLR	0	0	0	0	0	0	0	0	0	0	0	3	0	0
KLF6	0	0	0	0	0	0	0	0	0	0	0	0	1	0
FBP1	0	0	0	0	0	0	0	0	0	0	3	0	0	0
RAC2	0	0	0	0	0	1	0	0	0	0	0	0	0	0
APOC4	0	0	0	0	3	0	0	0	0	0	0	0	0	0
MATN2	0	0	0	0	0	0	0	0	0	0	0	3	0	0
IFI30	0	0	0	0	0	0	0	0	0	0	0	0	1	0
WIPF1	0	0	0	0	0	0	0	0	0	2	0	0	0	0
FN1	0	0	0	0	0	0	0	0	1	0	0	3	0	0
BST2	0	0	1	0	0	0	0	0	0	0	0	0	0	0
COL5A1	2	0	0	0	0	0	0	0	0	0	0	0	0	0
EPS8	0	0	0	0	0	0	0	0	0	2	0	0	0	0
SPARC	0	0	0	0	0	0	0	0	0	0	3	0	0	0
IRF7	1	0	0	0	0	0	0	0	0	0	0	0	0	1
BATF2	0	0	0	2	0	0	0	0	0	0	0	0	0	0
ZYX	0	0	0	0	0	0	0	0	0	0	0	0	1	0
MMT00081256	0	0	0	0	0	0	0	0	0	0	2	0	0	0
HEMGN	0	0	0	0	0	0	0	0	0	0	2	0	0	0
ZNF496	0	0	0	0	0	0	0	0	0	1	0	0	0	0
AW475929	0	0	0	0	2	0	0	0	0	0	0	0	0	0
CKLF	0	0	0	0	0	0	0	0	0	2	0	0	0	0
APOC3	0	0	0	0	2	0	0	0	0	0	0	0	0	0
NCOR2	0	0	0	0	0	0	0	0	4	0	0	0	0	0
WWC2	0	1	0	0	0	0	0	0	0	0	0	0	0	0
ASAH1	0	0	0	0	0	0	0	0	0	0	2	0	0	0
ACCN1	0	0	0	0	0	0	0	1	0	0	0	0	0	0
ISG15	0	0	0	0	0	1	0	0	0	0	0	0	0	0
ADAM9	0	1	0	0	0	0	0	0	0	0	0	0	0	0
SDCBP	0	1	0	0	0	0	0	0	0	0	0	0	0	0
CD74	2	0	0	0	0	0	0	0	0	0	0	0	0	0
MCOLN1	0	0	0	0	2	0	0	0	0	0	0	0	0	0
ZBTB44	0	0	0	0	0	0	0	0	0	2	0	0	0	0
IGFBP6	0	0	1	0	0	0	0	0	0	0	0	0	0	0
CTSB	0	0	0	0	0	0	0	0	0	0	0	0	1	0
SERPINC1	3	0	0	0	0	0	0	0	0	0	0	0	0	0
SLIT2	0	1	0	0	0	0	0	0	0	0	0	0	0	0
ABCG8	0	0	0	0	0	0	0	0	0	2	0	0	0	0
NME6	0	0	0	0	0	0	0	0	2	0	0	0	0	0
C1R	0	0	0	0	0	1	0	0	0	0	0	0	0	0
DPYD	0	0	0	0	0	1	0	0	0	0	0	0	0	0
AK021074	0	0	0	0	0	0	0	0	2	0	0	0	0	0
BNIP3L	0	1	0	0	0	0	0	0	0	0	0	0	0	0
LAMA2	2	0	0	0	0	0	0	0	0	0	0	0	0	0
M93275	0	0	0	0	1	0	0	0	0	0	0	0	0	0
RIF1	0	0	0	0	0	0	1	0	0	0	0	0	0	0
ANXA3	0	0	0	0	0	0	0	0	0	1	0	0	0	0
TRIM22	0	0	0	0	0	0	0	0	0	0	0	0	0	1
SLC1A5	0	0	0	0	0	0	0	0	0	0	1	0	0	0
AK007927	0	0	0	0	0	0	0	0	0	0	1	0	0	0
MAFF	0	0	0	0	0	0	0	0	0	1	0	0	0	0
STAT3	0	0	0	0	0	0	0	0	0	0	0	1	0	0
ITGA7	2	0	0	0	0	0	0	0	0	0	0	0	0	0
KL	0	0	0	0	2	0	0	0	0	0	0	0	0	0
CD14	2	0	0	0	0	0	0	0	0	0	0	0	0	0
GEM	0	0	0	0	0	0	0	0	2	0	0	0	0	0
ZNF467	0	0	0	0	0	0	0	0	0	1	0	0	0	0
SHC1	0	0	0	0	0	0	0	0	0	0	0	1	0	0
SMAD1	0	0	0	0	0	0	0	0	0	0	0	1	0	0
IGSF10	0	0	0	0	0	0	0	0	0	0	1	0	0	0
FBLN2	0	0	0	0	0	0	0	0	0	0	0	2	0	0
BTNL9	0	0	0	0	0	0	0	0	0	1	0	0	0	0
COASY	0	0	0	0	0	0	0	0	0	0	1	0	0	0
MMT00002956	0	0	0	0	0	0	0	0	0	1	0	0	0	0
TRAPPC3	0	0	0	0	1	0	0	0	0	0	0	0	0	0
PTCHD1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
THADA	0	0	0	0	1	0	0	0	0	0	0	0	0	0
LOXL1	0	0	0	0	0	0	0	0	0	0	1	0	0	0
PCOLCE2	0	0	0	0	0	0	0	0	0	1	0	0	0	0
CTNNB1	0	0	0	0	0	0	0	0	0	0	0	1	0	0
ALDOB	0	0	0	0	0	0	0	0	0	0	1	0	0	0
SCARA3	0	0	0	0	0	0	0	0	0	0	1	0	0	0
HELZ	0	0	0	0	0	0	0	0	0	0	1	0	0	0
VPS33A	1	0	0	0	0	0	0	0	0	0	0	0	0	0
PTPN11	0	0	0	0	0	0	0	0	0	0	0	1	0	0
TCF3	1	0	0	0	0	0	0	0	0	0	0	0	0	0
CYP1B1	0	0	0	0	1	0	0	0	0	0	0	0	0	0
COLEC12	0	0	0	0	0	0	0	0	1	0	0	0	0	0
BC042789	0	0	0	0	0	0	0	0	1	0	0	0	0	0
OAS2	0	0	0	0	0	0	0	0	1	0	0	0	0	0
ZDHHC17	0	0	0	0	1	0	0	0	0	0	0	0	0	0

Part 2:

Key Drivers	Z-Scores	Meta-P values	KD CAD GWAS P Values in CARDIoGRAM	KD CAD GWAS P Values in 1000 Genomes	Score 1	Score 2	Score 3	Summary Score
DUSP6	10.95	1.35E-34	7.29E-02	1.47E-03	1.00	0.54	1.00	2.54
DUSP1	9.64	2.77E-26	3.87E-03	2.07E-03	0.99	0.43	0.93	2.35
KNG1	8.26	8.60E-15	5.08E-03	2.65E-03	0.99	0.70	0.24	1.92
COL6A3	7.92	6.27E-14	1.08E-02	2.68E-04	0.98	0.09	0.59	1.67
F2	7.99	4.22E-13	2.04E-01	2.62E-04	0.97	0.92	0.23	2.13
APOA1	7.76	1.93E-09	8.02E-10	5.60E-05	0.96	0.62	0.15	1.74
HGD	7.46	1.05E-08	6.66E-02	4.15E-03	0.96	0.92	0.62	2.50
HLA-F	6.83	1.52E-08	2.83E-05	3.02E-03	0.95	0.12	0.85	1.91
GBP1	7.09	3.41E-08	6.74E-03	6.76E-04	0.94	0.23	0.96	2.13
LUM	7.05	5.74E-08	7.08E-02	2.33E-02	0.93	0.92	0.98	2.84
JAG1	6.87	9.49E-08	2.45E-03	8.01E-03	0.93	0.27	0.74	1.93
GBP2	6.94	1.60E-07	6.14E-03	6.76E-04	0.92	0.70	0.72	2.34
MTMR11	6.91	8.93E-07	1.67E-03	1.43E-02	0.91	0.92	0.49	2.32
ANXA1	6.72	9.70E-07	3.52E-03	9.12E-03	0.91	0.15	0.83	1.88
MMP9	6.96	9.76E-07	1.95E-04	5.81E-05	0.90	0.21	0.87	1.98
NM_009245	6.74	1.33E-06	1.00E+00	1.00E+00	0.89	0.54	0.20	1.62
IFI35	6.43	1.33E-06	6.95E-02	1.84E-03	0.89	0.16	0.96	2.01
CCL18	6.43	1.39E-06	2.15E-02	6.44E-03	0.88	0.47	0.95	2.30
PLG	6.72	3.13E-06	5.04E-06	2.88E-34	0.87	0.58	0.27	1.72
VEGFA	6.65	3.68E-06	9.02E-03	1.50E-05	0.86	0.43	0.38	1.67
COL4A2	6.94	4.04E-06	9.09E-08	1.83E-10	0.86	0.58	0.69	2.13
COL1A1	6.69	4.13E-06	1.06E-03	2.64E-03	0.85	0.92	0.82	2.59
ITGB4	6.36	4.35E-06	3.16E-02	3.37E-05	0.84	0.47	0.61	1.92
MMT00019644	6.63	4.58E-06	1.00E+00	1.00E+00	0.83	0.27	0.38	1.48
MSN	6.47	7.30E-06	1.00E+00	1.00E+00	0.83	0.62	0.99	2.44
KCNK13	6.43	1.13E-05	1.36E-02	1.12E-02	0.82	0.11	0.80	1.73
ANXA2	6.50	1.47E-05	5.14E-04	3.43E-03	0.81	0.24	0.72	1.77
TNFAIP2	6.27	2.20E-05	9.30E-04	5.55E-03	0.80	0.19	0.91	1.90
CXCL12	6.61	2.28E-05	2.62E-02	2.95E-10	0.80	0.92	0.65	2.37
ABCG5	6.35	3.70E-05	2.15E-06	1.35E-07	0.79	0.62	0.34	1.75
CFB	6.42	4.35E-05	9.12E-04	1.67E-03	0.78	0.92	0.28	1.99
APOC2	6.43	4.38E-05	2.14E-04	7.07E-11	0.78	0.92	0.25	1.94
APOB	6.44	6.48E-05	2.49E-04	3.09E-08	0.77	0.50	0.54	1.81
SORL1	6.19	6.66E-05	1.34E-02	1.00E-02	0.76	0.31	0.41	1.48
ACVR1C	6.26	6.98E-05	2.19E-03	3.05E-04	0.75	0.07	0.19	1.01
ADM	6.17	7.95E-05	3.66E-03	2.77E-04	0.75	0.14	0.91	1.79
RDH16	6.29	0.000115	3.07E-02	3.17E-03	0.74	0.92	0.29	1.95
PAPSS2	6.20	0.000136	6.32E-03	4.68E-03	0.73	0.47	0.70	1.91
LOXL2	6.29	0.000168	1.12E-02	5.28E-03	0.72	0.70	0.64	2.06
SLIT3	6.18	0.000204	8.02E-04	1.83E-04	0.72	1.00	0.51	2.22
MMT00021022	6.11	0.000206	1.00E+00	1.00E+00	0.71	1.00	0.00	1.71
TGFBI	6.31	0.000207	7.03E-02	7.89E-03	0.70	0.70	0.12	1.52
PHACTR1	6.26	0.000221	6.03E-12	1.81E-42	0.70	0.58	0.22	1.50
IL15RA	6.06	0.000223	3.36E-02	2.73E-04	0.69	0.62	0.43	1.74
TRIM8	6.09	0.000224	6.74E-05	5.08E-06	0.68	0.43	0.00	1.11
OSM	6.19	0.00024	2.39E-04	5.36E-07	0.67	0.70	0.09	1.47
LY96	6.09	0.000257	3.37E-02	1.02E-03	0.67	0.36	0.63	1.66
CXCL10	6.08	0.000274	5.74E-02	6.34E-03	0.66	0.43	0.97	2.06
SLC2A3	6.08	0.000274	2.18E-02	7.81E-03	0.65	0.50	0.88	2.04
LARGE	6.14	0.000336	3.02E-04	4.22E-04	0.64	0.21	0.39	1.25
IRF1	5.93	0.000357	1.78E-03	1.24E-04	0.64	0.27	0.99	1.90
AZGP1	6.12	0.000378	2.23E-02	5.77E-05	0.63	1.00	0.21	1.84
NGRN	6.13	0.000382	3.16E-02	3.67E-03	0.62	0.92	0.16	1.71
EFEMP1	6.04	0.000402	6.85E-04	1.95E-03	0.62	0.31	0.54	1.46
IRF9	5.91	0.000457	7.65E-02	3.18E-02	0.61	0.58	0.77	1.96
APOA5	6.10	0.0005	8.02E-10	5.60E-05	0.60	0.38	0.18	1.16
CFD	5.90	0.000506	5.49E-02	1.19E-02	0.59	0.27	0.90	1.76
NOTCH1	6.04	0.000591	3.08E-02	1.52E-03	0.59	0.77	0.44	1.79
APOF	6.08	0.000596	3.42E-02	4.16E-05	0.58	1.00	0.30	1.88
LDLR	6.06	0.000619	9.73E-10	4.44E-15	0.57	1.00	0.14	1.71
KLF6	5.89	0.000632	2.00E-02	3.53E-03	0.57	0.05	0.73	1.35
FBP1	6.07	0.000636	3.19E-03	7.08E-04	0.56	0.36	0.20	1.13
RAC2	5.88	0.000697	2.04E-04	2.30E-03	0.55	0.08	0.86	1.49
APOC4	6.05	0.000707	2.14E-04	7.07E-11	0.54	0.70	0.09	1.33
MATN2	6.10	0.000713	3.07E-02	3.12E-03	0.54	0.70	0.14	1.38
IFI30	5.87	0.000736	7.94E-04	8.19E-04	0.53	0.34	0.62	1.49
WIPF1	5.99	0.000743	5.86E-03	5.67E-05	0.52	0.19	0.26	0.97
FN1	6.10	0.000759	6.70E-05	5.14E-07	0.51	0.92	0.55	1.99
BST2	5.87	0.000796	7.38E-03	1.13E-02	0.51	0.27	0.78	1.55
COL5A1	5.97	0.000827	2.02E-02	1.84E-03	0.50	0.34	0.70	1.53
EPS8	5.97	0.00087	2.72E-02	9.44E-04	0.49	0.19	0.58	1.26
SPARC	6.03	0.000873	1.75E-03	3.24E-03	0.49	0.77	0.56	1.81
IRF7	5.94	0.000912	7.72E-03	8.68E-03	0.48	0.54	0.79	1.81
BATF2	5.96	0.00092	1.62E-01	1.88E-02	0.47	0.54	0.17	1.18
ZYX	5.85	0.000991	1.63E-02	2.04E-03	0.46	0.43	0.92	1.81
MMT00081256	5.95	0.001031	1.00E+00	1.00E+00	0.46	0.92	0.12	1.50
HEMGN	5.94	0.001131	6.54E-04	3.68E-03	0.45	0.12	0.28	0.85
ZNF496	5.84	0.001132	9.43E-03	4.32E-04	0.44	0.34	0.52	1.30
AW475929	5.94	0.00115	1.00E+00	1.00E+00	0.43	0.19	0.43	1.05
CKLF	5.94	0.00115	3.66E-02	5.66E-03	0.43	0.05	0.49	0.97
APOC3	5.93	0.001197	8.02E-10	5.60E-05	0.42	0.70	0.07	1.19
NCOR2	6.02	0.001216	1.59E-03	9.27E-04	0.41	0.92	0.10	1.44
WWC2	5.83	0.001306	1.32E-02	4.98E-04	0.41	0.00	0.53	0.93
ASAH1	5.92	0.001353	1.18E-02	1.36E-02	0.40	0.08	0.36	0.84
ACCN1	5.99	0.001379	4.40E-04	5.35E-04	0.39	1.00	0.00	1.39
ISG15	5.82	0.00139	1.27E-02	3.48E-04	0.38	0.38	0.84	1.61
ADAM9	5.82	0.001451	4.28E-02	4.45E-03	0.38	0.70	0.86	1.94
SDCBP	5.82	0.001466	4.09E-02	1.51E-02	0.37	0.17	0.80	1.34
CD74	5.90	0.001539	2.64E-02	3.41E-03	0.36	0.54	0.75	1.65
MCOLN1	5.90	0.001584	2.51E-02	2.89E-03	0.36	0.62	0.06	1.03
ZBTB44	5.89	0.001603	1.47E-02	3.93E-04	0.35	0.92	0.22	1.50

IGFBP6	**5.80**	**0.001759**	**2.16E-02**	**2.17E-03**	**0.34**	**0.27**	**0.59**	**1.19**
CTSB	**5.80**	**0.001791**	**3.68E-04**	**3.91E-03**	**0.33**	**0.43**	**0.71**	**1.47**
SERPINC1	**5.93**	**0.001813**	**4.02E-02**	**2.52E-03**	**0.33**	**0.31**	**0.11**	**0.74**
SLIT2	**5.79**	**0.001946**	**1.29E-04**	**1.57E-03**	**0.32**	**0.01**	**0.83**	**1.16**
ABCG8	**5.86**	**0.002066**	**2.15E-06**	**1.35E-07**	**0.31**	**0.43**	**0.57**	**1.31**
NME6	**5.85**	**0.002077**	**5.21E-03**	**3.69E-04**	**0.30**	**0.77**	**0.00**	**1.07**
C1R	**5.78**	**0.002115**	**1.46E-04**	**3.94E-04**	**0.30**	**0.34**	**0.75**	**1.38**
DPYD	**5.77**	**0.002352**	**4.79E-03**	**1.62E-03**	**0.29**	**0.27**	**0.51**	**1.07**
AK021074	**5.83**	**0.002375**	**1.00E+00**	**1.00E+00**	**0.28**	**0.77**	**0.00**	**1.05**
BNIP3L	**5.77**	**0.002409**	**4.72E-03**	**6.49E-04**	**0.28**	**0.34**	**0.64**	**1.26**
LAMA2	**5.82**	**0.002643**	**1.53E-02**	**5.77E-03**	**0.27**	**0.16**	**0.46**	**0.89**
M93275	**5.76**	**0.002662**	**1.00E+00**	**1.00E+00**	**0.26**	**0.77**	**0.08**	**1.11**
RIF1	**5.70**	**0.002841**	**5.05E-02**	**1.56E-03**	**0.25**	**1.00**	**0.00**	**1.25**
ANXA3	**5.74**	**0.00306**	**1.40E-02**	**2.15E-03**	**0.25**	**0.92**	**0.88**	**2.05**
TRIM22	**5.74**	**0.003272**	**1.43E-03**	**3.40E-05**	**0.24**	**0.38**	**0.76**	**1.38**
SLC1A5	**5.74**	**0.003283**	**9.83E-04**	**2.39E-04**	**0.23**	**0.40**	**0.60**	**1.23**
AK007927	**5.73**	**0.003364**	**1.00E+00**	**1.00E+00**	**0.22**	**0.70**	**0.32**	**1.24**
MAFF	**5.73**	**0.00349**	**3.41E-03**	**2.58E-03**	**0.22**	**0.23**	**0.93**	**1.38**
STAT3	**5.76**	**0.003503**	**4.35E-04**	**1.64E-06**	**0.21**	**1.00**	**0.81**	**2.02**
ITGA7	**5.77**	**0.003714**	**5.34E-03**	**1.19E-04**	**0.20**	**0.15**	**0.33**	**0.68**
KL	**5.77**	**0.003741**	**1.32E-02**	**2.82E-03**	**0.20**	**0.92**	**0.45**	**1.57**
CD14	**5.77**	**0.003769**	**1.35E-02**	**2.37E-02**	**0.19**	**0.01**	**0.68**	**0.88**
GEM	**5.76**	**0.004127**	**4.26E-03**	**1.82E-05**	**0.18**	**0.92**	**0.67**	**1.78**
ZNF467	**5.70**	**0.004247**	**1.33E-03**	**3.76E-04**	**0.17**	**0.70**	**0.46**	**1.34**
SHC1	**5.75**	**0.00426**	**6.14E-03**	**1.39E-05**	**0.17**	**0.92**	**0.94**	**2.03**
SMAD1	**5.73**	**0.004323**	**1.78E-02**	**4.89E-04**	**0.16**	**0.92**	**0.36**	**1.44**
IGSF10	**5.74**	**0.004506**	**1.30E-03**	**1.40E-03**	**0.15**	**0.03**	**0.66**	**0.84**
FBLN2	**5.73**	**0.004689**	**1.35E-02**	**5.59E-04**	**0.14**	**0.54**	**0.41**	**1.10**
BTNL9	**5.69**	**0.004803**	**2.75E-02**	**2.26E-02**	**0.14**	**0.24**	**0.35**	**0.73**
COASY	**5.69**	**0.004899**	**8.84E-02**	**3.37E-06**	**0.13**	**0.50**	**0.33**	**0.96**
MMT00002956	**5.68**	**0.004991**	**1.00E+00**	**1.00E+00**	**0.12**	**0.04**	**0.89**	**1.06**
TRAPPC3	**5.67**	**0.005347**	**1.67E-01**	**3.13E-02**	**0.12**	**0.04**	**0.37**	**0.52**
PTCHD1	**5.67**	**0.005398**	**1.00E+00**	**1.00E+00**	**0.11**	**0.77**	**0.67**	**1.54**
THADA	**5.67**	**0.005439**	**1.07E-03**	**9.84E-05**	**0.10**	**0.92**	**0.13**	**1.15**
LOXL1	**5.67**	**0.005516**	**3.96E-04**	**2.47E-04**	**0.09**	**0.58**	**0.25**	**0.93**
PCOLCE2	**5.67**	**0.005629**	**5.69E-02**	**6.24E-05**	**0.09**	**0.70**	**0.48**	**1.26**
CTNNB1	**5.66**	**0.005696**	**9.41E-05**	**1.67E-02**	**0.08**	**0.92**	**0.31**	**1.31**
ALDOB	**5.66**	**0.005725**	**2.81E-03**	**4.68E-03**	**0.07**	**0.43**	**0.17**	**0.67**
SCARA3	**5.66**	**0.005725**	**2.56E-02**	**1.52E-03**	**0.07**	**0.10**	**0.50**	**0.67**
HELZ	**5.65**	**0.006031**	**4.34E-02**	**2.34E-03**	**0.06**	**0.77**	**0.42**	**1.24**
VPS33A	**5.63**	**0.007027**	**3.80E-03**	**2.15E-04**	**0.05**	**0.92**	**0.07**	**1.04**
PTPN11	**5.65**	**0.007134**	**5.20E-07**	**1.47E-09**	**0.04**	**0.13**	**0.78**	**0.96**
TCF3	**5.62**	**0.007515**	**1.02E-01**	**1.46E-02**	**0.04**	**0.70**	**0.47**	**1.21**
CYP1B1	**5.61**	**0.007759**	**1.06E-02**	**2.99E-03**	**0.03**	**0.02**	**0.57**	**0.62**
COLEC12	**5.60**	**0.008186**	**1.38E-03**	**3.25E-03**	**0.02**	**0.54**	**0.30**	**0.86**
BC042789	**5.59**	**0.008305**	**1.00E+00**	**1.00E+00**	**0.01**	**0.47**	**0.00**	**0.49**
OAS2	**5.59**	**0.008663**	**6.10E-05**	**1.02E-03**	**0.01**	**1.00**	**0.00**	**1.01**
ZDHHC17	**5.57**	**0.009621**	**1.80E-03**	**4.50E-03**	**0.00**	**0.07**	**0.40**	**0.46**

Note: The numbers in columns B-O (Adipose-Vascular Endothelium) represent the number of CAD gene lists for which a gene was identified as a KD using the specific network, with cells showing values >1 in red. Column "Tissue Consistency" represents how many unique networks in which a gene was identified as a KD. Column "KDA List Consistency" represents the frequency of KDs in all the 7*14 =98 KDA results. "Z-Scores" and "Meta-P values" come from the meta-analysis of the 98 sets of KDA results. Columns "KD CAD GWAS P Values in CARDIoGRAM" and "KD CAD GWAS P Values in 1000 Genomes" annotate each KD with the most significant CAD association p values in CARDIoGRAM and CAD 1000 Genomes GWAS among all SNPs mapped to the gene, with cells highlighted in red satisfying GWAS P<10E-5. Columns "Score 1, "Score 2", and "Score 3" represent the normalized scores from KDA statistics and network consistency, CAD relevance of KD subnetworks in terms of CAD GWAS signal enrichment, and differential expression of KD subnetworks in CAD vs controls, respectively. Column "Summery score" is the sum of the three scores for each KD.

Supplemental Table III. Subnetworks with CARDIoGRAM GWAS information.

Key Drivers	Subnetwork Size	No. Genes with CAD 1000 Genomes GWAS P<0.001 in KD subnetworks	The percentage of Genes with CAD 1000 Genomes GWAS P<0.001 in KD subnetworks	Genes with CAD 1000 Genomes GWAS P<0.001 in KD subnetworks	P Values compared with random genes	P Values compared with GWAS genes
DUSP6	Aorta (952); Artery (193); Cardiac_muscle (304); Smooth_muscle (89); Vascular_endothelium (275)	Aorta (276); Artery (69); Cardiac_muscle (102); Smooth_muscle (35); Vascular_endothelium (93)	Aorta (0.289); Artery (0.357); Cardiac_muscle (0.335); Smooth_muscle (0.393); Vascular_endothelium (0.338)	Aorta (XAF1, VAT1, SFTPC, NEUROD6, CAV2, C4BPA, DNASE1L3, TNFSF15, CD40, PLA2G4A, MUC4, IFITM3, MT1H, POPDC3, ARL4A, C3, HLA-DRA, SLAMF1, PHLDA1, SPP1, SFTPD, CTSK, PTGIR, COL4A2, BLVRA, SRD5A1, TRIM68, NFE2, TNFSF10, PDE1A, FAP, TRIM21, MEST, NEDD9, SIK3, CCDC92, MREG, SLC26A10, NCOR2, APOE, AHR, SORBS2, SH3PXD2A, MT1G, LYPD3, GIMAP6, MMP1, RAD23A, FBLN2, ELMO1, HLA-DOB, AP1G1, PTHLH, GBP2, MCL1, CXCL12, PPAP2B, COL6A3, C1RL, MITF, KCNJ13, ARHGEF16, ATP2A3, WNT2, WDR37, NPBWR2, MMP10, XYLT1, GJB3, TCEA2, VWF, KDR, LEFTY2, TPO, NCALD, FSTL3, NPTX1, GRK5, TPM3, CAMTA1, IL24, TFAP2B, IL23A, AXL, LRP1, GALNT6, MT1F, LPL, KDELR2, NID1, ABCA8, COL3A1, PECAM1, CLDN5, HAAO, CTSH, TFF3, FRY, EPS8, PDGFD, PSMD8, PLXND1, C1S, PLCH1, CELF2, BNIP3L, IFITM1, GAS6, FNBP1, CSF1, KIAA1549L, MYOF, SDC4, VAV2, ENG, GRIN1, ASIC2, P2RX4, KCNMA1, PHYHIP, PTRF, WDR82, MCC, FOXF2, ARF4, PDXK, IFITM2, CDK2AP1, CX3CL1, HLA-B, TCF7L2, COL5A2, NR2F2, ACP5, ALDH1A3, MX1, MGRN1, SLC22A4, RGS19, WT1, CRIM1, XCL2, MICAL2, ARL15, MMP2, TEK, CD38, SDC2, FST, ARHGDIB, C14orf79, FNDC3B, WWC2, NEDD4, TIPARP, RAB23, CCNL1, ISG20, CXCL1, HOXB2, CUBN, IRF3, LIF, KCNN3, GPR1, FSCN1, LIPG, PDE4B, TFPI, ELK3, TMEM176B, DNAJB1, ECM1, IFIT2, DNALI1, HERPUD1, CBL, PROM1, CXCL6, DDX5, KIAA1324, SLC10A1, HS3ST2, FOSB, PROCR, KCNE4, IRF1, SNRPF, DPT, ME3, SORT1, LSAMP, ARL4D, F2R, C1R, TRIM22, CDH13, CCNG2, NKG7, SCGN, PVRL2, MFAP4, PTPRS, BACE1, FAM46A, UBA52, ANXA11, BBOX1, CDK14, ERG, PDGFRB, MAST4, MAGI1,	Aorta (p<10e-16); Artery (p<10e-16); Cardiac_muscle (p<10e-16); Smooth_muscle (p<10e-16); Vascular_endothelium (p<10e-16)	Aorta (0.0455); Artery (0.0261); Cardiac_muscle (0.017); Smooth_muscle (0.00682); Vascular_endothelium (0.0227)

				SLC7A7, SULF1, ABCG1, IGFBP7, CCL17, TCP11L1, ABCC3, PPIB, LILRB1, ZSCAN2, LDB2, RAB13, WWTR1, ZNF250, CABP1, EDNRA, MMP12, FTO, ADAMTS3, LOX, IL32, SPSB1, ZNF652, PRCP, ASPA, SLC4A2, CFI, ATP12A, GEM, TEAD1, GFPT2, ALAD, IL6R, FLI1, CX3CR1, TIMP3, OSMR, MERTK, SYNGR2, GRB10, CAV1, SCUBE2, CSF1R, ADAMTSL3, FOSL1, TTC39A, NAV3, LAMB2, CACNA1G, IFIT3, PLAU, FOXC1, THBS3, HLA-DQB1, CALR, TAGLN, KCNK2, MAGI2, HOMER1, CELSR1, CNKSR1, RAMP2, KCNN4); Artery (VAT1, CAV2, IFITM3, FOS, C3, PHLDA1, COL4A2, TNFSF10, ZCCHC24, AHR, MMP1, GBP2, MCL1, PPAP2B, JUN, FGFR3, TMEM123, ATP2A2, GRK5, MT1F, KDELR2, COL3A1, PECAM1, FGFR1, FRY, EPS8, PLXND1, CSF1, MYOF, SDC4, P2RX4, KCNMA1, VEGFA, MAP3K5, ARF4, PDXK, IFITM2, TCF7L2, COL5A2, NR2F2, ALDH1A3, MX1, TRIB1, FNDC3B, TIPARP, CXCL1, LIF, ZFP36, FSCN1, TFPI, ELK3, RRBP1, C16orf45, FOSB, GBP1, FSTL1, IGFBP7, ABCC3, CD302, HHEX, LOX, FLI1, ACTN1, TIMP3, SYNGR2, GRB10, CAV1, PLAU, TAGLN); Cardiac_muscle (CLIC4, CAV2, TNFRSF12A, FOS, RIT1, ST7, PHLDA1, COL4A2, DAZAP2, GRN, MEST, FDPS, MAPKAPK2, AHR, CPEB4, ITPR1, GBP2, MCL1, PPAP2B, JUN, PLIN2, SERINC1, GRK5, LRP1, ITGB5, NID1, TMED2, PLEC, PCDH9, FGFR1, FRY, SCP2, FN1, PLXND1, TGFBR3, IFITM1, GAS6, SSBP4, CSF1, MYOF, SLPI, LSM4, ACLY, VEGFA, PPARD, MAP3K5, ETS2, EIF5, TCF7L2, NR2F2, STEAP3, PNRC1, TRIB1, MMP2, ZEB1, COL18A1, TIPARP, ZFP36, TFPI, ADM, ELK3, ECM1, RRBP1, HEG1, SERPINH1, CD163, HSD17B12, ALDH3A2, SH3BP5, F2R, GPX1, ANXA4, FSTL1, SOD2, NR4A2, LRRFIP1, GBE1, HTRA1, SLC7A7, ABCC3, PPIB, NF2, EDNRA, RGL1, SGK1, RUNX1T1, CD302, HHEX, ZBTB20, ACTN1, TIMP3, EGR2, CAV1, NPC2, UMPS, GUCY1A3, HLA-DQB1, CALR, LAMC1, TAGLN, NFIB, RAB27A); Smooth_muscle (STK17A, IFITM3, PYGL, ZCCHC24, PRNP, JUN, FGFR3, GRK5, ITGB5, PECAM1, IFITM1, MYOF, VEGFA, ARF4, TCF7L2, MX1, PNRC1, TRIB1, FNDC3B, ISG20, CXCL1, LIF, ZFP36, ELK3, OAS1, YARS, TRIM22, ZNF274, MAST4, IGFBP7, GLI3, TIMP3, EGR2, CAV1, PLAU); Vascular_endothelium (KLF4, CAV2, IFITM3, FOS, PHLDA1, COL4A2, GRN, AHR, CDKN1A, GBP2, MCL1, CTGF, JUN, CXCR4, GRK5, TANK, KDELR2, SPRED2, ITGB5, NID1, PECAM1, FGFR1, FRY, EPS8, FN1, PLXND1, C1S, BNIP3L, MYOF, SDC4, ICAM1, VEGFA, MAP3K5, ARF4, ETS2, IFITM2, TCF7L2, PON2, COL5A2, NR2F2, TRIB1, PTPRK, SH2B3, FNDC3B, ISG20, CXCL1, ATP2B1, PALLD, LIF, ZFP36, TFPI, ADM, ELK3, EPHA2, IL15RA, PROCR, IRF1, CD163, GBP1, F2R, C1R, CCNG2, TES, DENND5A, SP100, ANXA4, EDN1, NR4A2, ITGA2, LRRFIP1, HTRA1, IGFBP7, ABCC3, PPIB, SLC20A1, WWTR1, SGK1, MAP1LC3B, HHEX, PRCP, BACH1, GEM, TRIB2, ACTN1, TIMP3, CAV1, NPC2, TGFB1, PLAU, SWAP70, LAMC1, TAGLN, RAB27A)		
DUSP1	Aorta (780); Artery (265); Smooth_muscle (263)	Aorta (243); Artery (90); Smooth_muscle (97)	Aorta (0.311); Artery (0.339); Smooth_muscle (0.368)	Aorta (EMILIN1, CNTN2, CALCOCO2, GNLY, MFGE8, CAV2, TNFSF15, LLGL1, IFITM3, PCSK5, GATM, ARL4A, C3, MEOX1, TNFSF10, ZCCHC24, GAB2, FAP, SIK3, NRG1, APOE, AHR, SORBS2, MMP1, MMP3, FBLN2, ELMO1, CDKN1A, CH25H, PTGER3, MBNL2, ATP11A, SPHK1, MYH11, GBP2, ACPP, CTGF, GPR65, PTGDS, CXCL12, PPAP2B, COL6A3, CDKN2A, DAAM1, ADAM12, MITF, WNT2, ST5, LILRB4, GJB3, LMOD1, VWF, KDR, IFIT1, FSTL3, FPR1, AXL, ITGBL1, CPA3, BLZF1, MARCO, CHPF, RBMS1, NID1, PLN, ABCA8, STAT3, COL3A1, PECAM1, CNPPD1, AHNAK2, HLA-DRB5, TLR1, FN1, RRAD, PLXND1, C1S, MAFB, BNIP3L, IFITM1, NRP1, PLK3, MNDA, SDC4, SLPI, ICAM1, STX4, RIT2, KCNMA1, FEV, PTRF, COL7A1, HLA-DQA1, HOXC4, GIMAP4, KIAA0922, PTN, MAP3K5, CCR9, ETS2, IFITM2, HLA-B, TCF7L2, OGDH, TRIM29, COL5A2, BCAR3, DOCK1, ACP5, CCPG1, TRPV4, ALDH1A3, RELB, PSG11, PIK3R3, RAF1, ARG1, LIPA, TPM1, CRIM1, NMI, MAT2A, CST7, SEC14L1, SDC2, BST1, PTCRA, FST, PRKD2, NINJ1, MMP13, TIPARP, SLC26A4, OASL, ISG20, LIF, PJA2, FHL5, PDE7B, SART1, TFPI, SEC11A, ADM, AGXT, ITGA7, ELK3, ECM1, GUCY1B3, CDK6, CADPS, MYO1A, CALCRL, SLC12A8, C16orf45, CRYBA1, IL15RA, RHOQ, PROCR, KCNE4, TBC1D2B, P2RX6, BCAR1, DPT, HIVEP2, SDC1, CER1, MYLK, TMED10, C1R, TRIM22, CDH13, COL15A1, CCNG2, MFAP4, SP100, IFIT5, ANKRD1, SEMA3C, RPS27, FSTL1, EDN1, SOD2, NR4A2, AIPL1, CGA, PDGFRB, DHX38, HTRA1, TWIST1, SMAD6, SEPT9, S100A1, PDPN, PTPRN2, ZSCAN2, FGF2, PTH1R, EDNRA, IL5, MMP12, CD302, FGF5, LOX, STXBP1, HSPB7, PLEK, CTSS, PRKG1, CFI, PDLIM3, GEM, ZBTB20, ADAMTS8, RPL28, OSMR, ZFP36L2, EGR2, KLF7, WIPI1, CAV1, SFTPB, KIAA0430, CSF1R, ADAMTSL3, PCOLCE, UTRN, LTBP1, LOXL1, PLEKHO2, LAMB2, GRAP, IFIT3, GUCY1A3, GJA1, RFTN1, SWAP70, HLA-DQB1, FBLN1, LAMC1, TAGLN, SLC7A5, ALOX12P2, BMPR1B); Artery (STK17A, KLF4, CAV2, SMAD3, IFITM3, ZCCHC24, GAB2, GRN, SIK3, APOE, CDKN1A, ABLIM1, SPHK1, MCL1, CTGF, PPAP2B, JUN, HMGCR, CXCR4, AXL, ITGB5, RBMS1, NID1, FGFR1, FN1, RRAD, PLXND1, C1S, MAFB, TPM2, IFITM1, SDC4, ICAM1, KLF2, FKBP5, VEGFA, ETS2, IFITM2, TCF7L2, ATP1B1, TPM1, CRIM1, TRIB1, SH2B3, MAT2A, SEC14L1, LDLR, PRKD2, TIPARP, PALLD, ALDH2, TFPI, ADM, ITGA7, ELK3, ECM1, HEG1, HERPUD1, PRKCA, SAMM50, RHOQ, PROCR, NEAT1, MYLK, CYBRD1, TRIM22, COL15A1, CCNG2, IFIT5, ANXA11, SOD2, NR4A2, FGF2, SGK1, BMP2, STXBP1, PFKFB3, GEM, ZBTB20, TIMP3, OSMR, ZFP36L2, GRB10, CAV1, LOXL1, PLEKHO2, LAMC1, TAGLN, SLC7A5, RAB27A); Smooth_muscle (STK17A, KLF4, SQLE, CLIC4, UBE2H, RIOK3, RIT1, CALHM2, NPC1, GDF15, PHLDA1, WEE1, YRDC, GRN, VCL, APOE, CDKN1A, LTBP3, TAGLN2, MCL1, CTGF, UBL3, JUN, UBC, SHC1, HMGCR, CAMSAP2, SPRED2, ITGB5, NID1, BNIP3L, GAS6, MYOF, SDC4, HSPA1B, BCL3, PTRF, CHST11, FKBP5, VEGFA, UCP2, MAP3K5, ETS2, IFITM2, STAT6, LRP10, TRIB1,	Aorta (p<10e-16); Artery (p<10e-16); Smooth_muscle (p<10e-16)	Aorta (0.0125); Artery (0.0318); Smooth_muscle (0.0102)

				JOSD1, MICAL2, FKBP1A, LDLR, CHP1, NEDD4, TIPARP, ATP2B1, ALDH2, ZFP36, ADM, DNAJB1, EPHA2, TUFT1, RRBP1, HERPUD1, RHOQ, CSTB, FOSB, PROCR, IRF1, TBC1D2B, ZNF274, RORA, DKK1, ANXA11, SOD2, NR4A2, ODC1, SMAD6, TMED5, FGF2, SGK1, BMP2, AKR1C1, GLI3, GEM, IL6R, RPL28, ZFP36L2, GRB10, CAV1, XBP1, NPC2, LTBP1, PLEKHO2, SLC7A5, KLC1, QSOX1, RAB27A)		
KNG1	Brain (56); Muscle (29)	Brain (14); Muscle (13)	Brain (0.25); Muscle (0.448)	Brain (C4BPA, APOC4, APOC3, APOB, APOA5, AZGP1, APOA4, AGXT, MAT1A, PAH, APOC2, CYP2A13, APOA1, FBP1); Muscle (APOC1, SEC14L4, APOC3, MBL1P, PFKL, APOB, APOA5, NIPSNAP1, CALN1, ITIH4, MST1, CFI, APOA1)	Brain (p<10e-16); Muscle (p<10e-16)	Brain (0.017); Muscle (0.00341)
COL6A3	Liver (69)	Liver (21)	Liver (0.304)	Liver (COL4A2, CXCL12, COL6A3, LARGE, BICC1, PSRC1, ITGBL1, NID1, COL3A1, GATA6, CRISPLD2, COL4A1, WT1, SERPINH1, DPT, FSTL1, PDGFRB, SMOC2, HTRA1, CX3CR1, PCOLCE)	Liver (p<10e-16)	Liver (0.0386)
F2	Adipose (49); Muscle (47)	Adipose (12); Muscle (19)	Adipose (0.244); Muscle (0.404)	Adipose (PLG, SERPIND1, SEC14L2, APOC3, APOA5, APOA4, APOF, LIPC, PAH, AKR1C1, APOA1, F2); Muscle (PLG, SERPIND1, HPX, APOC3, ATP2A2, KLKB1, UPB1, TNNT1, APOA5, MYL2, ARG1, ASGR1, GNMT, MAT1A, PAH, AKR1C1, CFI, APOA1, F2)	Adipose (p<10e-16); Muscle (p<10e-16)	Adipose (0.0182); Muscle (0.00114)
APOA1	Adipose (32); Brain (30); Muscle (16)	Adipose (9); Brain (8); Muscle (7)	Adipose (0.281); Brain (0.266); Muscle (0.437)	Adipose (PLG, SLC22A1, APOB, APOA4, FABP2, MAT1A, CYP2C18, APOA1, F2); Brain (APOC4, SLC22A1, APOC3, CEP97, KIAA0922, APOA4, CPS1, APOA1); Muscle (C4BPA, SERPIND1, APOC3, C8G, APOA4, APOA1, F2)	Adipose (p<10e-16); Brain (p<10e-16); Muscle (p<10e-16)	Adipose (0.00455); Brain (0.0136); Muscle (0.00909)
HGD	Brain (40); Muscle (48)	Brain (8); Muscle (12)	Brain (0.2); Muscle (0.25)	Brain (PLG, APOC4, HPX, APOA5, APOF, PAH, AKR1D1, APOA1); Muscle (PLG, APOC4, CA5A, UROC1, APOC3, UPB1, APOB, APOA5, AGXT, MAT1A, CYP2A13, FBP1)	Brain (p<10e-16); Muscle (p<10e-16)	Brain (0.00114); Muscle (0.0136)
HLA-F	Artery (189)	Artery (58)	Artery (0.306)	Artery (XAF1, ADAR, RIT1, C3, DPYSL2, TNFSF10, NLRC5, GRN, TSPAN3, GBP2, TREX1, MT1F, PLEC, CELF2, IFITM1, UCP2, PHF11, IFITM2, LRP10, HLA-B, ACP5, RELB, RGS19, OPTN, NMI, HLA-C, CAPG, OASL, ISG20, ALDH2, ELK3, OAS1, MMP14, CSTB, IRF1, GBP1, IFIH1, GPX1, C1R, TRIM22, UBA7, SP100, IFIT5, ANXA4, HERC6, HTRA1, ISG15, GBP3, HLA-DRB1, IL32, CTSS, IFI30, SYNGR2, OAZ1, PARP12, IFIT3, HLA-DQB1, CALR)	Artery (p<10e-16)	Artery (0.0318)
GBP1	Adipose (25); Blood (18); Vascular_endothelium (216)	Adipose (7); Blood (3); Vascular_endothelium (68)	Adipose (0.28); Blood (0.166); Vascular_endothelium (0.314)	Adipose (GBP2, NMI, EXTL2, GBP1, IFIH1, TRIM22, MTTP); Blood (P2RY14, GBP1, TRIM22); Vascular_endothelium (STK17A, KLF4, XAF1, ADAR, CAV2, MT1H, ATP1B3, HLA-DRA, PHLDA1, TNFSF10, CDKN1A, GBP2, PRNP, CTGF, DDX58, HLA-DPB1, IFIT1, CXCR4, TAP2, RBMS1, IFITM1, ICAM1, IFITM2, HLA-B, SMCO4, COL4A1, MX1, LIPA, NMI, ARHGDIB, FNDC3B, HLA-C, ISG20, PDE4B, ADM, IFIT2, PML, OAS1, IL15RA, IRF1, GBP1, TRIM22, SP100, IFIT5, ANXA4, EDN1, CMPK2, ISG15, GBP3, WWTR1, RGL1, LOX, IL32, PLEK, NRP2, CTSS, IFI30, ZFP36L2, CAV1, BAZ1A, MCM6, PARP12, TLR2, IFIT3, PLAU, HLA-DQB1, TAGLN, APOL3)	Adipose (p<10e-16); Blood (p<10e-16); Vascular_endothelium (p<10e-16)	Adipose (0.0193); Blood (0.0307); Vascular_endothelium (0.0182)
LUM	Brain (45)	Brain (12)	Brain (0.266)	Brain (CXCL12, COL3A1, TGFBR3, BMP6, FIBIN, TFPI, GBP1, ANXA4, SMOC2, SPOCK3, PCOLCE, ZFPM2)	Brain (p<10e-16)	Brain (0.00114)
JAG1	Vascular_endothelium (109)	Vascular_endothelium (39)	Vascular_endothelium (0.357)	Vascular_endothelium (KLF4, SMAD3, PHLDA1, COL4A2, F2RL1, PRNP, CTGF, JUN, AMIGO2, FGFR1, FN1, MYOF, ENG, VEGFA, TCF7L2, ENC1, COL4A1, CRIM1, FNDC3B, NOTCH3, ATP2B1, PALLD, TFPI, ADM, ABCC1, RAC1, EPHA2, HEG1, STK24, TES, WWTR1, TJP1, ZBTB20, GRB10, LOXL1, YES1, GJA1, ITGAV, PBX3)	Vascular_endothelium (p<10e-16)	Vascular_endothelium (0.0159)
GBP2	Blood (20); Kidney (12); Smooth_muscle (45)	Blood (3); Kidney (2); Smooth_muscle (18)	Blood (0.15); Kidney (0.166); Smooth_muscle (0.4)	Blood (GBP2, IRF1, FANCA); Kidney (GBP2, MTTP); Smooth_muscle (VAT1, GBP2, DDX58, SHC1, MX1, LIPA, OPTN, HLA-C, ATP2B1, SERPINB9, ADM, IRF1, GBP1, ARNTL, ANXA4, ISG15, LOX, PLAU)	Blood (p<10e-16); Kidney (p<10e-16); Smooth_muscle (p<10e-16)	Blood (0.033); Kidney (0.0159); Smooth_muscle (0.00341)
MTMR11	Liver (80)	Liver (25)	Liver (0.312)	Liver (DUSP8, ARHGAP22, ARL2BP, VCL, NRG1, SORBS2, TAGLN2, NID1, COL3A1, COL4A1, SMOX, SH2B3, ABCG5, MYO9B, FST, ARF5, HELLS, NUDT18, WFDC3, PDGFRB, SCD, SLC20A1, ST6GALNAC4, SGSM1, OTUD7B)	Liver (p<10e-16)	Liver (0.00114)
ANXA1	Artery (170); Smooth_muscle (290)	Artery (57); Smooth_muscle (81)	Artery (0.335); Smooth_muscle (0.279)	Artery (CLIC4, NAB1, PYGL, ATP1B3, COL4A2, AHR, HSPB8, SPHK1, TANK, PECAM1, FGFR1, PLXND1, C1S, BNIP3L, MYOF, SDC4, ENG, CDK2AP1, KRT17, ADAM17, SLC22A4, NMI, FST, ARHGDIB, NEDD4, TIPARP, PALLD, FSCN1, ELK3, RRBP1, SERPINH1, NPTN, TNFAIP6, PROCR, IRF1, GBP1, VAMP8, TRIM22, CDH13, SEMA3C, GBE1, HTRA1, SEPT11, TMED5, FGF2, EFEMP2, RAB13, WWTR1, PRCP, PLEK, CTSS, CFI, ACTN1, CAV1, PDLIM4, PLAU, TAGLN); Smooth_muscle (STK17A, KLF4, RIOK3, CBR1, ARL4A, PHLDA1, CTSK, TNFSF10, TLE1, MEST, AGRN, HSPB8, SPHK1, MCL1, PRNP, CTGF, DAAM1, MITF, SHC1, FGFR3, MAN2A2, JTB, CD2AP, RGS10, SERINC1, TANK, UVRAG, BNIP3L, SLBP, HSPG2, LSM4, STAG1, ARF4, IFITM2, EIF5, ENC1, ANP32E, PLD1, ARPC3, ME1, NMI, ARHGDIB, NEDD4, TIPARP, RRAS2, PALLD, FSCN1, ELK3, DDX5, TRAM2, PROCR, RYBP, IRF1, EFNA1, YWHAQ, ABHD2, CDC27, GBP1, TES, DKK1, ANXA4, SEMA3C, ATP11B, GBE1, SEPT11, IGFBP7, TMED5, FGF2, SLC20A1, PPP1R12A, CTSS, USP25, GLI3, ACTN1, MLLT3, XBP1, IFT20, NPC2, IP6K2, SWAP70, PSMD14)	Artery (p<1.0e-16); Smooth_muscle (p<1.0e-16)	Artery (0.0261); Smooth_muscle (0.0659)
MMP9	PPI (31)	PPI (11)	PPI (0.354)	PPI (PLG, COL4A2, COL4A3, MMP10, MMP9, FN1, COL4A1, CXCL1, TFPI, COL4A4, TIMP3)	PPI (p<1.0e-16)	PPI (0.0193)
NM_009245	Brain (26)	Brain (9)	Brain (0.346)	Brain (HPX, APOC3, APOA5, AZGP1, ARG1, MAT1A, CFI, APOA1, F2)	Brain (p<1.0e-16)	Brain (0.00682)
IFI35	Artery (165)	Artery (62)	Artery (0.375)	Artery (XAF1, ADAR, IFITM3, C3, TRAFD1, TRIM21, GRN, APOE, PTPN6, CDKN1A, GBP2, DDX58, LGALS1, IFIT1, STAT2, C1S, CELF2, IFITM1, PDXK, IFITM2, STAT6, HLA-B, ACP5, SLC35A2, COL4A1, MX1, RELB, RGS19, OPTN, NMI, HLA-C, CAPG, OASL, ISG20, IFIT2, RRBP1, PML, VAMP3, OAS1, IL15RA, IRF1, TNFAIP1, ABHD2, GBP1, ENO1, IFIH1, VAMP8, TRIM22, UBA7, SP100, ANXA4, HERC6, ISG15, HLA-DRB1, ECHDC2, PLEK, IFI30, NPC2, PLEKHO2, PARP12, IFIT3, HLA-DQB1)	Artery (p<1.0e-16)	Artery (0.025)
CCL18	Aorta (940)	Aorta (304)	Aorta (0.323)	Aorta (XAF1, VAT1, TOMM22, GNLY, AK1, MFGE8, CLIC4, ALOX5AP, TOX2, CAV2, APOC1, DRG2, KLRB1, PLTP, CD40, UFD1L, IFITM3, NOD1, RIN3, FOS, MT1H, HAS1, MPG, C3, SLAMF1, SPP1, COL4A2, MKNK2, BLVRA, SRD5A1, FASTK, FBN2, EIF2B3, ACTR1A, MCM3, GAB2, FAP, LRRK1, TRIM21, GRN, MEST, CLIP1, AGAP1, SH2D2A,	Aorta (p<1.0e-16)	Aorta (0.00909)

				CPVL, ACADVL, PTPN6, NCK1, RPL23A, CH25H, USP20, TAGLN2, DDAH2, GBP2, CTGF, ACAP1, GPR65, POMP, JUN, TREX1, ADAM12, MITF, LIMS2, GORASP2, APRT, AMIGO2, LGALS1, DEF6, EPB41L2, SYMPK, IFIT1, STAT2, FSTL3, ATP5G1, CXCR4, TMSB10, GRK5, ARHGAP15, SNTA1, FPR1, CACNA1C, TAP2, PIK3R1, RPS16, RBMS1, MGAT1, CTSW, SND1, CS, MT1X, SOAT1, PECAM1, FAM65B, PLEC, HAAO, CNPPD1, PSTPIP1, TLR1, SCP2, TNFSF12, FN1, PLXND1, ERAP2, CHI3L2, LTK, IFITM1, FNBP1, SERPINB7, MNDA, SDC4, SLPI, ZNF217, ASIC2, P2RX4, STX4, VKORC1, DNAJC15, COL7A1, DYRK4, OLR1, CD72, HLA-DQA1, UCP2, CNPY3, TUBGCP4, SSR2, RAP1A, TPP2, NCF2, ETS2, IFITM2, PVRIG, LRP10, BMPR2, IL1R2, FUT9, MYCBP2, HLA-B, OGDH, PLEKHO1, ARPC3, TRPM2, TMC6, BCAR3, ALDH1A3, RELB, MXD1, SLC39A1, LTA4H, ATP1B1, ABCA1, JOSD1, MICB, MICAL2, SH2B3, NMI, LRPAP1, FKBP1A, MMP2, CST7, NDUFAF1, AP2S1, ARHGDIB, FAM134C, CHP1, RRAS2, CAPG, CAMP, HEBP2, UBE2S, ISG20, CXCL1, PEMT, ADARB1, INSM1, ADM, PFKFB4, DNAJB1, ECM1, SMAD7, NDUFB6, HEG1, ACADS, PML, SERPINH1, HERPUD1, SCARB2, VAMP3, PPP2R3C, MED22, LUZP1, LMNB2, TRAM2, MMP14, CSTB, NXPE3, PROCR, MAST3, SF1, TNFAIP1, CD163, DPT, OPLAH, ERP29, HIVEP2, CAMK1D, TLN1, QDPR, AP4M1, GATA3, GBP1, F2R, DNM2, PLA2G7, YARS, GPX1, CNPY2, VAMP8, TRIM22, COL15A1, UBA7, SLC1A5, NKG7, SIT1, TES, SP100, IFIT5, FAM46A, CREG1, DKK1, FAM114A1, ERG, SOD2, EIF4E2, BICD1, PTP4A3, LGALS2, NFE2L3, SP140, HTRA1, SLC7A7, SH3BP1, LBH, SMAD6, IGFBP7, TCP11L1, SCD, ISG15, COL4A4, EFEMP2, RAB13, HLA-DRB1, DARS, MFSD11, RGL1, NUP88, SGK1, MAP1LC3B, MMP12, CD302, CD70, SSR1, LOX, IL32, IGF2R, PRCP, NRP2, FES, CTSS, BLM, PFKFB3, RALGDS, P2RY13, IFI30, CORO7, RUNX3, FGF1, NEU1, TRIP10, PLEKHJ1, ACTN1, MTFR1L, HMOX2, OSMR, SYNGR2, GRHPR, C10orf10, CAV1, YIPF5, AKR1C3, FOSL1, DDT, UTRN, NPC2, CEP170, PIP4K2A, PDLIM4, P4HA1, LAMB2, LPGAT1, TAGLN, TK1, SLC7A5, KCNN4)		
PLG	Adipose (46); Liver (43)	Adipose (14); Liver (16)	Adipose (0.304); Liver (0.372)	Adipose (PLG, HPX, APOC3, APOB, APOA5, AZGP1, OIT3, ASGR1, MAT1A, PAH, CYP2A13, APOA1, F2, ITIH1); Liver (PLG, SERPIND1, C3, ALDH6A1, ITIH3, LPAL2, VTN, FN1, C1S, C4B, ALDH2, APOF, CAT, HADHB, CFI, F2)	Adipose (p<1.0e-16); Liver (p<1.0e-16)	Adipose (0.00909); Liver (0.00568)
VEGFA	Adipose (36)	Adipose (10)	Adipose (0.277)	Adipose (SETD7, PODXL, TMEM204, AACS, MRAS, STAT5B, VEGFA, SCTR, CDH13, KLHL2)	Adipose (p<1.0e-16)	Adipose (0.0102)
COL4A2	Muscle (28); PPI (19)	Muscle (9); PPI (8)	Muscle (0.321428571428571); PPI (0.421052631578947)	Muscle (PLTP, COL4A2, CXCL12, COL4A1, SCARB1, COL15A1, PDGFRB, LOXL1, TP53I11); PPI (BMP3, COL4A2, OSM, FBLN2, MMP9, FN1, COL4A1, FAM46A)	Muscle (p<1.0e-16); PPI (p<1.0e-16)	Muscle (0.0136); PPI (0.00568)
COL1A1	Liver (73)	Liver (23)	Liver (0.315068493150685)	Liver (COL4A2, NCAM1, FBLN2, COL6A3, GINS2, TMSB10, ITGBL1, COL3A1, GAS6, COL4A1, LOXL4, WT1, SERPINH1, IGFBP2, CD163, PDGFRB, EFEMP2, MMP12, CCDC3, TREM2, EGR2, PCOLCE, LOXL1)	Liver (p<1.0e-16)	Liver (0.00114)
ITGB4	Aorta (200)	Aorta (63)	Aorta (0.315)	Aorta (CLIC4, C4BPA, CYP39A1, GDF15, TIAM2, CDKN1A, TAGLN2, GBP2, ACPP, SHC1, MMP10, EVPL, ADORA2B, PLXND1, MAFB, ICAM1, P2RX4, KCNMA1, CDC37, ITGB4, ETS2, RBMS2, LRP10, HLA-B, ALDH1A3, MX1, SEMA6A, TEK, HLA-C, SIPA1L1, CAMP, OASL, SART1, ABCC1, RAC1, EPHA2, PML, BCL2L11, CALCRL, TRIM47, SIPA1, GALNT2, GBP1, TRIM22, CDH13, PVRL2, VIPR1, ERG, GPR135, CDK18, SGK1, JUP, ACTN1, SYNGR2, FER, IFIT3, RFTN1, ZNF148, TSPAN8, CALR, AP3D1, QSOX1, APOL3)	Aorta (p<1.0e-16)	Aorta (0.00909)
MMT00019644	Adipose (37)	Adipose (13)	Adipose (0.351)	Adipose (MST1R, GPAM, ADRA2C, AXIN2, VEGFA, DTNA, SLC2A13, MICAL3, PRKCA, PTCH2, CENPA, CD320, TK1)	Adipose (p<1.0e-16)	Adipose (0.0159)
MSN	Liver (56); Vascular_endothelium (299)	Liver (15); Vascular_endothelium (97)	Liver (0.267); Vascular_endothelium (0.324)	Liver (MTHFD1L, PLTP, COL4A2, DPYSL2, SLCO3A1, TMSB10, WIPF1, ARHGDIB, RHOQ, EHD4, ST6GALNAC4, ITGAL, TEX35, TTC7B, SIPA1L3); Vascular_endothelium (VAT1, CLIC4, CAV2, TNFRSF12A, ATP1B3, COL4A2, DPYSL2, GRN, F2RL1, PODXL, TAGLN2, GBP2, PRNP, CTGF, SHC1, PLIN2, LGALS1, EPB41L2, TMSB10, AXL, ITGB5, RBMS1, NID1, STAT3, PECAM1, FGFR1, FN1, PLXND1, C1S, CELF2, TPM2, IFITM1, NRP1, MYOF, ICAM1, HSPG2, PTRF, ARF4, IFITM2, STAT6, HLA-B, COL5A2, COL4A1, MICAL2, SH2B3, NMI, FKBP1A, MMP2, COL18A1, ARHGDIB, FNDC3B, HLA-C, CAPG, ISG20, CXCL1, FSCN1, TFPI, ADM, ELK3, EPHA2, HEG1, SERPINH1, TRAM2, CSTB, ASAP1, GALNT2, MYLK, GBP1, F2R, TMED10, ENO1, GPX1, C1R, TRIM22, TES, CREG1, ANXA4, SOD2, LBH, SEPT9, ISG15, WWTR1, SSR1, NRP2, CTSS, ACTN1, TIMP3, OSMR, SNX10, AKR1C3, NPC2, LTBP1, CORO1C, TGFB1, PLAU, SWAP70, LAMC1)	Liver (p<1.0e-16); Vascular_endothelium (p<1.0e-16)	Liver (0.0239); Vascular_endothelium (0.00455)
KCNK13	Liver (45)	Liver (6)	Liver (0.133)	Liver (PLCG1, GPR65, S1PR5, NCAPG2, LPCAT2, ABCG1)	Liver (p<1.0e-16)	Liver (0.0364)
ANXA2	Cardiac_muscle (587); PPI (22)	Cardiac_muscle (187); PPI (8)	Cardiac_muscle (0.318); PPI (0.363)	Cardiac_muscle (SQLE, VAT1, CLIC4, ALOX5AP, CAV2, APOC1, UQCRH, SMAD3, PLTP, TNFRSF12A, IFITM3, RIT1, MT1H, CBR1, BCAM, PHLDA1, COL4A2, AQP3, PHB, ILF2, TNFSF10, GRN, SNX3, VCL, TOP1, SVIL, AGRN, CDKN1A, TSPAN3, TAGLN2, MDH1, DDAH2, MCL1, PRNP, CTGF, PPAP2B, JUN, DAAM1, UBC, SHC1, PLIN2, H2AFV, GORASP2, RPL37A, LGALS1, RHOA, TMSB10, PSMA5, STMN1, SSB, RPL31, KDELR2, DEK, RPS16, NID1, ARPC5, STAT3, RPL6, COL3A1, TIMP2, CNPPD1, CTSH, AHNAK2, FGFR1, DLGAP4, FN1, WWOX, PLXND1, IFITM1, GAS6, SDC4, HSPA1B, STX4, RPL7A, PTRF, YBX1, THSD7A, CTTN, ARF4, ETS2, IFITM2, STAT6, LRP10, HLA-B, PAPOLA, COL4A1, PSMB3, SLC22A4, RGS19, NRAS, LIPA, TPM1, CRIM1, CERS2, MAT2A, MMP2, GRB2, C1QBP, AP2S1, ARHGDIB, AP2A2, NEDD4, ATP6V0B, RRAS2, UBE2S, ALDH2, ZFP36, ERCC1, ADARB1, ACOT13, SEC11A, ADM, ELK3, COMT, ACOX1, RPSA, RRBP1, SERPINH1, HERPUD1, VAMP3, SCAMP3, TRAM2, STK24, CSTB, KDELR3, TNFAIP1, ERP29, PSMG1, TMED10, ENO1, YARS, ALG5, GPX1, VAMP8, CNN3, PRKAR1A, TXNDC5, CREG1, ANXA11, ERG, JUND, ATP11B, GBE1, SEPT11, EIF6, IGFBP7, TMED5, PPIB, WWTR1, SNX1, EDNRA, SGK1,	Cardiac_muscle (p<1.0e-16); PPI (p<1.0e-16)	Cardiac_muscle (0.0375); PPI (0.017)

				SSR1, PRCP, CTSS, TRIB2, DSTN, HBP1, RPL28, ACTN1, RPL10A, TIMP3, CGGBP1, SHMT1, MRPL18, CAV1, RELA, UTRN, NPC2, LTBP1, LOXL1, YES1, CFL1, MTAP, P4HA1, PLAU, LPGAT1, HLA-DQB1, PPIA, LAMC1, PSMD14, TK1, EIF4A1, RPL27A, RAB27A, PEPD, SNRPD2); PPI (PLG, PLA1A, PHB, CDC42, DYSF, GRB2, PRKCA, MAP3K4)		
TNFAIP2	Cardiac_muscle (334)	Cardiac_muscle (109)	Cardiac_muscle (0.326)	Cardiac_muscle (SUMO1, HS2ST1, KLF4, AK1, SMAD3, IFITM3, RIN3, NPC1, GDF15, ZCCHC24, CSK, FURIN, TLE1, NLRC5, ABI1, DENND3, TOP1, CDKN1A, UBE2I, SPHK1, ITPR1, LPAR2, SHC1, BCAP29, ASL, AMIGO2, AMPD3, ZMIZ2, HIP1, FGFR1, PLXND1, FNBP1, CSF1, SDC4, ICAM1, ETS2, STAT6, LRP10, HLA-B, NR2F2, RELB, ITSN2, RGS19, RAF1, TMEM9B, TRIB1, BAG6, SACS, OPTN, PPIF, SH2B3, MYO9B, SEC14L1, COL18A1, LDLR, ARHGAP26, TIPARP, RRAS2, KCNK1, CCNL1, NOTCH3, RHOT1, TMEM97, ADM, DNAJB1, PML, HERPUD1, OAS1, IL15RA, BID, IRF1, ANKRD10, LPAR1, TIAM1, CTSA, COL15A1, ARHGEF2, ANXA11, SOD2, JUND, LRRFIP1, NFE2L3, ZC3H12A, SEPT9, TOR1B, WWTR1, MAP1LC3B, AP2B1, SSR1, IL32, PRCP, TRIB2, RUNX3, TRIP10, MTF2, BRCA2, SYNGR2, MDM1, MRPL18, SMG6, CORO1C, YES1, CFL1, PLAU, SWAP70, DGKG, TTC28, QSOX1, SCAMP2)	Cardiac_muscle (p<1.0e-16)	Cardiac_muscle (0.0205)
CXCL12	Adipose (47); Cardiac_muscle (170); Liver (30); Muscle (36)	Adipose (10); Cardiac_muscle (54); Liver (9); Muscle (11)	Adipose (0.212); Cardiac_muscle (0.317); Liver (0.3); Muscle (0.305)	Adipose (PODXL, MMP3, CXCL12, TRERF1, KDR, SLC6A6, MRVI1, KLK10, SLC22A3, RAB19); Cardiac_muscle (CAV2, PYGL, HLA-DRA, COL4A2, ZCCHC24, CTGF, CXCL12, PPAP2B, ST5, GRK5, AXL, LRP1, NID1, ZCCHC14, PECAM1, SNED1, FGFR1, EPS8, WIPF1, VPS13D, PTRF, HLA-B, CRISPLD2, TMEM176A, NR2F2, COL4A1, LIPA, ZHX3, NPR1, CXCL1, SLC24A3, SFRP2, RHOQ, LPAR1, MYLK, RAB13, SGK1, CD302, FTO, PRCP, USP25, TRIB2, ZBTB20, PSD3, TIMP3, WIPI1, PCOLCE, LTBP1, LAMB2, GUCY1A3, LAMC1, ANGPT1, NFIB, KLC1); Liver (PLEKHA1, CXCL12, COL6A3, SLC2A1, RERG, SLC6A6, CUX2, HSD17B12, SFTPB); Muscle (COL4A2, AHR, PODXL, CXCL12, S100Z, SCUBE3, BRPF1, RNF213, ARHGDIB, CNIH3, OR4X2)	Adipose (p<1.0e-16); Cardiac_muscle (p<1.0e-16); Liver (p<1.0e-16); Muscle (p<1.0e-16)	Adipose (0.0534); Cardiac_muscle (0.0182); Liver (0.00341); Muscle (0.00114)
ABCG5	Adipose (18); Liver (33)	Adipose (5); Liver (11)	Adipose (0.277); Liver (0.333)	Adipose (TCF21, AZGP1, ABCG5, ABCG8, DYNC2LI1); Liver (SQLE, N4BP2L1, RAPH1, CPSF4L, HAAO, SREBF1, ABCG5, ABCG8, ADARB1, ODC1, DYNC2LI1)	Adipose (p<1.0e-16); Liver (p<1.0e-16)	Adipose (0.00455); Liver (0.00682)
CFB	Brain (20)	Brain (10)	Brain (0.5)	Brain (PLG, APOC1, C3, APOA5, C4B, APOF, HP, CFI, APOC2, APOA1)	Brain (p<1.0e-16)	Brain (0.00114)
APOC2	Muscle (27)	Muscle (10)	Muscle (0.370)	Muscle (APOC1, SLC22A1, APOC3, APOA5, AGT, CYP4F12, ARG1, ABCG5, APOF, APOC2)	Muscle (p<1.0e-16)	Muscle (0.00114)
APOB	Adipose (27); PPI (18)	Adipose (7); PPI (7)	Adipose (0.259); PPI (0.388)	Adipose (PLG, UPB1, APOB, AKR1C1, SLC26A1, AKR1D1, APOA1); PPI (APOB, LDLR, LIPC, PPIB, MTTP, APOA1, CALR)	Adipose (p<1.0e-16); PPI (p<1.0e-16)	Adipose (0.0114); PPI (0.00795)
SORL1	Vascular_endothelium (85)	Vascular_endothelium (25)	Vascular_endothelium (0.294)	Vascular_endothelium (MYO5C, ABLIM1, ITPR1, RGS10, CXCR4, CTSH, AHNAK2, FGFR1, TCF7L2, PTPRK, HNRNPH1, MUT, TFPI, NUP210, SH3BP5, VAMP8, CREG1, ANXA4, LOX, TULP4, TGOLN2, TRIB2, ZBTB20, TIMP3, SLC7A5)	Vascular_endothelium (p<1.0e-16)	Vascular_endothelium (0.0148)
ACVR1C	Brain (37)	Brain (7)	Brain (0.189)	Brain (SYNPO2, APOE, AKAP6, PLEKHG1, ATP2B1, ACVR1C, CYP17A1)	Brain (p<1.0e-16)	Brain (0.0420)
ADM	Artery (287); Smooth_muscle (183)	Artery (99); Smooth_muscle (56)	Artery (0.344); Smooth_muscle (0.306)	Artery (KLF4, TOMM22, TNFRSF12A, OS9, MT1H, SPP1, ZCCHC24, MMP1, SLC35G2, CDKN1A, PDGFRA, TSPAN3, MCL1, CTGF, PLIN2, FGFR3, AMIGO2, RGS10, GRK5, AMPD3, SMPD1, STAT3, MT1X, FGFR1, EPS8, PFKL, C1S, CSF1, SDC4, ICAM1, PTRF, VEGFA, CTTN, ARF4, ETS2, LRP10, COL5A2, COL4A1, ALDH1A3, ATP1B1, TPM1, TRIB1, SH2B3, FNDC3B, ISG20, CXCL1, PALLD, ZFP36, ERCC1, TFPI, ADM, ELK3, TUFT1, SMAD7, HEG1, SERPINH1, C16orf45, CSTB, PROCR, IRF1, TNS1, TNFAIP1, SH3BP5, C1R, CDH13, DENND5A, SP100, DKK1, EDN1, HTRA1, SMAD6, IGFBP7, CENPA, FGF2, SLC20A1, WWTR1, CES2, SGK1, PFKFB3, IFI30, BACH1, GEM, NAB2, ACTN1, TIMP3, OSMR, C10orf10, GRB10, CAV1, FOSL1, LTBP1, LOXL1, IGFBP5, LAMB2, PLAU, AKR1C2, TAGLN, SLC7A5, QSOX1); Smooth_muscle (KLF4, NPC1, PITPNB, SLC35G2, CDKN1A, GBP2, MCL1, CTGF, FGFR3, AMIGO2, TMSB10, STAT3, C1S, SDC4, PPP2CB, PTRF, PPARD, CTTN, HLA-B, CRIM1, PNRC1, TRIB1, OPTN, MICAL2, PPIF, FNDC3B, NEDD4, ISG20, ALDH2, ZFP36, ADM, TUFT1, SMAD7, MICAL3, KIF14, HIVEP2, GATA3, TES, DENND5A, CREG1, SCD, SLC20A1, SGK1, AKR1C1, PFKFB3, GLI3, IFI30, BACH1, GEM, GFPT2, GRB10, CAV1, LTBP1, LAMB2, AKR1C2, NFIB)	Artery (p<1.0e-16); Smooth_muscle (p<1.0e-16)	Artery (0.0273); Smooth_muscle (0.0273)
RDH16	Brain (43); Muscle (36)	Brain (10); Muscle (11)	Brain (0.232); Muscle (0.3056)	Brain (APOC4, SLC22A1, APOC3, KLKB1, MBL1P, APOA5, APOF, PON1, AKR1C1, CFI); Muscle (PLG, SEC14L2, APOC3, HAAO, APOB, ABCG5, C8G, APOA4, GNMT, CYP2A13, F2)	Brain (p<1.0e-16); Muscle (p<1.0e-16)	Brain (0.0273); Muscle (0.00114)
PAPSS2	Cardiac_muscle (263); Smooth_muscle (108)	Cardiac_muscle (87); Smooth_muscle (41)	Cardiac_muscle (0.330); Smooth_muscle (0.379)	Cardiac_muscle (SYT11, CAV2, HSPB6, TNFRSF12A, PYGL, RIT1, BCAM, PHLDA1, COL4A2, MAPRE2, DPYSL2, ZCCHC24, PODXL, TAGLN2, CTGF, PPAP2B, RAB5B, AMIGO2, SGPL1, PPFIA1, AXL, ITGB5, NID1, TBC1D1, HIP1, AHNAK2, FGFR1, FRY, GAS6, FNBP1, NRP1, MYOF, ENG, KIAA0922, CTTN, ARF4, PLEKHO1, BMP6, BCAR3, COL4A1, TPM1, OPTN, MICAL2, SH2B3, COL18A1, PALLD, ALDH2, GNA13, TFPI, ADM, GUCY1B3, SERPINH1, SCARB2, TRAM2, ENTPD6, SOCS5, NEAT1, TNS1, LPAR1, CNN3, DENND5A, GAB1, HTRA1, IGFBP7, TMED5, EFEMP2, CES2, SLC5A3, CD302, LOX, S1PR3, ACTN1, ZFP36L2, FAM171A1, GRB10, BAZ1A, LTBP1, YES1, TRIP6, PLAU, GJA1, SWAP70, FBLN1, ITGAV, ILF3, LAMC1, TAGLN); Smooth_muscle (TNFRSF12A, COL4A2, VCL, NCK1, CTGF, FGFR3, LGALS1, RGS10, PGPEP1, AXL, RBMS1, TIMP2, FN1, VEGFA, ARF4, RBMS2, LRP10, ENC1, PYGB, COL4A1, LTA4H, STEAP3, PTPRK, SH2B3, SEPT7, FNDC3B, RRAS2, RHOQ, PROCR, KDELR3, LPAR1, SH3BP5, FSTL1, GBE1, HTRA1, SULF1, SHB, PFKFB3, CEP170, P4HA1, LAMC1)	Cardiac_muscle (p<1.0e-16); Smooth_muscle (p<1.0e-16)	Cardiac_muscle (0.0182); Smooth_muscle (0.00909)
LOXL2	Liver (28)	Liver (11)	Liver (0.392)	Liver (COL4A2, PSRC1, NID1, COL3A1, ETS2, KCNJ2, COL4A1, SERPINH1, HPS1, CSTB, UNC5B)	Liver (p<1.0e-16)	Liver (0.00341)
SLIT3	Muscle (28)	Muscle (11)	Muscle (0.392)	Muscle (APOE, SLIT3, EPB41L2, NID1, FN1, TGFBR3, DOCK1, ADM, SCARA5, PROCR, THBS3)	Muscle (p<0.00114)	Muscle (p<0.00114)
MMT00021022	Heart (11)	Heart (2)	Heart (0.181)	Heart (OVOL1, TCP11)	Heart (p<0.00114)	Heart (p<0.00114)

TGFBI	PPI (10)	PPI (5)	PPI (0.5)	PPI (COL4A2, COL4A3, FN1, COL4A1, COL4A4)	PPI (p<1.0e-16)	PPI (0.00341)
PHACTR1	Brain (33)	Brain (12)	Brain (0.363)	Brain (DBNDD1, SMAD3, KIAA1462, DLGAP4, NKX2-6, PHYHIP, PHACTR1, PPP1R1B, KIT, NETO1, SEPT9, PTPRN2)	Brain (p<1.0e-16)	Brain (0.00568)
IL15RA	Liver (20)	Liver (8)	Liver (0.4)	Liver (SMAD3, CDKN1A, ARHGEF5, RASD1, TTF1, ADAMTS13, IL15RA, SPSB1)	Liver (p<1.0e-16)	Liver (0.00455)
TRIM8	Smooth_muscle (67)	Smooth_muscle (22)	Smooth_muscle (0.328)	Smooth_muscle (ACTR1A, CCDC92, JUN, UBE2D4, TCEA2, SMARCA2, ZNF7, UROD, UCP2, LRP10, FNDC3B, HLA-C, TUFT1, HEG1, UTP11L, KDELR3, CAPRIN2, SOD2, GLI3, CAV1, PLAU, TRIM8)	Smooth_muscle (p<1.0e-16)	Smooth_muscle (0.0102)
OSM	PPI (10)	PPI (6)	PPI (0.6)	PPI (COL4A2, OSM, COL4A3, COL4A1, COL4A4, OSMR)	PPI (p<1.0e-16)	PPI (0.00341)
LY96	Vascular_endothelium (75)	Vascular_endothelium (26)	Vascular_endothelium (0.346)	Vascular_endothelium (CALHM2, C3, AHR, CPVL, CXCL12, CXCR4, PECAM1, C1S, IFITM1, PHF11, IFITM2, HLA-B, COL5A2, ISG20, TNFAIP6, CD163, GBP1, TRIM22, ANXA4, CDK14, HTRA1, LOX, IFI30, FLI1, PLAU, HLA-DQB1)	Vascular_endothelium (p<1.0e-16)	Vascular_endothelium (0.0125)
CXCL10	Liver (46)	Liver (13)	Liver (0.282)	Liver (ITIH3, NRG1, IFIT1, IRG1, XCL1, RELB, MMP13, IL1RN, IFIT2, PROCR, GBP1, CMPK2, TLR2)	Liver (p<1.0e-16)	Liver (0.0102)
SLC2A3	Aorta (825)	Aorta (272)	Aorta (0.329)	Aorta (CD82, KLF4, XAF1, MFGE8, CLIC4, ADAR, CAV2, APOC1, DNASE1L3, IFITM3, NOD1, TNFRSF1B, TMEM121, CTNNAL1, POPDC3, ATP1B3, C3, SLAMF1, SPP1, CTSK, PTGIR, COL4A2, MAPRE2, MEOX1, TNFSF10, ACTR1A, SNX3, NEDD9, NRG1, SLC26A10, AHR, MT1G, CPVL, PODXL, MMP1, MMP3, FBLN2, KIAA1462, FCGR2B, PLCG1, PTHLH, RUNX1, SIM1, SLIT3, SPHK1, NEK1, GBP2, MCL1, PRNP, CTGF, PPAP2B, COL6A3, JUN, C1RL, NAP1L1, FLT1, MYL3, GLDC, ST5, SLCO5A1, AMIGO2, GABPB2, TNNI3, GALC, NFAM1, SLC4A10, IFIT1, STAT2, NPTX1, EDN2, MMP9, IL24, CLDN10, MRAS, AXL, PAPD7, CAMSAP2, NID1, RERG, MGAT1, MSI1, STAT3, H1F0, COL3A1, PECAM1, CLDN5, TIMP2, MDM4, EPS8, TLR1, RRAD, SLC1A6, C1S, CELF2, TPM2, IFITM1, NLRP3, AIDA, LILRA2, SDC4, SLPI, ENG, HSPA1B, SEMA5A, KCNMA1, PTRF, AGT, CD72, VEGFA, HLA-DQA1, THSD7A, HMGN3, ETS2, IFITM2, EIF5, IL1R2, FUT9, CST6, CX3CL1, RNF19A, COL4A1, ALDH1A3, MX1, ABCA1, ARG1, LIPA, TPM1, PTPRK, MICAL2, SH2B3, ABCG5, NMI, TMED1, FKBP1A, MYO9B, CST7, SEC14L1, COL18A1, MAS1, ARHGDIB, AMPH, PIK3C2B, PRKD2, KCNA3, OBFC1, GSTM5, MMP13, RRAS2, SULT4A1, DGKI, CLEC1A, ISG20, CXCL1, NOS3, RBMS3, MYO1F, CUBN, BIRC5, PJA2, ARFGEF2, PI3, FSCN1, BAZ2B, PDE4B, RASSF8, ADM, ELK3, ASB9, EPHA2, ECM1, GUCY1B3, PML, SERPINH1, HERPUD1, CALCRL, PROM1, MYH7B, DDX5, IRS1, TNFAIP6, TRAM2, IL15RA, RPP30, MMP14, MAP3K4, HS3ST2, PROCR, RYK, SPR, KDELR3, PRKAR2B, HIVEP2, LPAR1, H3F3B, KIT, SH3BP5, GBP1, PLA2G7, LPIN1, B4GALT5, C1R, UGGT1, TRIM22, CDH13, PQBP1, CNN3, TBKBP1, TES, IFIT5, ANKRD1, ANXA11, EDN1, CDK14, PDGFRB, LGALS2, ATP11B, F2RL2, VIP, SULF1, SEPT11, TWIST1, SEPT9, VPS11, ISG15, PDPN, WWTR1, RGL1, ENO2, CD302, LOX, IL32, POU5F1, MLLT11, PCSK7, SEC23B, NRP2, CTSS, CFI, GEM, RUNX3, CBS, FLI1, TREM2, TMEM50A, ACTN1, TIMP3, OSMR, MERTK, GRIK4, SNX10, GRB10, CACNB4, APOA1, FOSL1, UTRN, LTBP1, TGFB1, IGFBP5, DKK3, TTC39A, P4HA1, LAMB2, SOX18, IFIT3, PLAU, GUCY1A3, RFTN1, FOXC1, HLA-DQB1, SIPA1L3, TAGLN, KCNN4)	Aorta (p<1.0e-16)	Aorta (0.00795)
LARGE	Liver (20)	Liver (8)	Liver (0.4)	Liver (LSM6, COL6A3, LARGE, PRKCA, RHOQ, CSGALNACT1, OCEL1, VASN)	Liver (p<1.0e-16)	Liver (0.0193)
IRF1	Artery (207)	Artery (75)	Artery (0.362)	Artery (KLF4, ADAR, IFITM3, FOS, RIT1, MT1H, GDF15, C3, COL4A2, TNFSF10, TRIM21, DAGLB, AGRN, CDKN1A, GBP2, MCL1, DDX58, TREX1, MAP3K11, CDC42EP4, STAT3, MT1X, ELP5, FGFR1, IFITM1, ICAM1, BCL3, IFITM2, LRP10, HLA-B, PYGB, RELB, RGS19, MICB, MICAL2, SH2B3, NMI, ICAM3, HLA-C, CAPG, OASL, ISG20, CXCL1, IRF3, VASP, ADM, IFIT2, PML, IL15RA, IRF1, FAM89B, GBP1, TRIM22, ANXA4, HERC6, FAM129B, GBE1, ISG15, WWTR1, SGK1, BMP2, STX11, IFI30, RUNX3, TRIP10, ACTN1, IGF1R, PLEKHO2, PARP12, IFIT3, PLAU, HLA-DQB1, TAGLN, SLC7A5, QSOX1)	Artery (p<1.0e-16)	Artery (0.0159)
AZGP1	Adipose (23)	Adipose (8)	Adipose (0.347)	Adipose (PLG, SLC22A1, UPB1, APOA5, AZGP1, ABCG5, CYP2A13, FBP1)	Adipose (p<0.00114)	Adipose (p<0.00114)
NGRN	Liver (32)	Liver (10)	Liver (0.312)	Liver (HDDC3, TRIM68, FURIN, KLHL25, RCCD1, SPC24, SLC22A3, MESDC1, APOC2, AKAP13)	Liver (p<1.0e-16)	Liver (0.00114)
EFEMP1	Cardiac_muscle (182)	Cardiac_muscle (64)	Cardiac_muscle (0.351)	Cardiac_muscle (CLIC4, CAV2, SPON1, COL4A2, MEST, FBLN2, PDGFRA, LTBP3, CTGF, PPAP2B, COL6A3, AMIGO2, SLK, OBSL1, COL3A1, FGFR1, FN1, GAS6, PTRF, COL5A2, NR2F2, ATP1B1, TPM1, PTPRK, MICAL2, MMP2, NPR1, DTNA, PEMT, PALLD, ALDH2, TFPI, ADM, HEG1, SERPINH1, TRAM2, PROCR, TNS1, ALDH3A2, TMED10, MFAP4, FAM114A1, ANXA4, SEMA3C, LRRFIP1, IGFBP7, PPIB, EFEMP2, WWTR1, RGL1, LOX, PRCP, ACTN1, TIMP3, PCGF2, CAV1, CAMKK2, LTBP1, LOXL1, IGFBP5, LAMC1, PBX3, ANGPT1, TAGLN)	Cardiac_muscle (p<1.0e-16)	Cardiac_muscle (0.0148)
IRF9	Smooth_muscle (104)	Smooth_muscle (41)	Smooth_muscle (0.394)	Smooth_muscle (ADAR, GRN, TRIP4, PBXIP1, DDX58, ASL, IFIT1, STAT2, TMSB10, IFITM1, MYOF, RNF213, HLA-B, ARPC3, MX1, OPTN, NMI, CAPG, OASL, ISG20, ZFP36, VASP, PML, OAS1, EIF2AK2, IRF1, NEAT1, GBP1, ENO1, IFIH1, TRIM22, UBA7, SP100, IFIT5, SARS, JUND, ISG15, IL32, RELA, PARP12, IFIT3)	Smooth_muscle (p<1.0e-16)	Smooth_muscle (0.00568)
APOA5	Brain (32); Liver (23)	Brain (8); Liver (6)	Brain (0.25); Liver (0.260)	Brain (PLG, APOC3, APOA5, PHF2, ARG1, MAT1A, AKR1C1, FBP1); Liver (SEC14L4, APOA5, APOA4, ALDH2, ABHD2, ATOH8)	Brain (p<1.0e-16); Liver (p<1.0e-16)	Brain (0.0148); Liver (0.0114)
CFD	Aorta (773)	Aorta (238)	Aorta (0.307)	Aorta (CRTAP, ALOX5AP, C4BPA, N4BP2L1, APOC1, MAP4, SLC6A2, PLA1A, SPON1, IFITM3, PSORS1C1, LY75, KRT5, CDX1, PLCE1, C3, SLAMF1, MBD5, ZNF423, EIF2B3, C10orf76, FAP, HECTD3, AHR, HIC1, FBLN2, PTPN6, PDGFRA, HLA-DOB, PTGER3, MBNL2, TSPAN3, CRYAB, PCLO, MYH11, GBP2, MCL1, CTGF, PTGDS, GMPPB, COL6A3, C1RL, EPHX3, RYR1, WNT2, ST5, NPBWR2, LGALS1, STOML1, LMOD1, VTN, SLCO1A2, RGS10, FSTL3, NPTX1, TMSB10, MRAS, ITGBL1, MT1F, ITGB5, GPR137B, ABCA8, TMED2, TBC1D1, TUBG2, TIMP2, TFF3, ACVR2A, GP2, PARP8, GREM2, C1S, MAFB, BNIP3L, NAT8, NRP1,	Aorta (p<1.0e-16)	Aorta (0.0159)

				AKAP7, SERPINB7, C1orf21, LEFTY1, NDUFA4L2, SDC4, ZC2HC1C, PRG4, SLC18A2, RIT2, KLF2, HCFC1R1, FKBP5, HOXC4, GIMAP4, FAM46C, PREX1, PTN, NCF2, IFITM2, LRP10, AZGP1, CX3CL1, PRSS8, DMTN, PHACTR1, BMP6, COL5A2, DOCK1, CCPG1, PID1, COL4A1, RORC, RGS7, ZSWIM8, PNRC1, ATP6V0A4, ABCG5, MMP2, AEN, GDPD5, CST7, SEC14L1, BST1, ACSS3, C4B, FAM134C, FAM168A, HLA-C, GGT5, AMPD1, GALNT12, OASL, PDZRN4, ZNF34, HOXB2, ALDH2, GPR1, FSCN1, MUT, IL1RN, GABRB3, CAT, TMEM176B, ECM1, IFIT2, SMAD7, SCARB2, PROM1, THUMPD1, PSG6, MISP, SLC2A5, SLC12A8, IL15RA, LIPC, PROCR, MUC16, COLGALT2, TBC1D2B, CD163, DPT, PRKAR2B, COPB1, CHST5, LPAR1, ALDH3A2, KIT, P2RY14, C1R, CDH13, CCNG2, NKG7, ZNF521, SMYD3, CYP1A1, PDGFRB, LGALS2, HADHB, ARHGAP24, CCL17, CD226, TGDS, PDPN, PTPRN2, FGF2, EXTL1, WWTR1, ELF5, ECHDC2, CES2, EDNRA, RGL1, ATP8B4, SGK1, CD302, CNTLN, METTL21B, LOX, PLEK, MTTP, P2RY1, CFI, ALDH3A1, RYR2, ZEB2, RUNX3, VGLL3, GFPT2, FGF1, SHH, NAGLU, TREM2, FUT3, AKR1D1, GJB4, ARHGEF3, GRB10, CAV1, OTUD7B, MSRA, CSF1R, KLHL2, PCOLCE, UTRN, PLEKHO2, ADORA3, RDH14, PLAU, GJA1, RFTN1, MYCT1, PSG5, TAGLN, KLF1, IFNA17, AP3D1, ITIH1, CAB39L, RAB27A, APOL3, VAV1)		
NOTCH1	PPI (46)	PPI (12)	PPI (0.260)	PPI (SMAD3, FURIN, FBXW7, LFNG, DLL1, WDR12, ADAM17, ITCH, KAT2A, CBL, KAT2B, RELA)	PPI (p<1.0e-16)	PPI (0.00227)
APOF	Muscle (45)	Muscle (17)	Muscle (0.377)	Muscle (PLG, APOC4, ITIH3, GLS2, APOB, APOA5, ARG1, APOF, AGXT, LIPC, ITIH4, MAT1A, PAH, PON1, CFI, APOC2, CYP2A13)	Muscle (p<0.00114)	Muscle (p<0.00114)
LDLR	PPI (11)	PPI (7)	PPI (0.636)	PPI (APOE, APOB, LRPAP1, LDLR, PCSK9, DAB1, AP1M2)	PPI (p<0.00114)	PPI (p<0.00114)
KLF6	Smooth_muscle (400)	Smooth_muscle (114)	Smooth_muscle (0.285)	Smooth_muscle (KLF4, TAB2, UBE2H, CAV2, SMAD3, TNFRSF12A, PYGL, FOS, ARL4A, PHLDA1, WEE1, SMTN, PDE8A, NEDD9, RHBDF1, CDKN1A, RUNX1, GBP2, MCL1, PRNP, CTGF, JUN, DAAM1, FGFR3, CLSTN3, WDR37, LGALS1, IFIT1, FSTL3, SERINC1, ADORA2B, RBMS1, STAT3, HEXB, FGFR1, NTAN1, FN1, TCF7L1, CHI3L2, WIPF1, SREBF1, MYOF, ICAM1, HSPA1B, VEGFA, UCP2, MAP3K5, ETS2, TCF7L2, ENC1, LTA4H, ATP1B1, PNRC1, TRIB1, JOSD1, OPTN, MICB, MICAL2, SEC14L1, PRKD2, BMPR1A, TIPARP, RRAS2, ATP2B1, ALDH2, ZFP36, PUM2, ABCC1, TUFT1, RRBP1, TNFAIP6, FOSB, RYBP, ANKRD10, EFNA1, TNFAIP1, HIVEP2, TLN1, GATA3, GBP1, BMP1, LPIN1, ZNF274, TES, DENND5A, IFIT5, ANXA4, SOD2, CYP1A1, PTP4A3, LRRFIP1, SCD, SLC20A1, SGK1, LOX, AKR1C1, CTSS, GLI3, TGOLN2, GEM, PHYH, TIMP3, ZFP36L2, GRB10, AKR1C3, UTRN, NPC2, CORO1C, TGFB1, P4HA1, IFIT3, PLAU, SWAP70, QSOX1)	Smooth_muscle (p<1.0e-16)	Smooth_muscle (0.0477)
FBP1	Muscle (23)	Muscle (8)	Muscle (0.347)	Muscle (PLG, APOC4, SEC14L2, UROC1, APOC3, ASGR1, MAT1A, FBP1)	Muscle (p<1.0e-16)	Muscle (0.0125)
RAC2	Cardiac_muscle (179)	Cardiac_muscle (48)	Cardiac_muscle (0.268)	Cardiac_muscle (STK17A, PLTP, C3, SRRT, GRN, GBP2, CXCR4, C19orf12, FGFR1, PLXND1, CELF2, C14orf159, VPS13D, ICAM1, SSR2, MAP3K5, PVRIG, HLA-B, ACP5, NCAPG2, CIAO1, ARHGDIB, FNDC3B, IL1A, CAT, CDK6, SRSF2, OAS1, IL15RA, DBI, TESC, SIPA1, GBP1, CYBRD1, LRRC8C, FAM46A, MXRA7, CTSS, IFI30, TGOLN2, FLI1, SYNGR2, MCM6, C1orf131, DKK3, IFIT3, PLAU, RAB27A)	Cardiac_muscle (p<1.0e-16)	Cardiac_muscle (0.0409)
APOC4	Brain (25)	Brain (10)	Brain (0.4)	Brain (APOC1, C3, APOC4, HPX, ARG1, MAT1A, PAH, CFI, APOC2, APOA1)	Brain (p<1.0e-16)	Brain (0.00341)
MATN2	PPI (13)	PPI (7)	PPI (0.538)	PPI (COL4A2, FBN2, COL4A3, FN1, COL4A1, MATN4, COL4A4)	PPI (p<1.0e-16)	PPI (0.00341)
IFI30	Smooth_muscle (104)	Smooth_muscle (35)	Smooth_muscle (0.336)	Smooth_muscle (IFITM3, KPNA2, FGFR3, HLA-DPB1, JTB, IFIT1, SSB, C1S, UCP2, ALDH1A3, MX1, MICB, NMI, CAPG, ADM, SAMM50, RAB20, CSTB, PROCR, IRF1, VAMP8, TRIM22, ISYNA1, SP100, IFIT5, CREG1, LBH, ISG15, SGK1, IFI30, PARP12, LAMB2, IFIT3, HLA-DQB1, RAB27A)	Smooth_muscle (p<1.0e-16)	Smooth_muscle (0.0136)
WIPF1	Liver (20)	Liver (3)	Liver (0.15)	Liver (WIPF1, TFPI, DOCK10)	Liver (p<1.0e-16)	Liver (0.0205)
FN1	Kidney (16); PPI (75)	Kidney (3); PPI (21)	Kidney (0.187); PPI (0.28)	Kidney (ERBB4, ADAM12, FN1); PPI (COL4A2, FBLN2, COL4A3, ITGB6, CXCL12, FSTL3, MMP9, GALNT6, FN1, COL7A1, COL4A1, SDC2, FST, LPA, FASLG, COL4A4, SMAD9, MEP1B, LTBP1, IGFBP5, FBLN1)	Kidney (p<1.0e-16); PPI (p<1.0e-16)	Kidney (0.00114); PPI (0.0477)
BST2	Artery (91)	Artery (33)	Artery (0.362)	Artery (ADAR, APOC1, IFITM3, TNFSF10, TRIM21, TAGLN2, GBP2, RGS10, EPS8, IFITM1, SDC4, ICAM1, PDXK, IFITM2, HLA-B, MX1, NMI, HLA-C, OASL, UBE2S, IFIT2, IL15RA, CSTB, GBP1, SP100, IFIT5, ISG15, IFI30, TRIB2, SYNGR2, PARP12, IFIT3, HLA-DQB1)	Artery (p<1.0e-16)	Artery (0.0159)
COL5A1	Adipose (29)	Adipose (13)	Adipose (0.448)	Adipose (COL4A2, CDKN1A, COL6A3, COL3A1, OAF, ACLY, COL5A2, COL4A1, SERPINH1, KDELR3, COL15A1, DNAH10, PLAU)	Adipose (p<1.0e-16)	Adipose (0.0136)
EPS8	Liver (22)	Liver (7)	Liver (0.318)	Liver (GALNS, EPS8, PTPRO, TFPI, TSPAN33, C12orf5, MMP12)	Liver (p<1.0e-16)	Liver (0.0205)
SPARC	Muscle (34)	Muscle (11)	Muscle (0.323)	Muscle (PRND, COL4A2, NEDD9, TMSB10, NID1, COL3A1, FN1, COL5A2, COL4A1, RRBP1, SERPINH1)	Muscle (p<1.0e-16)	Muscle (0.00227)
IRF7	Adipose (24); Vascular_endothelium (42)	Adipose (8); Vascular_endothelium (16)	Adipose (0.333); Vascular_endothelium (0.380)	Adipose (ADAR, DHX58, IFIT1, STAT2, MX1, OASL, OAS1, ISG15); Vascular_endothelium (XAF1, IFITM3, OAS3, IFITM1, ICAM1, IFITM2, MX1, HLA-C, ZFP36, PML, OAS1, IRF1, SP100, ISG15, RELA, IFIT3)	Adipose (p<1.0e-16); Vascular_endothelium (p<1.0e-16)	Adipose (0.00682); Vascular_endothelium (0.00909)
BATF2	Blood (12)	Blood (4)	Blood (0.333)	Blood (TAP2, IL15RA, IRF1, GBP1)	Blood (p<1.0e-16)	Blood (0.00682)
ZYX	Smooth_muscle (231)	Smooth_muscle (86)	Smooth_muscle (0.372)	Smooth_muscle (VAT1, MED15, CAV2, SMAD3, PLTP, GNB2, COL4A2, SMTN, GRN, VCL, MAPKAPK2, RHBDF1, RAD23A, AGRN, SPHK1, MCL1, PRNP, INPP5A, FGFR3, JTB, LRP1, ITGB5, RBMS1, LPP, MGAT1, STAT3, TMEM214, PLEC, TIMP2, AHNAK2, DPAGT1, FGFR1, DLGAP4, PLXND1, TPM2, ICAM1, PTRF, FAM120A, UCP2, CDC37, ITGB4, LRP10, PLEKHO1, DOCK6, FXR2, RELB, PTPRK, OPTN, CERS2, MYO9B, PLXNA1, COL18A1, PRKD2, AP2A2, FSCN1, GRINA, VASP, EPHA2, CLPTM1, IRF1, FAM89B, SUPT5H, PRKCD, SCARB1, TNFAIP1, CSPG4, GALNT2, TES, DENND5A, WBP2, PTP4A3, SMAD6, IL32, GLI3, JUP, ACTN1, RALY, CAV1, RELA, FOSL1, NPC2, TRIP6, HNRNPUL1, LAMC1, QSOX1, RAB27A)	Smooth_muscle (p<1.0e-16)	Smooth_muscle (0.0102)
MMT00081256	Muscle (20)	Muscle (5)	Muscle (0.25)	Muscle (TNFSF10, NRG1, TMEM59L, GBP1, ZEB2)	Muscle (p<1.0e-16)	Muscle (0.00114)

HEMGN	Muscle (21)	Muscle (4)	Muscle (0.190)	Muscle (SLPI, ITGAD, MMP13, CAMP)	Muscle (p<1.0e-16)	Muscle (0.0307)
ZNF496	Liver (39)	Liver (11)	Liver (0.282)	Liver (SLC29A4, RAD50, SLC22A5, RASD1, LRRC48, ZNF496, SLC22A4, SMCR8, RNF123, SHMT1, DHRS7B)	Liver (p<1.0e-16)	Liver (0.0136)
AW475929	Brain (30)	Brain (8)	Brain (0.266)	Brain (KLHL10, TEX2, ACOX1, PRKCA, CRHR1, ARL4D, SLC25A39, MYL4)	Brain (p<1.0e-16)	Brain (0.0205)
CKLF	Liver (26)	Liver (6)	Liver (0.230)	Liver (LARGE, SLPI, LIPA, PRKCD, CDKN2B, PHYH)	Liver (p<1.0e-16)	Liver (0.0477)
APOC3	Brain (19)	Brain (5)	Brain (0.263)	Brain (APOC3, UPB1, APOA5, CCDC153, APOA1)	Brain (p<1.0e-16)	Brain (0.00341)
NCOR2	Kidney (12)	Kidney (7)	Kidney (0.583)	Kidney (NCOR2, ACAD10, UBC, AACS, CUX2, PTPN11, VPS33A)	Kidney (p<1.0e-16)	Kidney (0.00114)
WWC2	Aorta (262)	Aorta (70)	Aorta (0.267)	Aorta (MCOLN3, FAIM, CAV2, ARMC8, IFITM3, C3, PHLDA1, ALDH6A1, MKNK2, PDE1A, LRRK1, AGAP1, RPL23A, PTHLH, SLCO3A1, CTGF, MITF, EPHX3, AMIGO2, FSTL3, OSBPL8, SLC26A2, GPR137B, DNAJC7, COL3A1, FAM96B, FN1, TGFBR3, MCC, HEXA, IFITM2, TKT, DYSF, ARG1, TPM1, PTPRK, MICAL2, FNDC3B, WWC2, PALLD, FHIT, TMEM184C, TFF1, TMEM176B, IFIT2, WDR33, PROCR, C8orf4, CDH13, CREG1, ANKRD1, ANXA4, GAB1, MAGI1, DHX38, ATG4B, PEAK1, PDPN, WWTR1, ECHDC2, CABP1, GALNT15, P2RY13, ST6GALNAC5, KLF7, DKK3, LAMB2, MAGI2, DBR1, KCNN4)	Aorta (p<1.0e-16)	Aorta (0.0989)
ASAH1	Muscle (18)	Muscle (4)	Muscle (0.222)	Muscle (COL4A2, SPTY2D1, EDNRA, SGK223)	Muscle (p<1.0e-16)	Muscle (0.0409)
ACCN1	Islet (13)	Islet (4)	Islet (0.307)	Islet (LARGE, ACCN1, ITGA2, CYP17A1)	Islet (p<0.00114)	Islet (p<0.00114)
ISG15	Cardiac_muscle (162)	Cardiac_muscle (57)	Cardiac_muscle (0.351)	Cardiac_muscle (TCP1, XAF1, ADAR, IFITM3, MPG, MKNK2, MEST, ACADVL, ABLIM1, PTHLH, DDAH2, PLIN2, TMSB10, SND1, STAT3, FGFR1, IFITM1, WBP1L, PTRF, SSR2, PHF11, IFITM2, LRP10, HLA-B, TKT, MX1, PSMB3, SH2B3, PSMC3, AP2S1, PIK3C2B, HLA-C, ATP6V0B, EREG, ISG20, HERPUD1, IL15RA, GBP1, TRIM22, UBA7, CNN3, SP100, CREG1, ANXA11, CMPK2, LRRFIP1, ODC1, TOR1B, ISG15, MAP1LC3B, IFI30, ABCB4, NPC2, CORO1C, PARP12, IFIT3, PLAU)	Cardiac_muscle (p<1.0e-16)	Cardiac_muscle (0.0114)
ADAM9	Aorta (446)	Aorta (153)	Aorta (0.343)	Aorta (EMILIN1, PITX1, CAV2, C4BPA, PYGL, DSCAM, TNFRSF1B, MT1H, HAS1, C3, SPP1, ITGB8, PIGK, COL4A2, ADORA2A, ZCCHC24, NOX4, FAP, GUCA1A, ERMAP, MMP1, MMP3, FBLN2, PDGFRA, MBNL2, TAGLN2, FKBP10, ITGB6, CTGF, PTGDS, PPAP2B, SHC1, MAP3K7CL, WNT2, HLA-DPB1, MMP10, KDR, FSTL3, IL10, GLT8D1, MT1F, KDELR2, RBMS1, NID1, PLN, ARPC5, GSTT2, MT1X, COL3A1, DPAGT1, EPS8, FN1, RRAD, TPM2, PPP2R3A, NDUFA4L2, KCNMA1, TCF21, FOXF2, KCNS3, HYAL1, STT3A, NCF2, NINJ2, AZGP1, CST6, ENC1, PLD1, COL5A2, ACP5, COL4A1, ALDH1A3, ARG1, MMP2, SDC2, BST1, TPPP, EML1, NEDD4, HEBP2, TBR1, CXCL1, NOS3, FHL5, TFPI, DNALI1, CDK6, SERPINH1, CALCRL, SCNN1A, IGFBP2, MMP14, PROCR, KCNE4, DPT, LPAR1, TNIP3, ARHGEF38, CSGALNACT1, BMP1, C1R, CDH13, COL15A1, CNN3, NKG7, TXNDC5, TES, MFAP4, PTPRD, ADAM15, CGA, PDGFRB, ITGA2, SULF1, PDPN, COL4A4, WWTR1, HLA-DRB1, EDNRA, SGK1, IBSP, CD302, IL32, PCSK7, EYA2, ASPA, P2RY13, CFI, PDLIM3, GEM, TREM2, OSMR, EGR2, PCOLCE, UTRN, NPC2, GPR171, MYOZ2, KLK12, IGFBP5, P4HA1, NAV3, LAMB2, IFIT3, PLAU, GUCY1A3, GJA1, FOXC1, TSPAN8, TAGLN, C2orf54, TSPAN1, PMM2)	Aorta (p<1.0e-16)	Aorta (0.00341)
SDCBP	Aorta (616)	Aorta (175)	Aorta (0.284)	Aorta (PTPRG, CAV2, PRKCE, NOD1, PSORS1C1, LY75, TNFRSF1B, MT1H, C3, SPP1, CTSK, CNTN5, ITGB8, PTGIR, PHACTR2, ZNF423, ZCCHC24, NOX4, IQCG, TLE1, FAP, ABI1, FYTTD1, NCAM1, MT1G, ARHGAP10, MMP1, FBLN2, CD247, SLC35G2, HLA-DOB, GNAI3, FKBP10, MYH11, MCL1, CTGF, CXCL12, PPAP2B, TARBP1, WNT2, GLDC, MAP3K11, TMEM204, KDR, IL24, AXL, IL10, LRP1, PIK3R1, RBMS1, LPP, NMB, NID1, PLN, RERG, ABCA8, ROBO1, AHNAK2, HS3ST1, FN1, C1S, ERAP2, AIDA, EFHD1, C4A, KIAA1549L, SPIN1, KCNMA1, DYRK4, NINJ2, AZGP1, KCNJ2, DYSF, COL5A2, BCAR3, COL4A1, ALDH1A3, MX1, ME1, ABCA1, TMPRSS2, PTPRK, SH2B3, EWSR1, C6orf106, ARL15, MMP2, HLA-C, EML1, NEDD4, IPO8, CXCL1, FHL5, ADM, ITGA7, ASB9, IFIT2, RAMP1, HEG1, SERPINH1, CALCRL, CXCL6, NPTN, PRKCA, MMP14, CLCN3, CSTB, PROCR, KCNE4, IRF1, SPR, DPT, PRKAR2B, HIVEP2, TNFRSF10D, KIT, CSGALNACT1, PLA2G7, C1R, CDH13, COL15A1, MFAP4, PTPRD, BACE1, SP100, DKK1, BBOX1, EDN1, ERG, NR4A2, PDGFRB, GBE1, HTRA1, GAS2, SCD, TGDS, PDPN, FGF2, EFEMP2, WWTR1, SUSD1, EDNRA, CD302, FTO, SSR1, ADAMTS3, FPR3, CTSS, PRPF6, ASPA, PTPRT, MARCH2, CFI, GEM, LRRC41, CBS, TRIP10, TREM2, TIMP3, OSMR, C10orf10, CAV1, CD320, MT1B, ZFPM2, SMAD1, PDLIM4, FBP1, P4HA1, LAMB2, GUCY1A3, RFTN1, LPGAT1, ITGAV, CHN1)	Aorta (p<1.0e-16)	Aorta (0.0227)
CD74	Adipose (17)	Adipose (6)	Adipose (0.352)	Adipose (HLA-DRA, CIITA, HLA-DQA1, HLA-C, HLA-DRB1, HLA-DQB1)	Adipose (p<1.0e-16)	Adipose (0.00682)
MCOLN1	Brain (35)	Brain (13)	Brain (0.371)	Brain (TRAIP, CXCL12, RTN3, GGT7, CCDC85B, TKT, ARPC3, ATP2B1, STK32C, GIGYF1, CLCN3, CDH13, AFF3)	Brain (p<1.0e-16)	Brain (0.00455)
ZBTB44	Liver (25)	Liver (10)	Liver (0.4)	Liver (TOMM40, APOC3, CPEB3, ZBTB44, S1PR5, EI24, SPC24, OXR1, FOXRED1, ST3GAL4)	Liver (p<1.0e-16)	Liver (0.00114)
IGFBP6	Artery (189)	Artery (70)	Artery (0.370)	Artery (CAV2, GDF15, C3, BCAM, PHLDA1, COL4A2, ZCCHC24, APOE, AHR, ABLIM1, CTGF, C1RL, SHC1, FGFR3, IFIT1, AXL, LRP1, LPP, NID1, TIMP2, CTSH, AHNAK2, FGFR1, EPS8, FN1, ITGB4, COL4A1, TPM1, CRIM1, ZEB1, PALLD, ERCC1, TFPI, ADM, SMAD7, C16orf45, IRS1, TRIOBP, PROCR, GATA3, BMP1, C1R, TES, CREG1, ANXA4, SEMA3C, S100A13, PDGFRB, JUND, HTRA1, IGFBP7, FGF2, EFEMP2, WWTR1, RGL1, SGK1, LOX, AKR1C1, GFPT2, RTN2, CAV1, PCOLCE, TGFB1, IGFBP5, DKK3, PDLIM4, LAMB2, IFIT3, TAGLN, QSOX1)	Artery (p<1.0e-16)	Artery (0.0159)
CTSB	Smooth_muscle (224)	Smooth_muscle (79)	Smooth_muscle (0.35)	Smooth_muscle (KLF4, CLIC4, UBE2H, RIOK3, CALHM2, COL4A2, TNFSF10, GRN, APOE, CDKN1A, CUL7, DMWD, PRNP, GTPBP4, INPP5A, FGFR3, CLIC3, SERINC1, KDELR2, MGAT1, RRAGA, HEXB, CTSH, IFITM1, MYOF, SDC4, WBP1L, UCP2, ETS2, IFITM2, BMPR2, HLA-B, CCPG1, LIPA, TPM1, BAG6, MICAL2, C6orf106, LRPAP1, OASL, ATP2B1, PALLD, UGGT2, FSCN1, TMEM97, HERPUD1, OAS1, RHOQ, CSTB, CREB3, SH3BP5, CTSA, TRIM22, CDH13, PVRL2, CREG1, ANXA4, SOD2, HTRA1,	Smooth_muscle (p<1.0e-16)	Smooth_muscle (0.0102)

				IGFBP7, ISG15, SLC20A1, MAP1LC3B, AP1B1, IGF2R, PRCP, GLI3, SEC61A1, TP53I3, ACTN1, PCOLCE, NPC2, P4HA1, IFIT3, PLAU, SWAP70, LAMC1, SLC7A5, SCAMP2)		
SERPINC1	Adipose (34)	Adipose (10)	Adipose (0.294)	Adipose (PLG, C4BPA, CA5A, APOA5, APOF, MAT1A, PAH, AKR1C1, APOA1, F2)	Adipose (p<1.0e-16)	Adipose (0.0148)
SLIT2	Aorta (778)	Aorta (218)	Aorta (0.280)	Aorta (NEFH, ACOT2, OGFRL1, ALOX5AP, ZCCHC2, TRIM5, DNASE1L3, FOS, TNFRSF1B, HAS1, CBR1, ALDH6A1, SPATC1, MAPRE2, CYB5R2, GALNT1, DPYSL2, MEOX1, MRPL24, TMEM57, NOX4, GAB2, TAF1A, MEST, AHR, SORBS2, SH3PXD2A, MMP1, MMP3, PEBP1, ACTR2, TNIK, SLIT3, MYH11, ITPR1, GBP2, PRNP, PTGDS, PPAP2B, DAAM1, MITF, MAP3K7CL, FDX1, TEX2, NAT2, HLA-DPB1, MMP10, C1orf56, TCEA2, FAM155A, LEFTY2, NCR1, GRAMD3, CXCR4, ARSA, CACNA1C, MRAS, SLC26A2, PIK3R1, RBMS1, PLN, MGAT1, MSI1, ABCA8, CWF19L1, ZNF184, COL3A1, CLDN5, NFIX, CTSH, THSD4, HIP1, FRY, TLR1, HS3ST1, SLC6A6, PDGFD, FIGN, C1S, MAFB, TGFBR3, BNIP3L, IFITM1, EFHD1, TVP23B, GUCY1A2, SEMA5A, RETSAT, KCNMA1, ZNF646, AGT, LRRC48, KLF2, PNMA2, MCC, PTN, CCR9, HLA-B, TCF7L2, ENC1, CRISPLD2, PRKACB, EPHB1, NR2F2, ALDH1A3, MANSC1, HDAC9, PFN2, ARG1, TPM1, CRIM1, PNRC1, CLASP2, SEMA6A, OPTN, RTN1, CST7, BST1, ACSS3, AMPH, FABP2, WWC2, CLEC1A, HOXB2, ATP2B1, RHOT1, PALLD, FAM102A, ASB9, IFIT2, HEG1, HERPUD1, CALCRL, SCARB2, FIG4, FAM19A2, RHOQ, PROCR, DPT, PRKAR2B, EZH1, HIPK2, PRICKLE1, TESC, SORT1, TSPAN14, MYLK, GBP1, CLASRP, C1R, CDH13, COL15A1, UBA7, CNN3, PVRL2, RORA, SP100, CREG1, VIPR1, ANKRD1, ANXA4, GAB1, SEMA3C, EDN1, ERG, SOD2, FGF12, TLR5, MXRA7, TLE4, PLA2G12A, APBB1, CYP4F3, LILRB1, FGF2, WWTR1, SGK1, GAP43, GAL3ST1, CD302, HHEX, LOX, STXBP1, MLLT11, NRP2, FES, ASPA, STX11, ZEB2, ARID4A, BACH1, VGLL3, SLC4A5, NR1D2, SLC22A3, CAMTA2, PSD3, ITGA1, CNTN3, PCOLCE, NPC2, LTBP1, NR2C2, ZFPM2, CORO1C, NAV3, LAMB2, IFIT3, GUCY1A3, SWAP70, FOXC1, TSPAN8, ITGAV, PBX3, TAGLN, NFIB, TTC28, TSPAN1)	Aorta (p<1.0e-16)	Aorta (0.0670)
ABCG8	Liver (30)	Liver (10)	Liver (0.333)	Liver (GNL3, CPSF4L, NFIX, SLC22A4, CRIM1, ABCG5, ABCG8, BCL2L11, OSMR, DYNC2LI1)	Liver (p<1.0e-16)	Liver (0.0102)
NME6	Kidney (10)	Kidney (4)	Kidney (0.4)	Kidney (NME6, HYAL1, CSPG5, CDC25A)	Kidney (p<1.0e-16)	Kidney (0.00227)
C1R	Cardiac_muscle (304)	Cardiac_muscle (101)	Cardiac_muscle (0.332)	Cardiac_muscle (EMILIN1, ACOT2, VAT1, CLIC4, IFITM3, PYGL, CALHM2, ATP1B3, CTSK, ACAA2, COL4A2, GRN, PODXL, PCOLCE2, TAGLN2, MYH11, CTGF, SLC27A3, LGALS1, RGS10, NINL, TYMS, PSMA5, AXL, SND1, PECAM1, AHNAK2, FGFR1, EPS8, SCP2, FN1, PLXND1, C1S, TPM2, IFITM1, GAS6, PHLDB2, C4A, MYOF, VKORC1, PTRF, HADHA, FAM20C, DIP2C, MAP3K5, IFITM2, TCF7L2, CRISPLD2, ANP32E, TPM1, OPTN, NPR1, ARHGDIB, RRAS2, HEBP2, PALLD, ALDH2, FSCN1, ADM, SMAD7, TNS1, KDELR3, LPAR1, MYLK, MPRIP, LPIN1, GPX1, C1R, COL15A1, CNN3, TXNDC5, DENND5A, CREG1, FAM114A1, S100A13, PSMD12, GBE1, HTRA1, SEPT11, IGFBP7, EFEMP2, WWTR1, CD302, LOX, PRCP, TGOLN2, GFPT2, DSTN, ACTN1, SYNGR2, GRB10, CAV1, ADAMTSL3, LTBP1, CORO1C, PSMD9, MTAP, SWAP70, CALR, LAMC1, TAGLN)	Cardiac_muscle (p<1.0e-16)	Cardiac_muscle (0.0136)
DPYD	Cardiac_muscle (143)	Cardiac_muscle (44)	Cardiac_muscle (0.307)	Cardiac_muscle (VAT1, OGFRL1, CLIC4, CAV2, PLA2G4A, PLCE1, MT1G, TAGLN2, PRNP, PLIN2, MTSS1, KDELR2, ITGB5, CTSH, FGFR1, PLXND1, C1S, NRP1, ALKBH5, ETS2, IFITM2, HLA-B, ABCA1, CRIM1, TACC1, HLA-C, HLA-DRB3, ZFP36, HEG1, SERPINH1, F2R, WWTR1, CES2, IFI30, ZEB2, TIMP3, CAV1, PCOLCE, LTBP1, PLAU, SWAP70, CALR, ITGAV, LAMC1)	Cardiac_muscle (p<1.0e-16)	Cardiac_muscle (0.0159)
AK021074	Kidney (11)	Kidney (4)	Kidney (0.363)	Kidney (GNA13, PRKCA, RPRML, RUNDC3A)	Kidney (p<1.0e-16)	Kidney (0.00227)
BNIP3L	Aorta (286)	Aorta (88)	Aorta (0.307)	Aorta (VAT1, GNLY, GALNS, PLA1A, PKMYT1, MT1H, HAS1, C3, PHLDA1, SPP1, NOX4, TRIM21, MT1G, MMP1, MMP3, FBLN2, SLC35G2, GPR65, TREX1, DAAM1, INSRR, ARHGEF5, PDE4A, FUT5, GRK5, AMPD3, UPB1, SLC26A2, EPS8, HS3ST1, GREM2, TPM2, BNIP3L, NAT6, TVP23B, KCNMA1, HLA-DQA1, PTN, NCF2, LRP10, TCF7L2, ALDH1A3, MX1, CKM, MMP13, EML1, CAMP, ISG20, CXCL1, GPR1, LIPG, GDF5, MMP14, HS3ST2, PROCR, KCNE4, PRKAR2B, LPAR1, KIT, GBP1, ARTN, SUSD5, NGF, CDH13, DKK1, EDN1, ERG, KDM4B, PDGFRB, TWIST1, NRXN2, RGL1, FGF5, LOX, P2RY1, LDB3, ZBTB20, MTF2, TIMP3, CAV1, SCUBE2, UTRN, CEP170, ZFPM2, LAMB2, GJA1, TBX2, TSPAN1)	Aorta (p<1.0e-16)	Aorta (0.0136)
LAMA2	Adipose (33)	Adipose (11)	Adipose (0.333)	Adipose (PLA1A, PDGFRA, ITGBL1, COL3A1, EPS8, FN1, SCARA5, NUP210, ACSS2, SLC22A3, LAMC1)	Adipose (p<1.0e-16)	Adipose (0.025)
M93275	Brain (16)	Brain (6)	Brain (0.375)	Brain (FGGY, ZDHHC21, PEMT, CDKN2B, MLLT3, NFIB)	Brain (p<1.0e-16)	Brain (0.00227)
RIF1	Heart (11)	Heart (2)	Heart (0.181)	Heart (MALAT1, NBEAL1)	Heart (p<0.00114)	Heart (p<0.00114)
ANXA3	Liver (49)	Liver (14)	Liver (0.285)	Liver (GIMAP8, LPL, PARP8, SLPI, SIGLEC5, EML1, ADM, CXCL6, EHD4, SCD, CTSS, TBXAS1, GCA, PLAU)	Liver (p<1.0e-16)	Liver (0.00114)
TRIM22	Vascular_endothelium (90)	Vascular_endothelium (33)	Vascular_endothelium (0.366)	Vascular_endothelium (IFITM3, TNFSF10, CDKN1A, GBP2, CTGF, DDX58, IFIT1, CXCR4, STAT3, C1S, IFITM1, ICAM1, UCP2, IFITM2, HLA-B, PON2, MX1, NMI, HLA-C, OAS1, PROCR, IRF1, GBP1, F2R, C1R, TRIM22, SP100, ANXA4, CMPK2, ISG15, PRCP, IFI30, IFIT3)	Vascular_endothelium (p<1.0e-16)	Vascular_endothelium (0.0114)
SLC1A5	Muscle (40)	Muscle (11)	Muscle (0.275)	Muscle (APOC1, APOE, PPP2R1B, RASD1, C14orf180, TRIM67, SLC1A5, RTN4RL1, CCDC61, SLC22A3, FBXO21)	Muscle (p<1.0e-16)	Muscle (0.01136)
AK007927	Muscle (16)	Muscle (5)	Muscle (0.3125)	Muscle (SLC22A5, LRRC48, SLC22A4, SMCR8, LIN52)	Muscle (p<1.0e-16)	Muscle (0.00341)
MAFF	Liver (27)	Liver (10)	Liver (0.370)	Liver (TNFRSF12A, GDF15, PHLDA1, MCL1, NAV2, TRIB1, LDLR, ZFP36, EPHA2, SLC20A1)	Liver (p<1.0e-16)	Liver (0.0182)
STAT3	PPI (102)	PPI (35)	PPI (0.343)	PPI (CDKN1A, PDGFRA, JUN, FGFR3, FLT1, CXCR4, RPS6KA5, BRCA1, HDAC3, STMN1, NLK, STAT5B, STAT3, ZNF467, MAP3K7, MTOR, NMI, RAC1, PML, KAT5, EIF2AK2, PRKCD, PTPN11, JAK3, FOXM1, PDGFRB, HNF1A, SUMO4, FES, IL2RA, IL6R, IGF1R, RELA, FER, ZNF148)	PPI (p<0.00114)	PPI (p<0.00114)
ITGA7	Adipose (37)	Adipose (8)	Adipose (0.216)	Adipose (COL4A2, VTN, PNPLA3, ADAMTS7, COL4A1, NPR1, ITGA7, DCBLD1)	Adipose (p<1.0e-16)	Adipose (0.0261)
KL	Brain (42)	Brain (8)	Brain (0.190)	Brain (KCNJ13, CLIC6, FN1, KCNE2, IGFBP2, COL4A4, SLC2A12, PRLR)	Brain (p<1.0e-16)	Brain (0.00114)

CD14	Adipose (48)	Adipose (10)	Adipose (0.208)	Adipose (ALOX5AP, C19orf38, KCNK5, P2RX4, PRKCA, C4orf19, CENPA, SLC9A9, SLC22A3, IGFBP5)	Adipose (p<1.0e-16)	Adipose (0.067)
GEM	Kidney (18)	Kidney (6)	Kidney (0.333)	Kidney (RASGEF1B, RASD1, TAL2, CXCL1, SGK1, GEM)	Kidney (p<1.0e-16)	Kidney (0.00114)
ZNF467	Liver (22)	Liver (9)	Liver (0.409)	Liver (ARHGEF5, PDE4A, ADAMTS7, SNED1, ZNF467, GREM2, VAMP5, LDLR, PARP12)	Liver (p<1.0e-16)	Liver (0.00341)
SHC1	PPI (118)	PPI (46)	PPI (0.389)	PPI (CALCOCO2, ERBB4, MST1R, GRAP2, CSK, GAB2, MAPKAPK2, CD247, PTPN6, PLCG1, PPAP2B, SHC1, FLT1, KDR, AXL, LRP1, STAT5B, PIK3R1, FGFR1, EPS8, NGFR, PIK3R2, LTK, BCL3, ITGB4, TEK, GRB2, TPR, AP2A2, DAG1, EPHA2, CBL, PRKCA, NTRK1, IRS1, PRKCD, PAK1, PTPN11, GAB1, PDGFRB, PLCG2, ESR1, CSF1R, PTK2, GRAP, VAV1)	PPI (p<1.0e-16)	PPI (0.00114)
SMAD1	PPI (111)	PPI (35)	PPI (0.315)	PPI (SMAD3, ZNF423, RAB30, NEDD9, UBE2Z, ING2, ZNF8, SOX5, ZBTB44, TNNT1, TTF1, HOXD13, COL4A1, EWSR1, AP2A2, BMPR1A, PLEKHB1, FHL5, BTBD2, HIPK2, PAK1, ARL4D, ZNF76, ZNF521, UBA52, SMAD6, KAT2B, GLI3, ZEB2, HBP1, SNIP1, TRIP6, SMAD1, RAB34, VEPH1)	PPI (p<1.0e-16)	PPI (0.00114)
IGSF10	Muscle (45)	Muscle (7)	Muscle (0.155)	Muscle (MEOX1, CXCL12, COL6A3, COL3A1, OLR1, SERTAD4, COL5A2)	Muscle (p<1.0e-16)	Muscle (0.0545)
FBLN2	PPI (22)	PPI (13)	PPI (0.590)	PPI (COL4A2, FBLN2, COL4A3, NID1, ATN1, FN1, HSPG2, COL4A1, COL18A1, ACAN, LAMC2, LAMA1, COL4A4)	PPI (p<1.0e-16)	PPI (0.00682)
BTNL9	Liver (26)	Liver (5)	Liver (0.192)	Liver (FLT1, LIPA, TBC1D2B, TBC1D8, DDX59)	Liver (p<1.0e-16)	Liver (0.0170)
COASY	Muscle (26)	Muscle (11)	Muscle (0.423)	Muscle (EPHX2, ACAD10, PAFAH2, PFKL, RBPMS2, COASY, ACSF3, HSD17B12, MPDU1, TGOLN2, DDT)	Muscle (p<1.0e-16)	Muscle (0.00795)
MMT00002956	Liver (36)	Liver (7)	Liver (0.194)	Liver (RGS1, RASGEF1B, CPSF4L, KLF2, IFIH1, ITGAX, PLEK)	Liver (p<1.0e-16)	Liver (0.05)
TRAPPC3	Brain (40)	Brain (11)	Brain (0.275)	Brain (PRMT1, PODXL, DNAJC7, GGT7, PYGB, ALDH2, CALCRL, TRAF4, RAPGEF4, SURF6, ALG8)	Brain (p<1.0e-16)	Brain (0.0523)
PTCHD1	Adipose (104)	Adipose (18)	Adipose (0.173)	Adipose (DNASE1L3, FOS, PKIB, CTSK, RGS1, RHPN2, MYH11, NPTX1, ATP6V0D2, CHN2, MYO1E, KCNJ2, CD200R1L, CALCRL, TNIP3, CLEC7A, ABCB4, PLAU)	Adipose (p<1.0e-16)	Adipose (0.00227)
THADA	Brain (19)	Brain (8)	Brain (0.421)	Brain (THADA, HAAO, ABCG5, LRPPRC, ACAD9, PLEKHH2, ZFP36L2, DYNC2LI1)	Brain (p<1.0e-16)	Brain (0.00114)
LOXL1	Muscle (30)	Muscle (12)	Muscle (0.4)	Muscle (COL4A2, CSK, PDGFRA, COL6A3, MRGPRF, LRRC16A, SERPINH1, BACE1, PCOLCE, LOXL1, VASN, MGAT5)	Muscle (p<1.0e-16)	Muscle (0.00568)
PCOLCE2	Liver (32)	Liver (14)	Liver (0.437)	Liver (MORF4L1, PCOLCE2, ATP11A, ARHGEF16, CTSH, LRP10, CLEC4F, EMR1, PILRB, PAQR9, SLCO1B1, PROCR, RGL1, SLC9A9)	Liver (p<1.0e-16)	Liver (0.00341)
CTNNB1	PPI (135)	PPI (37)	PPI (0.274)	PPI (SMAD3, PTPN6, PYGO1, MITF, FLT1, KDR, PIK3R1, PECAM1, AXIN2, TCF7L1, GRIN1, BCL3, TCF7L2, CTNNA3, PTPRK, IGF2BP1, GNA13, FSCN1, CDK6, SMAD7, GLIS2, RUVBL1, CDK5R1, GRIK2, MAGI1, SMARCA4, HNF1A, NF2, ESR1, NEURL2, CA9, TRIP10, PTPRJ, CBY1, CDH15, FER, MAGI2)	PPI (p<1.0e-16)	PPI (0.00114)
ALDOB	Muscle (30)	Muscle (9)	Muscle (0.3)	Muscle (APOC3, UPB1, MARCO, APOA5, MAT1A, ANKRD1, CYP2A13, F2, FBP1)	Muscle (p<1.0e-16)	Muscle (0.0102)
SCARA3	Muscle (30)	Muscle (8)	Muscle (0.266)	Muscle (FCGR2B, TIMP2, FN1, EFHD1, GPC6, MMP2, SFRP2, CSF1R)	Muscle (p<1.0e-16)	Muscle (0.0375)
HELZ	Muscle (32)	Muscle (12)	Muscle (0.375)	Muscle (CEP95, RYR1, SRP68, SMG7, PRKCA, SMARCA4, METTL23, C17orf58, MYL4, ING5, ZBTB20, CELSR2)	Muscle (p<1.0e-16)	Muscle (0.00227)
VPS33A	Adipose (21)	Adipose (9)	Adipose (0.428)	Adipose (NCOR2, ACAD10, UBC, CUX2, PTPN11, VPS33A, MAFK, CAMKK2, GPC2)	Adipose (p<1.0e-16)	Adipose (0.00114)
PTPN11	PPI (109)	PPI (40)	PPI (0.366)	PPI (SLAMF1, TREML1, GAB2, NEDD9, PTPN6, PDGFRA, PLCG1, SHC1, FLT1, LILRB4, KDR, CXCR4, AXL, STAT5B, PIK3R1, STAT3, PECAM1, PILRA, BDKRB2, TEK, GRB2, PILRB, CAT, EPHA2, CBL, PRKCA, NTRK1, IRS1, MAP3K4, KIT, PTPN11, SIT1, GAB1, PDGFRB, ARHGAP1, IGF1R, CAV1, PTK2, DAB1, PRLR)	PPI (p<1.0e-16)	PPI (0.0295)
TCF3	Adipose (25)	Adipose (9)	Adipose (0.36)	Adipose (SEMA5A, ADAMTS10, RETSAT, MAT2A, GGCX, GSTT1, VAMP8, HSPA12B, SNX10)	Adipose (p<1.0e-16)	Adipose (0.00341)
CYP1B1	Brain (49)	Brain (11)	Brain (0.224)	Brain (CTGF, CXCL12, KDR, SLC6A20, PDXDC1, RBPMS2, BMP6, SLC6A13, CD163, DYNC2LI1, FOXC1)	Brain (p<1.0e-16)	Brain (0.0580)
COLEC12	Kidney (17)	Kidney (6)	Kidney (0.352)	Kidney (NCAM1, TMSB10, FN1, IFITM2, KCNE4, FSTL1)	Kidney (p<1.0e-16)	Kidney (0.00682)
BC042789	Kidney (11)	Kidney (2)	Kidney (0.181)	Kidney (APOC3, ST3GAL4)	Kidney (p<1.0e-16)	Kidney (0.00909)
OAS2	Kidney (12)	Kidney (4)	Kidney (0.333)	Kidney (IFIT1, APOA4, OAS1, MMP12)	Kidney (p<0.00114)	Kidney (p<0.00114)
ZDHHC17	Brain (61)	Brain (11)	Brain (0.180)	Brain (SKI, PRMT1, PYGO1, MTSS1, JAZF1, PPP2R3A, RAP1A, HLA-C, SF3A3, CAMK2A, FGF5)	Brain (p<1.0e-16)	Brain (0.0466)

Note: "Genes with CAD 1000 Genomes GWAS P<0.001 in KD subnetworks" annotate the genes with its CAD association strength from CAD 1000 Genomes based on the most significant SNP among all SNPs mapped to a gene based on chromosome distance or eQTLs.

Supplemental Table IV. Gene expression alterations of KD subnetworks in CAD patients using GSEA.

Part 1

Subnetworks	Blood		Endothelial_Cell		Epicardial_Adipose		Macrophages		PBMC		Resting_Monocytes	
	P_Values	FDRs	P_Values	FDRs	P_Values	FDRs	P_Values	FDRs	P_Values	FDRs	P_Values	FDRs
DUSP6_AORTA	1.2E-02	1.1E-01	4.6E-10	7.9E-07	4.2E-03	1.1E-01	5.0E-02	5.1E-01	4.0E-01	9.9E-01	5.1E-10	8.7E-08
IRF1_ARTERY	4.7E-03	3.3E-02	2.0E-07	6.5E-06	1.2E-12	1.1E-10	5.7E-05	2.0E-02	1.2E-01	7.1E-01	7.9E-01	8.8E-01
MSN_VASCULAR_ENDOTHELIUM	1.5E-02	1.1E-01	7.5E-09	9.1E-07	9.7E-11	9.1E-09	5.9E-01	8.4E-01	1.4E-02	4.4E-01	3.8E-04	8.1E-03
LUM_BRAIN	NA	NA	<1.0E-16	<1.0E-16	9.5E-01	9.6E-01	7.6E-02	5.9E-01	8.1E-01	1.0E+00	<1.0E-16	2.7E-14
CXCL10_LIVER	3.9E-01	5.8E-01	<1.0E-16	2.5E-06	1.0E-02	2.3E-02	<1.0E-16	1.1E-14	6.9E-01	9.1E-01	1.6E-02	4.8E-02
GBP1_VASCULAR_ENDOTHELIUM	4.7E-02	2.2E-01	2.4E-07	6.3E-05	9.8E-10	1.4E-08	3.8E-02	4.4E-01	1.1E-01	8.1E-01	6.3E-01	7.6E-01
IFI35_ARTERY	4.9E-05	3.7E-03	1.1E-01	1.9E-01	2.0E-03	1.6E-02	1.3E-01	6.3E-01	5.1E-01	9.9E-01	6.1E-04	1.5E-01
CCL18_AORTA	3.2E-02	2.8E-01	5.1E-06	2.1E-04	2.9E-04	7.2E-03	2.4E-01	7.5E-01	1.5E-02	5.1E-01	1.5E-02	1.8E-01
DUSP6_VASCULAR_ENDOTHELIUM	2.1E-01	9.0E-01	7.6E-06	8.9E-04	2.0E-05	6.5E-03	2.6E-01	7.5E-01	8.7E-01	9.3E-01	4.9E-11	9.0E-09
SHC1_PPI	1.5E-01	3.7E-01	<1.0E-16	1.0E-07	9.1E-02	1.7E-01	5.6E-02	4.7E-01	3.7E-01	9.7E-01	2.2E-04	4.7E-03
MAFF_LIVER	4.2E-01	7.8E-01	<1.0E-16	<1.0E-16	4.8E-02	8.4E-02	5.1E-01	8.4E-01	7.4E-01	9.3E-01	3.9E-11	8.2E-09
DUSP1_AORTA	7.2E-02	2.7E-01	3.9E-07	5.1E-05	5.8E-02	2.1E-01	2.1E-01	6.6E-01	4.6E-01	8.9E-01	1.9E-05	4.0E-04
ZYX_SMOOTH_MUSCLE	4.4E-04	3.6E-03	2.0E-06	5.8E-04	1.6E-01	3.0E-01	7.9E-01	1.0E+00	5.2E-06	1.4E-02	2.2E-01	4.4E-01
TNFAIP2_CARDIAC_MUSCLE	2.1E-01	4.3E-01	2.3E-06	7.8E-05	4.9E-06	1.6E-03	6.7E-01	8.3E-01	4.3E-04	1.6E-01	4.4E-01	6.4E-01
ADM_ARTERY	4.5E-02	2.1E-01	8.6E-06	9.0E-05	1.2E-04	2.9E-02	5.4E-01	8.6E-01	7.3E-01	1.0E+00	1.3E-03	5.0E-02
DUSP6_ARTERY	3.9E-01	5.9E-01	1.6E-11	6.6E-10	1.0E-04	1.5E-03	6.1E-01	8.6E-01	9.0E-01	1.0E+00	1.4E-03	1.6E-02

CFD_AORTA	1.6E-01	3.7E-01	3.2E-07	6.8E-05	5.7E-05	1.5E-02	4.1E-01	8.0E-01	6.1E-01	1.0E+00	1.3E-02	5.9E-02
MMT00002956_LIVER	4.8E-02	4.5E-01	<1.0E-16	5.9E-08	1.2E-07	3.2E-05	2.9E-01	7.1E-01	5.0E-01	9.8E-01	6.8E-01	8.2E-01
SLC2A3_AORTA	8.6E-02	3.0E-01	6.0E-09	7.5E-08	2.1E-03	3.5E-02	1.8E-02	3.9E-01	3.4E-01	8.8E-01	8.3E-02	3.1E-01
ANXA3_LIVER	5.4E-01	7.1E-01	<1.0E-16	9.2E-07	7.3E-02	7.9E-01	3.4E-01	7.9E-01	4.3E-02	4.4E-01	3.0E-01	5.1E-01
DUSP1_SMOOTH_MUSCLE	3.1E-02	1.1E-01	3.1E-10	1.1E-08	8.9E-05	7.6E-03	4.2E-01	7.6E-01	6.7E-01	9.3E-01	4.2E-04	8.8E-03
MMP9_PPI	NA	NA	<1.0E-16	<1.0E-16	6.0E-01	7.5E-01	4.8E-01	7.8E-01	4.0E-01	8.4E-01	5.4E-02	1.3E-01
ADAM9_AORTA	7.5E-01	9.1E-01	2.6E-07	7.5E-06	6.4E-02	1.5E-01	3.0E-04	2.1E-02	9.9E-01	9.8E-01	2.8E-03	2.6E-02
RAC2_CARDIAC_MUSCLE	2.1E-03	2.8E-02	1.0E-01	2.0E-01	5.6E-10	2.1E-08	8.1E-01	9.3E-01	1.1E-02	3.3E-01	1.0E+00	9.7E-01
HLA-F_ARTERY	2.2E-03	4.5E-02	1.9E-02	6.7E-02	4.9E-05	1.2E-03	1.5E-01	6.3E-01	6.5E-01	1.0E+00	9.1E-01	9.5E-01
ISG15_CARDIAC_MUSCLE	6.5E-03	2.0E-02	8.9E-03	4.3E-02	2.1E-03	1.5E-02	3.4E-01	7.7E-01	3.0E-01	8.8E-01	6.9E-01	7.8E-01
SLIT2_AORTA	7.5E-01	8.8E-01	1.2E-08	2.1E-06	3.9E-01	5.1E-01	1.6E-01	6.6E-01	6.8E-01	1.0E+00	1.6E-02	1.3E-01
ANXA1_ARTERY	5.8E-01	9.6E-01	3.7E-06	6.7E-04	2.2E-01	3.7E-01	4.4E-02	3.0E-01	6.6E-02	4.8E-01	4.9E-02	1.3E-01
COL1A1_LIVER	9.6E-01	9.7E-01	1.7E-09	1.7E-07	3.6E-01	8.6E-01	2.0E-01	6.9E-01	4.6E-02	4.8E-01	1.0E-01	2.4E-01
DUSP1_ARTERY	9.5E-01	9.8E-01	7.6E-11	5.9E-10	1.4E-04	3.9E-02	4.4E-01	7.4E-01	9.8E-01	9.8E-01	6.5E-04	1.7E-02
STAT3_PPI	6.9E-01	9.4E-01	2.4E-02	9.9E-02	2.2E-01	3.9E-01	4.0E-01	7.5E-01	8.8E-01	1.0E+00	9.7E-13	7.6E-11
KCNK13_LIVER	3.8E-01	5.7E-01	<1.0E-16	1.2E-04	4.5E-01	5.8E-01	7.2E-02	3.7E-01	3.5E-01	8.3E-01	9.5E-01	1.0E+00
SDCBP_AORTA	3.5E-01	5.7E-01	1.3E-07	6.1E-05	2.2E-01	4.1E-01	3.2E-04	1.0E-02	7.8E-01	9.3E-01	9.8E-02	2.5E-01
DUSP6_CARDIAC_MUSCLE	6.1E-01	9.1E-01	4.4E-10	7.4E-08	3.1E-01	4.6E-01	8.5E-01	9.1E-01	5.2E-01	1.0E+00	3.1E-04	6.6E-03
IRF7_ADIPOSE	6.3E-03	1.8E-02	6.4E-03	9.1E-02	NA	NA	1.1E-02	8.8E-02	2.0E-01	7.2E-01	2.3E-02	1.6E-01
PTPN11_PPI	2.8E-01	5.1E-01	1.1E-07	5.2E-03	2.5E-01	4.3E-01	5.4E-01	8.4E-01	6.8E-01	1.0E+00	6.1E-02	2.4E-01
ANXA1_SMOOTH_MUSCLE	4.5E-01	7.7E-01	7.6E-07	5.9E-05	2.3E-05	5.7E-03	3.6E-01	7.7E-01	7.6E-01	9.5E-01	3.7E-01	6.3E-01
BST2_ARTERY	1.3E-04	6.6E-03	8.4E-01	8.9E-01	6.1E-03	1.9E-02	8.3E-02	4.7E-01	1.1E-01	6.4E-01	7.7E-01	8.1E-01
IRF9_SMOOTH_MUSCLE	4.4E-04	8.5E-03	3.9E-02	8.2E-02	6.2E-02	1.2E-01	3.6E-01	7.3E-01	9.1E-01	1.0E+00	6.1E-01	7.6E-01
TRIM22_VASCULAR_ENDOTHELIUM	1.2E-04	1.0E-03	3.9E-01	9.5E-01	8.6E-03	1.5E-02	3.6E-01	7.7E-01	2.9E-01	7.6E-01	9.0E-01	9.5E-01
CD74_ADIPOSE	2.2E-02	6.0E-02	3.4E-01	4.0E-01	3.8E-08	4.4E-06	4.1E-08	2.1E-06	9.5E-01	9.9E-01	6.3E-01	8.0E-01
C1R_CARDIAC_MUSCLE	4.1E-01	6.0E-01	5.7E-10	9.3E-08	9.2E-01	1.0E+00	9.1E-01	9.6E-01	4.9E-01	1.0E+00	1.2E-03	2.1E-02
JAG1_VASCULAR_ENDOTHELIUM	2.7E-01	8.3E-01	1.5E-06	5.7E-04	3.2E-01	4.2E-01	2.7E-01	6.7E-01	2.1E-01	8.2E-01	4.2E-04	8.9E-03
KLF6_SMOOTH_MUSCLE	8.6E-01	8.9E-01	2.8E-07	2.6E-05	8.9E-03	8.3E-02	7.6E-01	8.9E-01	5.7E-01	9.3E-01	2.3E-03	4.9E-02
GBP2_BLOOD	8.9E-06	8.5E-04	1.5E-02	1.8E-02	NA	NA	2.2E-01	6.4E-01	5.7E-04	1.4E-01	2.3E-01	4.7E-01
ANXA2_CARDIAC_MUSCLE	9.7E-01	9.1E-01	8.2E-06	2.1E-04	6.6E-03	1.5E-01	9.9E-01	1.0E+00	2.3E-01	9.2E-01	3.5E-03	7.3E-02
CTSB_SMOOTH_MUSCLE	2.9E-01	5.2E-01	2.9E-06	7.5E-05	8.0E-02	1.6E-01	8.6E-01	1.0E+00	4.1E-02	4.4E-01	2.8E-01	4.9E-01
PAPSS2_CARDIAC_MUSCLE	1.3E-01	8.1E-01	8.2E-05	2.5E-04	8.7E-01	1.0E+00	3.5E-01	7.6E-01	2.3E-01	7.6E-01	1.6E-02	8.6E-02
COL5A1_ADIPOSE	NA	NA	4.5E-01	5.2E-01	4.7E-02	9.0E-01	7.2E-01	9.3E-01	1.4E-01	8.0E-01	4.7E-01	6.3E-01
COL4A2_PPI	NA	NA	<1.0E-16	<1.0E-16	8.7E-01	1.0E+00	NA	NA	9.2E-01	1.0E+00	NA	NA
GBP1_BLOOD	4.8E-02	1.2E-01	7.5E-01	8.6E-01	NA	NA	1.5E-02	1.1E-01	6.0E-03	1.3E-01	6.9E-02	2.6E-01
CD14_ADIPOSE	2.5E-01	3.7E-01	1.4E-02	4.6E-02	5.9E-01	6.9E-01	1.9E-03	1.6E-02	1.2E-02	2.8E-01	2.6E-01	4.4E-01
GEM_KIDNEY	NA	NA	<1.0E-16	3.5E-14	7.3E-02	1.2E-01	4.9E-01	8.3E-01	5.6E-01	9.1E-01	NA	NA
PTCHD1_ADIPOSE	4.1E-01	5.8E-01	1.0E-02	5.1E-02	2.0E-01	3.4E-01	6.1E-01	9.5E-01	6.2E-01	9.0E-01	6.0E-01	7.7E-01
IGSF10_MUSCLE	NA	NA	3.6E-03	1.4E-02	6.6E-01	1.0E+00	6.3E-01	8.4E-01	9.7E-01	1.0E+00	5.1E-03	3.4E-02
CXCL12_CARDIAC_MUSCLE	3.0E-01	7.5E-01	7.1E-03	2.1E-02	3.0E-01	4.2E-01	7.1E-01	9.1E-01	6.3E-01	1.0E+00	2.2E-01	4.0E-01
CXCL12_ADIPOSE	9.3E-02	1.8E-01	8.4E-02	1.2E-01	4.9E-01	6.0E-01	4.4E-01	8.3E-01	1.7E-01	7.5E-01	4.2E-01	6.2E-01
BNIP3L_AORTA	3.5E-01	8.4E-01	2.6E-07	7.1E-05	7.2E-01	8.1E-01	5.4E-01	8.5E-01	2.6E-01	8.1E-01	6.9E-02	1.8E-01
ANXA2_PPI	1.0E-01	4.0E-01	4.6E-02	7.8E-02	9.1E-01	9.7E-01	3.8E-01	7.5E-01	5.7E-04	1.7E-02	3.8E-01	5.9E-01
LOXL2_LIVER	5.0E-01	6.8E-01	9.0E-05	2.5E-03	5.4E-01	6.4E-01	2.2E-01	5.7E-01	2.3E-01	7.9E-01	5.8E-01	7.7E-01
LY96_VASCULAR_ENDOTHELIUM	1.5E-02	5.5E-02	1.9E-03	1.0E-02	3.1E-01	4.1E-01	2.9E-02	1.2E-01	8.9E-02	4.8E-01	6.9E-01	8.5E-01
IFI30_SMOOTH_MUSCLE	6.3E-03	4.7E-02	4.8E-02	5.4E-02	3.9E-01	5.1E-01	5.3E-01	8.3E-01	4.2E-01	9.7E-01	4.8E-01	6.8E-01
HGD_MUSCLE	NA	NA	2.9E-01	3.7E-01	NA	NA	NA	NA	5.4E-01	9.5E-01	NA	NA
ADM_SMOOTH_MUSCLE	1.3E-02	6.6E-02	4.6E-05	1.2E-03	7.2E-01	8.2E-01	9.0E-01	9.7E-01	7.7E-01	1.0E+00	5.5E-02	1.3E-01
ITGB4_AORTA	4.4E-01	6.4E-01	1.8E-03	4.8E-03	3.5E-01	4.8E-01	9.0E-01	9.7E-01	1.7E-01	7.8E-01	1.4E-01	3.0E-01
SLC1A5_MUSCLE	NA	NA	5.9E-02	1.0E-01	3.3E-01	9.9E-01	7.0E-02	7.1E-01	4.9E-01	1.0E+00	4.5E-01	6.4E-01
COL6A3_LIVER	4.2E-01	8.3E-01	1.1E-02	4.6E-02	9.2E-01	1.0E+00	5.5E-01	8.5E-01	1.2E-01	7.6E-01	3.0E-01	4.9E-01
IGFBP6_ARTERY	8.5E-01	9.3E-01	8.3E-04	2.6E-03	3.3E-01	9.0E-01	5.9E-01	8.5E-01	6.0E-01	9.0E-01	8.7E-02	2.1E-01
EPS8_LIVER	NA	NA	2.4E-02	4.6E-02	NA	NA	8.2E-01	9.6E-01	8.6E-01	9.8E-01	4.7E-02	1.1E-01
ABCG8_LIVER	NA	NA	2.8E-01	3.5E-01	NA	NA	1.3E-01	6.6E-01	8.3E-02	5.5E-01	3.3E-01	5.2E-01
CYP1B1_BRAIN	5.7E-01	7.2E-01	1.5E-06	5.1E-04	9.3E-01	1.0E+00	2.2E-01	6.0E-01	8.7E-01	9.9E-01	2.8E-01	4.9E-01
SPARC_MUSCLE	9.7E-01	9.8E-01	1.3E-02	2.3E-02	9.9E-02	9.2E-01	3.3E-01	7.4E-01	9.3E-01	1.0E+00	8.3E-01	9.3E-01
FN1_PPI	1.2E-01	2.6E-01	8.3E-03	3.4E-02	3.9E-01	5.0E-01	4.0E-01	7.9E-01	4.3E-01	9.9E-01	8.8E-01	9.4E-01
GBP1_ADIPOSE	NA	NA	9.6E-01	9.8E-01	NA	NA	1.0E-01	4.4E-01	3.5E-02	3.6E-01	6.9E-04	1.4E-02
APOB_PPI	6.3E-02	3.6E-01	6.3E-01	7.6E-01	8.5E-01	9.2E-01	1.7E-01	4.9E-01	4.1E-01	8.3E-01	2.7E-01	4.4E-01
EFEMP1_CARDIAC_MUSCLE	8.6E-01	9.5E-01	3.2E-06	9.0E-04	9.3E-01	1.0E+00	8.4E-01	9.5E-01	9.8E-01	1.0E+00	2.9E-03	1.4E-02
WWC2_AORTA	4.8E-01	6.5E-01	1.6E-02	3.4E-02	8.7E-01	1.0E+00	7.4E-02	3.8E-01	2.3E-01	7.8E-01	1.1E-01	2.1E-01
ZNF496_LIVER	NA	NA	3.7E-01	1.0E+00	NA	NA	7.6E-01	9.2E-01	6.8E-02	4.8E-01	6.0E-02	2.4E-01
DPYD_CARDIAC_MUSCLE	6.1E-01	8.1E-01	1.7E-02	4.2E-02	8.6E-01	9.0E-01	3.7E-01	8.4E-01	8.2E-01	1.0E+00	1.1E-01	2.4E-01
COL4A2_MUSCLE	NA	NA	3.9E-02	5.7E-02	8.5E-01	1.0E+00	5.6E-01	8.5E-01	1.7E-01	7.2E-01	3.6E-01	5.5E-01
SLIT3_MUSCLE	NA	NA	3.2E-01	3.9E-01	9.0E-02	1.0E+00	1.2E-01	5.6E-01	9.2E-01	1.0E+00	1.1E-01	2.1E-01
SCARA3_MUSCLE	NA	NA	5.9E-02	9.2E-02	4.3E-01	9.3E-01	1.6E-01	5.5E-01	9.9E-02	5.8E-01	NA	NA
CKLF_LIVER	2.0E-01	6.9E-01	2.0E-01	2.9E-01	3.5E-01	4.6E-01	9.1E-01	9.7E-01	6.5E-01	1.0E+00	6.2E-01	8.0E-01
MTMR11_LIVER	1.4E-01	3.0E-01	2.4E-01	3.6E-01	1.0E+00	1.0E+00	6.1E-01	8.4E-01	2.8E-01	9.0E-01	4.2E-01	6.2E-01
PCOLCE2_LIVER	7.2E-01	9.0E-01	2.0E-02	3.1E-02	7.4E-01	1.0E+00	2.9E-01	6.7E-01	3.6E-01	9.3E-01	4.3E-01	6.2E-01
DUSP6_SMOOTH_MUSCLE	3.2E-01	7.7E-01	4.1E-06	8.0E-04	9.1E-01	1.0E+00	1.0E+00	1.0E+00	6.3E-01	1.0E+00	3.1E-02	7.3E-02
TCF3_ADIPOSE	NA	NA	7.2E-01	8.3E-01	NA	NA	NA	NA	3.7E-01	8.4E-01	4.4E-01	6.3E-01
ZNF467_LIVER	NA	NA	5.3E-01	8.4E-01	NA	NA	2.2E-01	6.6E-01	4.3E-02	4.1E-01	5.7E-01	7.9E-01
MSN_LIVER	8.8E-01	9.3E-01	2.1E-01	2.9E-01	4.4E-02	7.5E-02	9.3E-01	9.9E-01	5.8E-01	9.1E-01	2.2E-01	4.4E-01
LAMA2_ADIPOSE	NA	NA	6.2E-02	9.2E-02	8.1E-01	8.8E-01	2.6E-01	7.0E-01	7.5E-01	1.0E+00	5.6E-01	7.6E-01
KL_BRAIN	7.8E-01	9.4E-01	2.0E-01	2.9E-01	8.4E-01	1.0E+00	1.4E-01	4.8E-01	2.1E-01	7.9E-01	NA	NA
NOTCH1_PPI	2.1E-01	4.0E-01	6.3E-01	7.2E-01	5.1E-02	1.0E-01	2.1E-01	6.7E-01	8.2E-01	1.0E+00	7.9E-01	8.8E-01
AW475929_BRAIN	9.5E-02	2.0E-01	9.5E-01	9.7E-01	NA	NA	2.5E-01	6.4E-01	5.8E-01	1.0E+00	5.1E-01	7.1E-01
IL15RA_LIVER	NA	NA	6.5E-02	8.3E-02	NA	NA	8.5E-01	1.0E+00	8.1E-01	1.0E+00	6.4E-01	7.3E-01
HELZ_MUSCLE	NA	NA	6.0E-01	8.7E-01	NA	NA	4.1E-01	8.0E-01	3.4E-01	8.6E-01	2.0E-01	5.2E-01
CXCL12_LIVER	NA	NA	9.5E-01	9.8E-01	3.0E-01	1.0E+00	NA	NA	7.5E-01	1.0E+00	1.4E-01	3.0E-01
FBLN2_PPI	NA	NA	1.6E-02	2.6E-02	NA	NA	NA	NA	2.1E-01	7.6E-01	NA	NA
SORL1_VASCULAR_ENDOTHELIUM	4.7E-02	7.7E-01	3.1E-01	3.8E-01	NA	NA	8.9E-01	9.6E-01	7.7E-02	5.7E-01	9.7E-01	9.8E-01
ZDHHC17_BRAIN	3.5E-01	7.7E-01	5.8E-01	8.3E-01	5.3E-01	6.5E-01	8.6E-01	9.7E-01	7.2E-01	9.1E-01	3.5E-01	5.9E-01
LARGE_LIVER	NA	NA	3.5E-01	4.1E-01	2.3E-01	9.6E-01	NA	NA	4.8E-01	1.0E+00	6.9E-01	8.3E-01
MMT00019644_ADIPOSE	NA	NA	4.3E-01	5.2E-01	NA	NA	4.4E-01	8.0E-01	4.5E-01	9.9E-01	NA	NA
VEGFA_ADIPOSE	9.3E-01	9.7E-01	3.7E-03	2.3E-02	8.7E-01	1.0E+00	6.3E-01	8.5E-01	9.3E-01	9.7E-01	2.2E-01	5.8E-01
TRAPPC3_BRAIN	7.5E-01	9.1E-01	2.9E-01	3.9E-01	2.9E-01	1.0E+00	1.0E+00	1.0E+00	9.1E-01	1.0E+00	8.1E-01	9.0E-01
ASAH1_MUSCLE	NA	NA	1.1E-01	1.4E-01	NA	NA	9.7E-02	3.7E-01	9.7E-01	9.8E-01	1.8E-01	2.9E-01
SMAD1_PPI	7.3E-01	8.6E-01	1.8E-01	3.0E-01	7.7E-01	1.0E+00	9.7E-01	9.6E-01	5.3E-02	5.2E-01	4.0E-01	6.3E-01
BTNL9_LIVER	NA	NA	8.1E-02	1.1E-01	3.4E-01	1.0E+00	NA	NA	8.2E-01	1.0E+00	2.2E-01	5.1E-01
ABCG5_LIVER	6.7E-01	9.2E-01	3.3E-01	4.1E-01	NA	NA	3.8E-01	7.8E-01	5.2E-01	9.9E-01	5.5E-01	7.4E-01
ITGA7_ADIPOSE	NA	NA	1.1E-01	1.5E-01	3.6E-01	8.6E-01	NA	NA	6.1E-01	1.0E+00	9.5E-01	9.9E-01
COASY_MUSCLE	7.8E-01	9.3E-01	6.9E-01	8.8E-01	NA	NA	6.3E-01	8.2E-01	7.6E-01	1.0E+00	2.8E-01	4.7E-01

AK007927_MUSCLE	NA	NA	1.6E-02	3.2E-02	NA	NA	NA	NA	1.8E-01	7.1E-01	NA	NA
CTNNB1_PPI	7.3E-01	9.2E-01	9.2E-01	8.7E-01	1.3E-01	1.0E+00	9.9E-01	9.5E-01	9.4E-01	1.0E+00	7.8E-01	8.7E-01
APOF_MUSCLE	NA	NA	8.9E-02	1.5E-01	NA	NA	NA	NA	4.5E-02	6.3E-01	NA	NA
COLEC12_KIDNEY	NA	NA	4.4E-02	5.5E-02	NA	NA	NA	NA	1.5E-01	6.4E-01	NA	NA
RDH16_BRAIN	NA	NA	2.8E-01	3.3E-01	NA	NA	NA	NA	1.7E-02	2.9E-01	NA	NA
CFB_BRAIN	NA	NA	1.5E-02	1.7E-02	NA	NA	NA	NA	3.0E-01	9.0E-01	NA	NA
PAPSS2_SMOOTH_MUSCLE	NA	NA	3.0E-02	4.6E-02	7.2E-01	1.0E+00	NA	NA	2.6E-01	7.5E-01	NA	NA
HEMGN_MUSCLE	NA	NA	9.6E-03	2.4E-02	NA	NA	NA	NA	4.4E-01	9.8E-01	NA	NA
PLG_LIVER	NA	NA	2.2E-01	2.9E-01	NA	NA	NA	NA	4.4E-01	8.5E-01	NA	NA
WIPF1_LIVER	NA	NA	1.9E-01	1.0E+00	NA	NA	NA	NA	1.2E-01	5.0E-01	NA	NA
LOXL1_MUSCLE	NA	NA	8.2E-01	8.9E-01	9.8E-01	1.0E+00	NA	NA	7.8E-01	1.0E+00	NA	NA
APOC2_MUSCLE	NA	NA	5.3E-02	8.3E-02	NA	NA	NA	NA	2.7E-01	7.6E-01	NA	NA
KNG1_MUSCLE	NA	NA	7.6E-01	8.6E-01	NA	NA	NA	NA	5.7E-01	9.1E-01	NA	NA
CXCL12_MUSCLE	NA	NA	5.9E-02	8.4E-02	NA	NA	NA	NA	3.0E-01	9.2E-01	NA	NA
F2_MUSCLE	NA	NA	2.4E-01	3.2E-01	NA	NA	NA	NA	7.2E-01	1.0E+00	NA	NA
ZBTB44_LIVER	NA	NA	1.6E-01	9.8E-01	NA	NA	8.3E-01	9.7E-01	4.0E-01	9.7E-01	8.9E-01	9.7E-01
PHACTR1_BRAIN	NA	NA	7.0E-02	1.0E-01	NA	NA	NA	NA	5.8E-01	1.0E+00	NA	NA
AZGP1_ADIPOSE	NA	NA	1.2E-01	1.2E-01	NA	NA	NA	NA	5.8E-01	9.0E-01	NA	NA
FBP1_MUSCLE	NA	NA	1.1E-01	1.2E-01	NA	NA	NA	NA	6.5E-01	1.0E+00	NA	NA
NM_009245_BRAIN	NA	NA	2.5E-01	3.0E-01	NA	NA	NA	NA	4.6E-01	9.0E-01	NA	NA
KNG1_BRAIN	NA	NA	5.4E-01	6.1E-01	NA	NA	NA	NA	1.9E-01	7.4E-01	NA	NA
ACVR1C_BRAIN	NA	NA	6.0E-01	7.0E-01	NA	NA	NA	NA	2.0E-01	7.6E-01	NA	NA
APOA5_BRAIN	NA	NA	2.1E-02	2.1E-02	NA	NA	NA	NA	9.3E-01	1.0E+00	NA	NA
ALDOB_MUSCLE	NA	NA	4.3E-01	4.8E-01	NA	NA	NA	NA	4.0E-01	8.7E-01	NA	NA
RDH16_MUSCLE	NA	NA	1.9E-01	2.4E-01	NA	NA	NA	NA	7.6E-01	1.0E+00	NA	NA
BATF2_BLOOD	NA	NA	2.0E-01	2.4E-01	NA	NA	NA	NA	NA	NA	NA	NA
NGRN_LIVER	NA	NA	2.1E-01	8.3E-01	NA	NA	7.2E-01	1.0E+00	9.8E-01	9.8E-01	4.8E-01	7.3E-01
FN1_KIDNEY	NA	NA	4.4E-01	9.4E-01	NA	NA	NA	NA	6.2E-01	9.0E-01	NA	NA
APOA1_MUSCLE	NA	NA	4.6E-01	8.1E-01	NA	NA	NA	NA	6.1E-01	9.2E-01	NA	NA
MATN2_PPI	NA	NA	3.4E-01	3.8E-01	NA	NA	NA	NA	7.3E-01	9.6E-01	NA	NA
LDLR_PPI	NA	NA	3.8E-01	1.0E+00	NA	NA	NA	NA	7.0E-01	1.0E+00	NA	NA
APOA5_LIVER	8.8E-01	9.6E-01	7.0E-01	8.0E-01	NA	NA	NA	NA	2.7E-01	7.9E-01	NA	NA
THADA_BRAIN	NA	NA	8.0E-01	9.7E-01	NA	NA	NA	NA	2.8E-01	7.6E-01	NA	NA
F2_ADIPOSE	NA	NA	7.3E-01	8.3E-01	NA	NA	NA	NA	3.6E-01	8.3E-01	NA	NA
ABCG5_ADIPOSE	NA	NA	NA	NA	NA	NA	NA	NA	2.9E-01	7.7E-01	NA	NA
MMT00081256_MUSCLE	NA	NA	3.2E-01	3.5E-01	NA	NA	NA	NA	NA	NA	NA	NA
TGFBI_PPI	NA	NA	NA	NA	NA	NA	NA	NA	3.4E-01	8.6E-01	NA	NA
SERPINC1_ADIPOSE	NA	NA	9.9E-01	9.9E-01	NA	NA	NA	NA	3.6E-02	4.9E-01	NA	NA
NCOR2_KIDNEY	NA	NA	4.7E-01	8.8E-01	NA	NA	NA	NA	NA	NA	NA	NA
PLG_ADIPOSE	NA	NA	5.0E-01	5.8E-01	NA	NA	NA	NA	8.9E-01	9.9E-01	NA	NA
OSM_PPI	NA	NA	NA	NA	NA	NA	NA	NA	6.7E-01	9.2E-01	NA	NA
HGD_BRAIN	NA	NA	3.9E-01	1.0E+00	NA	NA	NA	NA	9.4E-01	9.9E-01	NA	NA
APOB_ADIPOSE	NA	NA	9.4E-01	9.8E-01	NA	NA	NA	NA	4.1E-01	8.7E-01	NA	NA
APOC4_BRAIN	NA	NA	4.9E-01	5.8E-01	NA	NA	NA	NA	9.4E-01	9.7E-01	NA	NA
M93275_BRAIN	NA	NA	8.3E-01	9.3E-01	NA	NA	NA	NA	NA	NA	NA	NA
APOC3_BRAIN	NA	NA	NA	NA	NA	NA	NA	NA	8.4E-01	1.0E+00	NA	NA
VPS33A_ADIPOSE	NA	NA	7.5E-01	9.7E-01	NA	NA	NA	NA	8.9E-01	1.0E+00	NA	NA
APOA1_ADIPOSE	NA	NA	7.2E-01	8.2E-01	NA	NA	NA	NA	9.1E-01	1.0E+00	NA	NA
MCOLN1_BRAIN	NA	NA	8.6E-01	9.1E-01	NA	NA	6.4E-01	9.7E-01	8.4E-01	9.8E-01	7.5E-01	8.8E-01
APOA1_BRAIN	NA	NA	9.7E-01	1.0E+00	NA	NA	NA	NA	9.0E-01	1.0E+00	NA	NA

Part 2

Subnetworks	Stem_Cell		Stimulated_Monocytes		Subcutaneous_Adipose		T_cell		Dataset Consistency	Z-Scores	Meta-Pvalues
	P_Values	FDRs	P_Values	FDRs	P_Values	FDRs	P_Values	FDRs			
DUSP6_AORTA	8.9E-03	2.8E-01	1.6E-02	4.8E-01	1.1E-01	5.5E-01	2.1E-02	2.9E-01	2	8.466	p<1.0E-16
IRF1_ARTERY	2.2E-01	5.5E-01	7.9E-03	6.8E-02	2.2E-03	2.6E-02	2.9E-01	5.5E-01	5	8.052	4.44E-16
MSN_VASCULAR_ENDOTHELIUM	2.8E-03	2.5E-01	2.7E-01	7.2E-01	3.2E-01	7.5E-01	2.0E-02	2.2E-01	3	8.038	4.44E-16
LUM_BRAIN	4.8E-01	7.4E-01	7.5E-01	9.7E-01	9.6E-01	9.8E-01	1.9E-03	5.0E-02	3	7.306	1.38E-13
CXCL10_LIVER	4.8E-01	7.7E-01	1.6E-01	4.8E-01	7.5E-01	9.4E-01	2.5E-01	5.0E-01	4	6.863	3.37E-12
GBP1_VASCULAR_ENDOTHELIUM	1.0E-01	3.8E-01	1.3E-03	3.8E-02	2.6E-01	7.3E-01	1.9E-01	4.7E-01	3	6.699	1.05E-11
IFI35_ARTERY	7.6E-01	9.3E-01	4.9E-06	1.6E-03	1.7E-02	1.5E-01	2.1E-03	9.5E-02	3	6.651	1.46E-11
CCL18_AORTA	1.4E-01	5.0E-01	1.7E-01	5.8E-01	2.2E-01	7.3E-01	4.1E-03	3.6E-01	2	6.384	8.61E-11
DUSP6_VASCULAR_ENDOTHELIUM	8.9E-03	1.3E-01	4.7E-03	1.4E-01	9.3E-01	1.0E+00	9.6E-02	3.8E-01	3	6.347	1.10E-10
SHC1_PPI	7.3E-02	3.6E-01	2.0E-01	6.4E-01	5.9E-01	8.5E-01	5.5E-01	6.4E-01	2	5.953	1.32E-09
MAFF_LIVER	4.1E-02	2.2E-01	6.0E-01	8.5E-01	2.9E-01	5.8E-01	4.1E-01	5.9E-01	2	5.946	1.37E-09
DUSP1_AORTA	9.4E-03	2.5E-01	2.8E-01	6.4E-01	8.3E-01	9.0E-01	1.2E-02	2.1E-01	2	5.454	2.46E-08
ZYX_SMOOTH_MUSCLE	2.7E-01	5.8E-01	5.2E-03	4.1E-01	8.3E-01	1.0E+00	1.6E-01	3.6E-01	3	5.239	8.06E-08
TNFAIP2_CARDIAC_MUSCLE	1.4E-02	2.4E-01	8.7E-01	9.6E-01	4.7E-03	1.6E-01	5.7E-01	6.5E-01	2	5.173	1.15E-07
ADM_ARTERY	5.2E-02	3.1E-01	5.3E-01	7.6E-01	1.2E-02	8.4E-02	3.1E-01	5.5E-01	2	5.146	1.33E-07
DUSP6_ARTERY	1.4E-02	2.2E-01	2.1E-02	4.2E-01	8.4E-01	9.3E-01	3.0E-01	6.0E-01	3	5.015	2.65E-07
CFD_AORTA	4.1E-03	2.3E-01	9.2E-01	9.6E-01	1.2E-01	4.9E-01	9.2E-02	3.7E-01	2	4.996	2.93E-07
MMT00002956_LIVER	3.9E-01	6.8E-01	9.5E-01	9.6E-01	7.7E-02	3.0E-01	3.4E-01	5.5E-01	2	4.937	3.97E-07
SLC2A3_AORTA	7.8E-02	4.0E-01	2.8E-01	7.1E-01	7.4E-01	8.8E-01	3.7E-01	5.8E-01	2	4.901	4.76E-07
ANXA3_LIVER	5.0E-02	2.4E-01	7.9E-01	9.6E-01	2.5E-01	5.8E-01	3.4E-01	5.4E-01	1	4.825	7.02E-07
DUSP1_SMOOTH_MUSCLE	1.5E-02	2.3E-01	3.4E-01	7.1E-01	9.8E-01	9.5E-01	7.3E-01	7.6E-01	3	4.666	1.54E-06
MMP9_PPI	3.4E-01	6.3E-01	5.6E-03	2.3E-01	7.2E-02	3.0E-01	NA	NA	1	4.607	2.05E-06
ADAM9_AORTA	7.5E-02	3.4E-01	2.0E-02	4.1E-01	6.3E-01	8.9E-01	1.2E-01	4.4E-01	3	4.406	5.26E-06
RAC2_CARDIAC_MUSCLE	5.1E-01	7.5E-01	8.9E-01	9.4E-01	1.1E-01	4.8E-01	2.0E-03	1.6E-01	2	4.330	7.45E-06
HLA-F_ARTERY	1.7E-01	4.3E-01	1.7E-02	1.6E-01	1.8E-01	5.1E-01	7.1E-02	5.0E-01	2	4.307	8.29E-06
ISG15_CARDIAC_MUSCLE	9.3E-01	9.7E-01	9.9E-03	9.2E-02	1.0E-04	1.2E-03	2.5E-01	5.3E-01	4	4.249	1.07E-05
SLIT2_AORTA	4.0E-02	3.5E-01	5.2E-01	7.5E-01	4.8E-03	1.9E-01	1.2E-01	4.7E-01	1	4.210	1.28E-05
ANXA1_ARTERY	1.7E-01	3.8E-01	8.5E-02	6.0E-01	5.3E-01	8.0E-01	1.3E-01	3.8E-01	1	4.200	1.34E-05
COL1A1_LIVER	1.6E-01	4.8E-01	6.0E-01	7.8E-01	2.5E-01	6.0E-01	5.1E-01	6.4E-01	1	4.166	1.55E-05
DUSP1_ARTERY	1.1E-03	1.6E-02	4.5E-01	7.7E-01	6.5E-01	8.7E-01	2.7E-01	5.7E-01	4	4.120	1.90E-05
STAT3_PPI	6.9E-01	8.8E-01	6.3E-01	8.4E-01	7.4E-01	9.6E-01	8.6E-01	8.5E-01	1	3.992	3.27E-05
KCNK13_LIVER	1.5E-01	4.0E-01	3.8E-01	7.1E-01	4.0E-02	1.9E-01	2.8E-01	4.9E-01	1	3.945	3.98E-05
SDCBP_AORTA	3.2E-01	6.4E-01	2.2E-01	7.0E-01	6.6E-01	8.9E-01	1.2E-01	3.7E-01	2	3.861	5.64E-05
DUSP6_CARDIAC_MUSCLE	4.1E-03	2.3E-01	3.3E-01	7.1E-01	5.2E-01	8.5E-01	3.7E-01	5.8E-01	2	3.811	6.92E-05
IRF7_ADIPOSE	9.5E-01	9.7E-01	5.1E-04	1.5E-02	NA	NA	3.9E-02	2.4E-01	2	3.745	9.02E-05
PTPN11_PPI	4.3E-02	3.0E-01	2.8E-02	4.9E-01	4.7E-01	7.6E-01	2.8E-01	6.0E-01	1	3.697	1.09E-04
ANXA1_SMOOTH_MUSCLE	3.9E-02	2.4E-01	6.3E-02	5.6E-01	6.8E-01	8.6E-01	7.0E-01	7.6E-01	2	3.565	1.82E-04
BST2_ARTERY	4.4E-01	7.2E-01	1.6E-02	7.6E-02	1.2E-02	1.6E-01	6.4E-01	7.5E-01	2	3.559	1.86E-04

IRF9_SMOOTH_MUSCLE	8.9E-01	9.7E-01	2.7E-05	8.2E-04	9.1E-02	3.3E-01	6.7E-02	5.6E-01	2	3.487	2.45E-04
TRIM22_VASCULAR_ENDOTHELIUM	9.6E-01	9.9E-01	2.3E-03	2.0E-02	6.4E-03	4.9E-02	1.6E-01	3.5E-01	4	3.324	4.44E-04
CD74_ADIPOSE	5.7E-01	8.3E-01	9.7E-01	9.9E-01	NA	NA	1.2E-02	2.1E-01	2	3.318	4.53E-04
C1R_CARDIAC_MUSCLE	7.5E-02	4.0E-01	7.1E-01	8.5E-01	1.0E-01	4.8E-01	8.0E-02	3.5E-01	2	3.223	6.34E-04
JAG1_VASCULAR_ENDOTHELIUM	6.0E-01	8.8E-01	6.4E-01	8.6E-01	2.2E-01	5.1E-01	NA	NA	2	3.120	9.05E-04
KLF6_SMOOTH_MUSCLE	2.8E-03	2.3E-01	9.7E-01	9.8E-01	2.9E-01	7.5E-01	4.1E-01	6.0E-01	2	3.118	9.11E-04
GBP2_BLOOD	7.9E-01	9.7E-01	2.3E-01	4.9E-01	NA	NA	3.7E-01	5.8E-01	2	3.108	9.42E-04
ANXA2_CARDIAC_MUSCLE	8.2E-03	1.2E-01	1.1E-02	5.7E-01	4.0E-01	8.3E-01	8.6E-01	7.7E-01	1	3.054	1.13E-03
CTSB_SMOOTH_MUSCLE	6.7E-02	3.0E-01	9.4E-01	9.7E-01	3.2E-02	2.2E-01	4.6E-01	6.3E-01	1	3.037	1.19E-03
PAPSS2_CARDIAC_MUSCLE	1.7E-01	4.6E-01	5.0E-01	7.2E-01	1.3E-01	4.5E-01	3.5E-01	5.1E-01	1	2.992	1.39E-03
COL5A1_ADIPOSE	7.9E-02	4.0E-01	2.2E-01	6.1E-01	1.3E-04	1.6E-03	1.8E-02	1.5E-01	1	2.984	1.42E-03
COL4A2_PPI	4.4E-01	5.8E-01	NA	NA	3.3E-01	5.6E-01	NA	NA	1	2.887	1.94E-03
GBP1_BLOOD	2.1E-02	1.8E-01	8.9E-03	3.2E-02	NA	NA	NA	NA	1	2.850	2.19E-03
CD14_ADIPOSE	8.7E-01	9.7E-01	9.0E-02	2.4E-01	NA	NA	3.1E-01	5.4E-01	2	2.637	4.18E-03
GEM_KIDNEY	4.1E-01	6.9E-01	9.2E-01	9.8E-01	NA	NA	NA	NA	1	2.635	4.21E-03
PTCHD1_ADIPOSE	6.7E-02	3.0E-01	1.3E-01	6.6E-01	7.3E-01	9.8E-01	4.1E-01	5.7E-01	0	2.454	7.06E-03
IGSF10_MUSCLE	3.7E-01	6.1E-01	9.6E-02	6.1E-01	1.7E-02	8.0E-02	8.2E-02	2.9E-01	2	2.193	1.42E-02
CXCL12_CARDIAC_MUSCLE	3.7E-01	5.7E-01	1.8E-01	6.7E-01	2.3E-02	1.7E-01	4.5E-01	6.1E-01	1	2.140	1.62E-02
CXCL12_ADIPOSE	2.1E-02	2.8E-01	8.5E-01	9.9E-01	6.1E-01	8.8E-01	3.0E-02	2.1E-01	0	2.109	1.75E-02
BNIP3L_AORTA	1.9E-01	4.1E-01	5.6E-01	8.7E-01	9.0E-01	9.4E-01	3.8E-01	5.4E-01	1	2.091	1.83E-02
ANXA2_PPI	6.3E-02	2.9E-01	1.8E-01	6.9E-01	7.7E-01	9.5E-01	8.4E-01	9.1E-01	1	1.975	2.42E-02
LOXL2_LIVER	4.3E-01	6.0E-01	3.3E-01	6.9E-01	1.1E-01	3.2E-01	NA	NA	1	1.887	2.96E-02
LY96_VASCULAR_ENDOTHELIUM	7.7E-01	9.8E-01	2.8E-01	5.5E-01	9.2E-01	9.7E-01	NA	NA	1	1.871	3.06E-02
IFI30_SMOOTH_MUSCLE	8.3E-01	9.8E-01	6.9E-02	1.7E-01	2.5E-01	5.9E-01	5.3E-01	6.5E-01	1	1.819	3.44E-02
HGD_MUSCLE	1.4E-02	2.2E-01	NA	NA	NA	NA	NA	NA	0	1.779	3.76E-02
ADM_SMOOTH_MUSCLE	4.7E-02	2.3E-01	8.0E-01	9.4E-01	4.8E-01	8.7E-01	6.8E-01	7.4E-01	1	1.750	4.00E-02
ITGB4_AORTA	6.4E-01	8.7E-01	2.8E-01	5.7E-01	1.8E-01	4.8E-01	4.8E-01	6.1E-01	1	1.709	4.38E-02
SLC1A5_MUSCLE	8.1E-01	9.9E-01	2.7E-01	5.2E-01	1.3E-02	9.3E-02	3.1E-01	5.1E-01	0	1.661	4.83E-02
COL6A3_LIVER	3.3E-01	5.6E-01	3.4E-01	7.2E-01	3.0E-01	5.3E-01	1.3E-01	3.8E-01	1	1.648	4.97E-02
IGFBP6_ARTERY	4.5E-01	7.2E-01	5.3E-01	7.6E-01	5.1E-01	8.3E-01	4.6E-02	2.3E-01	1	1.630	5.15E-02
EPS8_LIVER	5.6E-01	8.0E-01	4.8E-01	7.3E-01	NA	NA	3.7E-02	2.3E-01	1	1.618	5.28E-02
ABCG8_LIVER	8.8E-02	4.4E-01	1.9E-01	4.5E-01	NA	NA	4.8E-02	2.1E-01	0	1.556	5.99E-02
CYP1B1_BRAIN	1.4E-01	3.7E-01	4.2E-01	7.1E-01	8.4E-01	9.7E-01	8.3E-02	4.5E-01	1	1.542	6.16E-02
SPARC_MUSCLE	1.2E-02	1.2E-01	4.7E-01	7.5E-01	7.2E-03	8.0E-02	3.8E-01	5.2E-01	1	1.503	6.64E-02
FN1_PPI	2.4E-01	5.5E-01	4.2E-01	7.3E-01	8.5E-01	9.6E-01	7.5E-02	2.9E-01	1	1.396	8.14E-02
GBP1_ADIPOSE	9.4E-01	9.9E-01	4.4E-03	2.1E-02	NA	NA	1.2E-01	5.4E-01	2	1.323	9.30E-02
APOB_PPI	3.4E-01	5.3E-01	1.4E-01	6.7E-01	6.6E-01	8.8E-01	1.5E-01	3.6E-01	0	1.300	9.67E-02
EFEMP1_CARDIAC_MUSCLE	8.0E-01	9.4E-01	1.7E-01	6.9E-01	2.4E-01	5.5E-01	8.7E-02	4.0E-01	2	1.239	1.08E-01
WWC2_AORTA	2.3E-01	4.5E-01	2.8E-01	6.9E-01	8.9E-01	9.4E-01	NA	NA	1	1.172	1.21E-01
ZNF496_LIVER	1.2E-02	1.7E-01	5.2E-01	7.7E-01	NA	NA	1.3E-01	3.9E-01	0	1.097	1.36E-01
DPYD_CARDIAC_MUSCLE	1.2E-01	3.7E-01	1.6E-01	4.3E-01	6.3E-01	8.8E-01	4.9E-01	6.4E-01	1	1.029	1.52E-01
COL4A2_MUSCLE	3.0E-01	5.3E-01	5.7E-01	7.9E-01	1.2E-01	3.8E-01	4.2E-01	5.3E-01	0	0.883	1.89E-01
SLIT3_MUSCLE	1.1E-01	4.0E-01	9.0E-01	9.6E-01	1.4E-01	4.6E-01	NA	NA	0	0.695	2.44E-01
SCARA3_MUSCLE	1.8E-01	3.7E-01	7.6E-01	9.8E-01	4.8E-01	8.7E-01	NA	NA	0	0.553	2.90E-01
CKLF_LIVER	3.6E-01	6.4E-01	2.1E-01	7.1E-01	3.6E-01	7.5E-01	5.9E-01	7.0E-01	0	0.430	3.33E-01
MTMR11_LIVER	4.4E-01	7.2E-01	1.7E-01	6.4E-01	4.8E-01	7.5E-01	3.5E-01	5.4E-01	0	0.357	3.61E-01
PCOLCE2_LIVER	2.8E-01	5.6E-01	8.9E-01	9.8E-01	9.0E-01	9.5E-01	1.9E-01	3.7E-01	1	0.282	3.89E-01
DUSP6_SMOOTH_MUSCLE	3.4E-01	6.1E-01	6.8E-01	9.1E-01	7.8E-01	9.8E-01	NA	NA	1	0.197	4.22E-01
TCF3_ADIPOSE	4.1E-01	6.9E-01	1.2E-01	6.4E-01	NA	NA	3.8E-03	1.5E-01	0	0.187	4.26E-01
ZNF467_LIVER	1.5E-01	3.7E-01	4.8E-01	7.1E-01	NA	NA	NA	NA	0	-0.015	5.06E-01
MSN_LIVER	4.4E-01	7.0E-01	7.8E-01	9.3E-01	8.7E-01	9.8E-01	1.0E-01	3.7E-01	0	-0.031	5.12E-01
LAMA2_ADIPOSE	3.6E-01	5.8E-01	4.2E-01	7.0E-01	3.4E-01	5.4E-01	NA	NA	0	-0.064	5.25E-01
KL_BRAIN	3.5E-01	6.2E-01	2.6E-01	6.9E-01	8.5E-01	9.6E-01	NA	NA	0	-0.237	5.94E-01
NOTCH1_PPI	9.2E-01	9.6E-01	6.0E-01	8.7E-01	7.1E-01	8.9E-01	4.1E-01	5.2E-01	0	-0.245	5.97E-01
AW475929_BRAIN	6.5E-01	7.9E-01	2.3E-01	6.7E-01	NA	NA	3.6E-01	5.7E-01	0	-0.263	6.04E-01
IL15RA_LIVER	3.4E-02	2.6E-01	8.6E-01	9.6E-01	NA	NA	1.2E-01	4.7E-01	0	-0.422	6.63E-01
HELZ_MUSCLE	9.0E-01	9.7E-01	4.1E-01	6.9E-01	NA	NA	1.6E-01	3.6E-01	0	-0.425	6.65E-01
CXCL12_LIVER	1.6E-01	3.9E-01	2.5E-01	6.2E-01	4.1E-01	7.5E-01	NA	NA	0	-0.449	6.73E-01
FBLN2_PPI	7.0E-02	5.3E-01	NA	NA	NA	NA	NA	NA	1	-0.468	6.80E-01
SORL1_VASCULAR_ENDOTHELIUM	6.4E-01	8.6E-01	1.0E+00	1.0E+00	NA	NA	2.2E-01	3.6E-01	0	-0.487	6.87E-01
ZDHHC17_BRAIN	5.3E-02	2.2E-01	8.9E-01	9.9E-01	6.2E-01	9.0E-01	7.3E-01	7.8E-01	0	-0.545	7.07E-01
LARGE_LIVER	5.3E-01	7.7E-01	NA	NA	1.6E-01	3.7E-01	NA	NA	0	-0.569	7.15E-01
MMT00019644_ADIPOSE	6.3E-01	8.8E-01	3.9E-01	7.2E-01	NA	NA	1.2E-01	4.3E-01	0	-0.570	7.16E-01
VEGFA_ADIPOSE	6.7E-01	9.0E-01	1.4E-01	5.7E-01	NA	NA	NA	NA	1	-0.625	7.34E-01
TRAPPC3_BRAIN	1.8E-01	5.0E-01	4.3E-01	7.1E-01	5.6E-03	1.1E-01	8.4E-01	8.9E-01	0	-0.637	7.38E-01
ASAH1_MUSCLE	4.6E-01	7.1E-01	6.5E-01	8.8E-01	NA	NA	NA	NA	0	-0.674	7.50E-01
SMAD1_PPI	2.4E-01	5.8E-01	4.8E-01	7.6E-01	5.1E-01	7.9E-01	1.0E+00	9.6E-01	0	-0.751	7.74E-01
BTNL9_LIVER	9.8E-01	9.9E-01	4.5E-01	7.4E-01	5.0E-01	8.1E-01	NA	NA	0	-0.865	8.06E-01
ABCG5_LIVER	6.4E-01	7.8E-01	6.0E-01	8.3E-01	NA	NA	NA	NA	0	-0.957	8.31E-01
ITGA7_ADIPOSE	7.9E-01	9.2E-01	8.3E-01	9.6E-01	1.3E-01	3.5E-01	NA	NA	0	-1.111	8.67E-01
COASY_MUSCLE	7.6E-01	9.7E-01	2.8E-01	6.6E-01	NA	NA	5.3E-01	6.3E-01	0	-1.137	8.72E-01
AK007927_MUSCLE	NA	NA	NA	NA	NA	NA	NA	NA	1	-1.158	8.77E-01
CTNNB1_PPI	9.6E-01	9.7E-01	4.4E-01	7.5E-01	2.5E-01	5.7E-01	2.1E-03	2.7E-01	0	-1.169	8.79E-01
APOF_MUSCLE	NA	NA	NA	NA	NA	NA	NA	NA	0	-1.169	8.79E-01
COLEC12_KIDNEY	NA	NA	NA	NA	NA	NA	NA	NA	0	-1.258	8.96E-01
RDH16_BRAIN	NA	NA	NA	NA	NA	NA	NA	NA	0	-1.268	8.98E-01
CFB_BRAIN	NA	NA	NA	NA	NA	NA	NA	NA	1	-1.285	9.01E-01
PAPSS2_SMOOTH_MUSCLE	NA	NA	NA	NA	8.3E-01	9.4E-01	NA	NA	1	-1.288	9.01E-01
HEMGN_MUSCLE	NA	NA	NA	NA	NA	NA	NA	NA	1	-1.343	9.10E-01
PLG_LIVER	2.4E-01	4.6E-01	NA	NA	NA	NA	NA	NA	0	-1.354	9.12E-01
WIPF1_LIVER	6.7E-01	8.9E-01	NA	NA	NA	NA	NA	NA	0	-1.362	9.13E-01
LOXL1_MUSCLE	5.1E-01	6.4E-01	NA	NA	1.6E-02	7.0E-02	2.9E-01	5.6E-01	0	-1.383	9.17E-01
APOC2_MUSCLE	NA	NA	NA	NA	NA	NA	NA	NA	0	-1.421	9.22E-01
KNG1_MUSCLE	1.5E-01	4.1E-01	3.5E-01	7.2E-01	NA	NA	NA	NA	0	-1.429	9.24E-01
CXCL12_MUSCLE	NA	NA	NA	NA	NA	NA	NA	NA	0	-1.467	9.29E-01
F2_MUSCLE	5.3E-01	7.9E-01	6.1E-01	8.4E-01	NA	NA	NA	NA	0	-1.676	9.53E-01
ZBTB44_LIVER	7.8E-01	9.7E-01	8.2E-01	9.6E-01	NA	NA	6.2E-01	7.2E-01	0	-1.728	9.58E-01
PHACTR1_BRAIN	8.4E-01	9.3E-01	7.8E-01	9.4E-01	NA	NA	NA	NA	0	-1.752	9.60E-01
AZGP1_ADIPOSE	NA	NA	NA	NA	NA	NA	NA	NA	0	-1.817	9.65E-01
FBP1_MUSCLE	NA	NA	NA	NA	NA	NA	NA	NA	0	-1.860	9.69E-01
NM_009245_BRAIN	NA	NA	NA	NA	NA	NA	NA	NA	0	-1.882	9.70E-01
KNG1_BRAIN	NA	NA	NA	NA	NA	NA	NA	NA	0	-1.885	9.70E-01
ACVR1C_BRAIN	8.1E-01	9.7E-01	NA	NA	NA	NA	NA	NA	0	-1.949	9.74E-01

APOA5_BRAIN	NA	NA	NA	NA	NA	NA	NA	NA	1	-1.960	9.75E-01
ALDOB_MUSCLE	NA	NA	NA	NA	NA	NA	NA	NA	0	-1.986	9.76E-01
RDH16_MUSCLE	NA	NA	NA	NA	NA	NA	NA	NA	0	-2.077	9.81E-01
BATF2_BLOOD	NA	NA	NA	NA	NA	NA	NA	NA	0	-2.129	9.83E-01
NGRN_LIVER	9.8E-01	9.9E-01	3.0E-01	6.9E-01	NA	NA	8.3E-01	9.1E-01	0	-2.132	9.83E-01
FN1_KIDNEY	NA	NA	NA	NA	NA	NA	NA	NA	0	-2.176	9.85E-01
APOA1_MUSCLE	NA	NA	NA	NA	NA	NA	NA	NA	0	-2.185	9.86E-01
MATN2_PPI	NA	NA	NA	NA	NA	NA	NA	NA	0	-2.191	9.86E-01
LDLR_PPI	NA	NA	NA	NA	NA	NA	NA	NA	0	-2.201	9.86E-01
APOA5_LIVER	NA	NA	NA	NA	NA	NA	NA	NA	0	-2.210	9.86E-01
THADA_BRAIN	NA	NA	NA	NA	NA	NA	NA	NA	0	-2.210	9.86E-01
F2_ADIPOSE	NA	NA	NA	NA	NA	NA	NA	NA	0	-2.212	9.87E-01
ABCG5_ADIPOSE	NA	NA	NA	NA	NA	NA	NA	NA	0	-2.219	9.87E-01
MMT00081256_MUSCLE	NA	NA	NA	NA	NA	NA	NA	NA	0	-2.245	9.88E-01
TGFBI_PPI	NA	NA	NA	NA	NA	NA	NA	NA	0	-2.263	9.88E-01
SERPINC1_ADIPOSE	NA	NA	NA	NA	NA	NA	NA	NA	0	-2.285	9.89E-01
NCOR2_KIDNEY	NA	NA	NA	NA	NA	NA	NA	NA	0	-2.373	9.91E-01
PLG_ADIPOSE	NA	NA	NA	NA	NA	NA	NA	NA	0	-2.505	9.94E-01
OSM_PPI	NA	NA	NA	NA	NA	NA	NA	NA	0	-2.534	9.94E-01
HGD_BRAIN	NA	NA	1.7E-02	2.7E-01	NA	NA	NA	NA	0	-2.544	9.95E-01
APOB_ADIPOSE	NA	NA	NA	NA	NA	NA	NA	NA	0	-2.554	9.95E-01
APOC4_BRAIN	NA	NA	NA	NA	NA	NA	NA	NA	0	-2.598	9.95E-01
M93275_BRAIN	NA	NA	NA	NA	NA	NA	NA	NA	0	-2.699	9.97E-01
APOC3_BRAIN	NA	NA	NA	NA	NA	NA	NA	NA	0	-2.706	9.97E-01
VPS33A_ADIPOSE	NA	NA	NA	NA	NA	NA	NA	NA	0	-2.731	9.97E-01
APOA1_ADIPOSE	NA	NA	NA	NA	NA	NA	NA	NA	0	-2.744	9.97E-01
MCOLN1_BRAIN	7.8E-01	9.8E-01	8.1E-01	9.5E-01	NA	NA	9.7E-01	9.8E-01	0	-2.884	9.98E-01
APOA1_BRAIN	NA	NA	NA	NA	NA	NA	NA	NA	0	-3.125	9.99E-01

Note: The minimum and maximum sizes of the KD subnetworks in GSEA are set to 10 and 500 separately. The subnetworks out of the range in all the expression profiles are not shown here ("NA" represents that the subnetwork is out of range in the expression profiles). "P_Values" represent the the nominal p-value in GSEA, which estimates the statistical significance of a single subnetwork's enrichment score. "Dataset Consistency" represent the statistical consistency of the KD subnetworks in expression perturbation (FDR<0.05).

Supplemental Table V. Functional annoations of KD subnetworks in Molecular Signatures Database (MSigDB).

Subnetworks	Subnet Size	Pathway Sources	Gene Category	P values in Fisher's Exact Test	Bonferroni corrected P values	Subnetwork Genes in the functional categories
ABCG5_adipose	18	REACTOME	Abca transporters in lipid homeostasis	1.60E-04	2.10E-01	ABCG5;ABCG8
ABCG5_adipose	18	REACTOME	Abc family proteins mediated transport	5.80E-04	7.80E-01	ABCG5;ABCG8
ABCG5_liver	33	REACTOME	Metabolism of lipids and lipoproteins	3.90E-04	5.20E-01	CHKA;SREBF1;ABCG8;SQLE;SPHK2;ABCG5
ABCG5_liver	33	REACTOME	Abca transporters in lipid homeostasis	6.70E-04	8.90E-01	ABCG8;ABCG5
ABCG8_liver	30	REACTOME	Abca transporters in lipid homeostasis	5.40E-04	7.20E-01	ABCG8;ABCG5
ABCG8_liver	30	REACTOME	Abc family proteins mediated transport	2.00E-03	1.00E+00	ABCG8;ABCG5
ACCN1_islet	13	REACTOME	Abca transporters in lipid homeostasis	5.40E-04	7.20E-01	ABCG8;ABCG5
ACCN1_islet	13	REACTOME	Abc family proteins mediated transport	2.00E-03	1.00E+00	ABCG8;ABCG5
ACCN1_islet	13	REACTOME	ABCA transporters in lihomeostasis	7.20E-01	5.40E-04	ABCG8;ABCG5
ACVR1C_brain	37	REACTOME	Glutamate neurotransmitter release cycle	1.90E-04	2.50E-01	GLS;SLC17A7
ACVR1C_brain	37	REACTOME	Neurotransmitter release cycle	1.00E-03	1.00E+00	GLS;SLC17A7
ADAM9_aorta	93	NABA	Core matrisome	7.60E-08	5.70E-11	POSTN;COL15A1;COL16A1;COMP;VCAN;AEBP1;FBN1;NID2;FN1;IGFBP3;IGFBP6;LAMA4;LAMB2;LUM;MGP;ASPN
ADAM9_aorta	93	PID	Integrin3 pathway	2.40E-05	1.80E-08	FBN1;FN1;KDR;LAMA4;PDGFRB;PLAU;PLAUR
ADM_artery	89	PID	ATF2 pathway	3.60E-04	2.70E-07	GADD45A;DUSP1;DUSP5;IL6;JUNB;ATF3;PLAU
ADM_artery	89	PID	AP1 pathway	1.20E-03	8.80E-07	DUSP1;FOSL2;CYR61;IL6;JUNB;ATF3;PLAU
ADM_smooth_muscle	41	PID	HIF1 tf pathway	9.90E-02	7.40E-05	ADM;HMOX1;BHLHE40;NDRG1
AK007927_muscle	16	REACTOME	Organic cation anion zwitterion transport	3.80E-05	5.10E-02	SLC22A4;SLC22A5
AK007927_muscle	16	REACTOME	Transport of glucose and other sugars bile salts and organic acids metal ions and amine compounds	1.90E-03	1.00E+00	SLC22A4;SLC22A5
AK007927_muscle	16	REACTOME	Organic cation anion zwitterion transport	5.10E-02	3.80E-05	SLC22A4;SLC22A5
AK021074_kidney	11	BIOCARTA	Myosin pathway	3.30E-05	4.40E-02	GNA13;PRKCA
AK021074_kidney	11	BIOCARTA	Par1 pathway	4.70E-05	6.20E-02	GNA13;PRKCA
AK021074_kidney	11	BIOCARTA	Myosin pathway	4.40E-02	3.30E-05	GNA13;PRKCA
ALDOB_muscle	30	KEGG	Ppar signaling pathway	1.30E-05	1.70E-02	SLC27A5;FABP1;APOA5;APOC3
ALDOB_muscle	30	PID	Hnf3bpathway	1.20E-04	1.60E-01	ALDOB;F2;TTR
ANXA1_artery	34	BIOCARTA	Platelet APP pathway	9.50E-03	7.10E-06	PLAT;PLAU;COL4A2
ANXA1_artery	34	REACTOME	Hemostasis	3.00E-01	2.30E-04	IRF1;ATP1B3;PLAT;PLAU;TIMP1;CAV1;F3
ANXA1_smooth_muscle	59	PID	IL6 7pathway	3.10E-03	2.30E-06	IRF1;JUNB;MCL1;TIMP1;CEBPD
ANXA1_smooth_muscle	59	PID	AP1 pathway	2.20E-02	1.70E-05	HIF1A;JUNB;MAF;TIMP1;DUSP1
ANXA2_cardiac_muscle	233	REACTOME	Response to elevated platelet cytosolic ca2	3.40E-07	2.60E-10	SERPINE1;PFN1;SERPINA1;PSAP;STX4;THBS1;TIMP1;VCL;CALM1;CALU;CD9;CD63;WDR1;ALDOA;FN1
ANXA2_cardiac_muscle	233	REACTOME	Platelet activation signaling and aggregation	1.70E-06	1.20E-09	ITPR3;RHOA;LYN;SERPINE1;PFN1;SERPINA1;PSAP;SHC1;STX4;THBS1;TIMP1;VCL;YWHAZ;CALM1;CALU;CD9;CD63;WDR1;ALDOA;FN1;GRB2
ANXA2_PPI	22	BIOCARTA	Srcrptp pathway	2.00E-09	2.60E-06	PRKCB;PRKCA;SRC;GRB2
ANXA2_PPI	22	BIOCARTA	Cbl pathway	4.30E-09	5.70E-06	PRKCB;PRKCA;SRC;GRB2
ANXA3_liver	49	NABA	Matrisome associated	5.90E-04	7.80E-01	LGALS3;SERPINB6;CXCL6;ANXA3;PLAU;PLXDC2;CTSS;SLPI
ANXA3_liver	49	NABA	ECM regulators	3.60E-03	1.00E+00	SERPINB6;PLAU;CTSS;SLPI
ANXA3_liver	49	NABA	Matrisome associated	7.80E-01	5.90E-04	CXCL6;PLAU;PLXDC2;SERPINB6;SLPI;ANXA3;CTSS;LGALS3
APOA1_adipose	32	PID	Hnf3bpathway	5.50E-08	7.30E-05	TAT;ALB;F2;APOA1;TTR
APOA1_adipose	32	BIOCARTA	Ami pathway	1.20E-07	1.50E-04	FGA;PLG;SERPINC1;F2
APOA1_brain	30	REACTOME	Hdl mediated lipid transport	2.60E-04	3.40E-01	APOA1;APOC3
APOA1_brain	30	REACTOME	Chylomicron mediated lipid transport	2.90E-04	3.90E-01	APOA1;APOC3
APOA1_muscle	16	KEGG	Complement and coagulation cascades	1.30E-10	1.70E-07	FGG;C4BPA;SERPIND1;C8G;F2;KNG1
APOA1_muscle	16	BIOCARTA	Intrinsic pathway	2.90E-06	3.90E-03	FGG;F2;KNG1
APOA5_brain	32	REACTOME	Gamma carboxylation transport and amino terminal cleavage of proteins	1.40E-03	1.00E-06	PROC;PROZ;F10
APOA5_liver	23	KEGG	Beta alanine metabolism	2.40E-04	3.20E-01	MLYCD;ALDH2
APOA5_liver	23	KEGG	Propanoate metabolism	5.50E-04	7.30E-01	MLYCD;ALDH2

APOA5_liver	23	KEGG	Beta alanine metabolism	3.20E-01	2.40E-04	ALDH2;MLYCD
APOB_adipose	27	REACTOME	Synthesis of bile acids and bile salts via 7alpha hydroxycholesterol	1.30E-06	1.70E-03	AKR1D1;CYP8B1;BAAT
APOB_adipose	27	KEGG	Primary bile acid biosynthesis	1.50E-06	2.00E-03	AKR1D1;CYP8B1;BAAT
APOB_PPI	18	REACTOME	Chylomicron mediated lipid transport	6.70E-11	8.90E-08	APOA1;MTTP;LDLR;LIPC;APOB
APOB_PPI	18	REACTOME	Lipoprotein metabolism	1.50E-09	2.00E-06	APOA1;MTTP;LDLR;LIPC;APOB
APOC2_muscle	27	REACTOME	Lidigestion mobilization and transport	7.10E-07	9.50E-04	APOC2;APOA5;APOC3;ABCG5
APOC2_muscle	27	REACTOME	Chylomicron mediated lipid transport	1.90E-06	2.60E-03	APOC2;APOA5;APOC3
APOC3_brain	19	REACTOME	Chylomicron mediated lipid transport	5.10E-07	6.80E-04	APOA1;APOA5;APOC3
APOC3_brain	19	REACTOME	Lipoprotein metabolism	3.00E-06	4.00E-03	APOA1;APOA5;APOC3
APOC4_brain	25	KEGG	Complement and coagulation cascades	1.30E-05	1.70E-02	CFI;KNG1;MBL2;C3
APOC4_brain	25	REACTOME	Complement cascade	4.20E-05	5.50E-02	CFI;MBL2;C3
APOF_muscle	45	KEGG	Complement and coagulation cascades	5.50E-09	7.30E-06	PLG;SERPINC1;F13B;CFI;MASP1;C5;FGB
APOF_muscle	45	REACTOME	Lipoprotein metabolism	5.40E-08	7.20E-05	ALB;APOC2;APOA5;LIPC;APOB
AW475929_brain	30	REACTOME	Striated muscle contraction	4.50E-04	5.90E-01	MYL4;TCAP
AW475929_brain	30	REACTOME	Muscle contraction	1.40E-03	1.00E+00	MYL4;TCAP
AZGP1_adipose	23	KEGG	Complement and coagulation cascades	1.40E-04	1.80E-01	PLG;KNG1;C9
AZGP1_adipose	23	REACTOME	Lidigestion mobilization and transport	2.10E-03	1.00E+00	APOA5;ABCG5
BATF2_blood	12	REACTOME	Interferon signaling	7.70E-08	1.00E-04	GBP1;UBE2L6;GBP5;IRF1;IRF9
BATF2_blood	12	REACTOME	Interferon gamma signaling	1.40E-07	1.80E-04	GBP1;GBP5;IRF1;IRF9
BNIP3L_aorta	53	NABA	Core matrisome	5.30E-02	4.00E-05	SPARC;THBS1;COL16A1;COMP;VCAN;FBLN2;NID2;MXRA5
BNIP3L_aorta	53	REACTOME	Class A1 rhodopsin like receptors	1.10E-01	8.20E-05	C3;S1PR1;EDN1;CXCL1;ANXA1;PTGDR;CCL20;CCL21
BST2_artery	33	REACTOME	Interferon signaling	4.00E-11	3.00E-14	IFITM1;UBE2L6;ISG15;ADAR;IRF9;IFITM3;HLA-B;HLA-C;IFI27;IFIT3;MX2;STAT1
C1R_cardiac_muscle	111	PID	Integrin1 pathway	1.40E-05	1.00E-08	CD81;COL5A1;COL6A2;ITGA3;LAMA2;LAMA4;MDK;TGFBI;THBS1
CCL18_aorta	214	REACTOME	Immune system	3.50E-07	2.60E-10	SELL;STAT5A;TAP1;TYROBP;UBA7;CANX;IFITM1;PSTPIP1;UBE2L6;CD14;ISG15;CD74;CD79A;IFITM3;CNPY3;CTSC;CISH;CTSB;CYBA;EGR1;LY96;FYB;FYN;GBP2;HLA-DRB1;HLA-F;HLA-G;BIRC3;IFI27;IFNGR1;IL2RB;ITGB7;JUN;MYD88;NFKB2;NFKBIA;HERC5;B2M;PSMB8;PSMB9;PSMD7;PSME1;PTPN6;PTPRC
CCL18_aorta	214	REACTOME	Cytokine signaling in immune system	1.50E-06	1.10E-09	STAT5A;UBA7;IFITM1;UBE2L6;ISG15;IFITM3;CISH;EGR1;FYN;GBP2;HLA-DRB1;HLA-F;HLA-G;IFI27;IFNGR1;IL2RB;MYD88;NFKB2;HERC5;B2M;PSMB8;PTPN6
CD14_adipose	48	REACTOME	Antigen processing cross presentation	1.00E+00	1.20E-03	MRC1;NCF4;PSMA8
CD74_adipose	17	KEGG	Antigen processing and presentation	<1.0E-16	<1.0E-16	HLA-DQB1;HLA-DRA;HLA-DMA;HLA-DRB1;CIITA;HLA-F;HLA-C;HLA-DQA1;HLA-DOA;HLA-DMB;CD74
CD74_adipose	17	KEGG	Type i diabetes mellitus	<1.0E-16	<1.0E-16	HLA-DQB1;HLA-DRA;HLA-DMA;HLA-DRB1;HLA-F;HLA-C;HLA-DQA1;HLA-DOA;HLA-DMB
CFB_brain	20	KEGG	Complement and coagulation cascades	4.00E-10	5.40E-07	CFB;C4B;PLG;CFI;F10;C3
CFB_brain	20	REACTOME	Regulation of complement cascade	1.00E-06	1.30E-03	CFB;CFI;C3
CFB_brain	20	KEGG	Complement and coagulation cascades	5.40E-07	4.00E-10	CFB;C3;C4B;CFI;F10;PLG
CFD_aorta	166	KEGG	Complement and coagulation cascades	1.20E-06	9.20E-10	CFD;F3;F13A1;CFI;SERPING1;C1R;C1S;C3;C3AR1;C4BPA;C5AR1
CFD_aorta	166	REACTOME	Degradation of the extracellular matrix	3.90E-02	2.90E-05	MMP2;MMP7;TIMP1;TPSAB1;CMA1
CKLF_liver	26	KEGG	Complement and coagulation cascades	4.00E-10	5.40E-07	CFB;C4B;PLG;CFI;F10;C3
CKLF_liver	26	REACTOME	Regulation of complement cascade	1.00E-06	1.30E-03	CFB;CFI;C3
CKLF_liver	26	KEGG	Complement and coagulation cascades	1.20E-06	9.20E-10	CFD;F3;F13A1;CFI;SERPING1;C1R;C1S;C3;C3AR1;C4BPA;C5AR1
COASY_muscle	26	KEGG	Peroxisome	2.50E-04	3.30E-01	HACL1;EHHADH;EPHX2
COASY_muscle	26	BIOCARTA	Ptdins pathway	6.10E-04	8.20E-01	PFKL;PFKP
COL1A1_liver	73	REACTOME	Extracellular Matrix	<1.0E-16	<1.0E-16	COL5A1;COL1A2;COL3A1;COL4A1;COL6A3;COL4A2;COL1A1;ADAMTS2;COL8A1;COL16A1;SERPINH1;COL6A1;PCOLCE;PLOD2
COL1A1_liver	73	REACTOME	Collagen formation	<1.0E-16	<1.0E-16	COL5A1;COL1A2;COL3A1;COL4A1;COL6A3;COL4A2;COL1A1;ADAMTS2;COL8A1;COL16A1;SERPINH1;COL6A1;PCOLCE;PLOD2
COL4A2_muscle	28	NABA	Collagens	9.90E-11	1.30E-07	COL5A1;COL4A1;COL5A3;COL4A2;COL6A2;COL15A1
COL4A2_muscle	28	REACTOME	Collagen formation	5.60E-10	7.40E-07	COL5A1;COL4A1;COL5A3;COL4A2;COL6A2;COL15A1
COL4A2_PPI	19	NABA	Extracellular Matrix	1.80E-07	2.40E-04	BGN;COL4A1;COL4A2;MATN2;FBLN2;FN1;TGFBI
COL4A2_PPI	19	BIOCARTA	Plateletapp pathway	1.50E-06	2.00E-03	COL4A1;COL4A2;APP
COL5A1_adipose	29	REACTOME	Extracellular Matrix	<1.0E-16	<1.0E-16	COL16A1;COL5A1;COL1A2;COL3A1;COL4A1;COL6A3;SERPINH1;COL5A3;COL4A2;COL5A2;COL15A1;ADAMTS2;COL6A2
COL5A1_adipose	29	REACTOME	Collagen formation	<1.0E-16	<1.0E-16	COL16A1;COL5A1;COL1A2;COL3A1;COL4A1;COL6A3;SERPINH1;COL5A3;COL4A2;COL5A2;COL15A1;ADAMTS2;COL6A2
COL5A1_adipose	29	REACTOME	Extracellular matrix organization	0.00E+00	0.00E+00	COL5A1;ADAMTS2;COL15A1;COL16A1;COL4A1;COL5A2;COL5A3;COL6A3;SERPINH1;COL1A2;COL3A1;COL4A2;COL6A2
COL6A3_liver	69	REACTOME	Collagen formation	<1.0E-16	<1.0E-16	COL1A2;COL3A1;COL4A1;COL6A3;COL4A2;COL1A1;ADAMTS2;COL8A1;COL14A1;SERPINH1;COL6A1;PCOLCE
COL6A3_liver	69	NABA	Extracellular Matrix	<1.0E-16	<1.0E-16	COL1A2;DCN;COL3A1;COL4A1;FBLN7;COL6A3;DPT;LAMA2;COL4A2;COL1A1;WISP1;MATN2;COL8A1;NID1;SVEP1;LGI2;LTBP4;COL14A1;FBN1;CRISPLD2;COL6A1;PCOLCE;TGFBI;SMOC2;THBS2
COL6A3_liver	69	REACTOME	Collagen formation	0.00E+00	0.00E+00	COL6A3;ADAMTS2;COL14A1;COL1A1;COL1A2;COL3A1;COL4A1;COL4A2;COL6A1;COL8A1;PCOLCE;SERPINH1
COLEC12_kidney	17	NABA	Core matrisome	1.90E-01	1.40E-04	FN1;FNDC1;IGSF10;SVEP1
CTNNB1_PPI	135	KEGG	Wnt signaling pathway	<1.0E-16	<1.0E-16	DVL1;BTRC;LEF1;CHD8;TCF7L1;EP300;AXIN1;TBL1X;PSEN1;APC;SMAD4;SMAD2;CREBBP;DVL3;TCF7L2;CSNK1A1;CSNK2A1;CTNNBIP1;GSK3B;RUVBL1;SMAD3;CSNK2B;CTNNB1;SOX17;APC2;AXIN2;CCND1
CTNNB1_PPI	135	KEGG	Adherens junction	<1.0E-16	<1.0E-16	CDH1;IQGAP1;LEF1;TCF7L1;EP300;SMAD4;TGFBR2;SMAD2;PTPN1;ACP1;FYN;MET;CREBBP;PTPRM;TCF7L2;CTNNA1;CSNK2A1;CTNNA3;FER;PTPRJ;SMAD3;CSNK2B;PTPN6;CTNNB1;PTPRF;EGFR;TGFBR1;SRC;ERBB2
CTNNB1_PPI	135	KEGG	WNT signaling pathway	0.00E+00	0.00E+00	CTNNB1;APC;CHD8;GSK3B;BTRC;SMAD4;SOX17;AXIN1;LEF1;TBL1X;CSNK1A1;PSEN1;SMAD2;CSNK2A1;CSNK2B;CTNNBIP1;DVL3;SMAD3;CCND1;CREBBP;RUVBL1;TCF7L2;APC2;AXIN2;DVL1;EP300;TCF7L1
CTSB_smooth_muscle	42	NABA	ECM regulators	2.30E-01	1.70E-04	CTSB;CTSD;CTSH;PLAU;CST3;CSTB
CXCL10_liver	46	REACTOME	Chemokine receptors bind chemokines	4.40E-16	5.90E-13	XCL1;CXCL10;CCL2;CCL3L1;CCL7;CCL5;CCL3L3;CXCL11;CXCL9;CCL4
CXCL10_liver	46	KEGG	Chemokine signaling pathway	3.40E-12	4.50E-09	XCL1;CXCL10;CCL2;CCL3L1;CCL7;CCL5;CCL3L3;CXCL11;STAT1;CXCL9;CCL4

CXCL12_adipose	47	REACTOME	Adenylate cyclase activating pathway	3.40E-04	4.50E-01	ADCY1;ADCY5
CXCL12_adipose	47	REACTOME	Adenylate cyclase inhibitory pathway	5.90E-04	7.80E-01	ADCY1;ADCY5
CXCL12_cardiac_muscle	41	PID	Syndecan 4 pathway	1.60E-01	1.20E-04	CXCL12;FZD7;FGFR1
CXCL12_cardiac_muscle	41	KEGG	Viral myocarditis	1.00E+00	1.40E-03	FYN;HLA-B;LAMA2
CXCL12_liver	30	KEGG	Intestinal immune network for iga production	3.00E-03	1.00E+00	CXCL12;HLA-DOA
CXCL12_liver	30	REACTOME	Amino acid and oligopeptide slc transporters	3.20E-03	1.00E+00	SLC1A1;SLC6A6
CYP1B1_brain	49	NABA	Core matrisome	7.00E-03	5.20E-06	DCN;ELN;EMILIN2;ESM1;BGN;CTGF;FMOD;LUM
DPYD_cardiac_muscle	35	REACTOME	Regulation of insulin like growth factor IGF activity by insulin like growth factor binding proteins igfbps	2.20E-02	1.70E-05	IGFBP3;IGFBP4;IGFBP6
DUSP1_aorta	179	NABA	Core matrisome	9.90E-07	7.40E-10	NID2;FMOD;FN1;MXRA5;CYR61;LAMA4;MATN2;MFGE8;NID1;CRIM1;ASPN;PRELP;SPARC;COL21A1;SRPX;WISP2;POSTN;COL6A3;COL15A1;CTGF;DPT
DUSP1_aorta	179	NABA	ECM glycoproteins	3.10E-04	2.30E-07	NID2;FN1;MXRA5;CYR61;LAMA4;MATN2;MFGE8;NID1;CRIM1;SPARC;SRPX;WISP2;POSTN;CTGF;DPT
DUSP1_artery	71	PID	Integrin1 pathway	6.20E-02	4.60E-05	FN1;ITGA5;LAMC1;NID1;THBS1
DUSP1_smooth_muscle	63	PID	HIF1 tf pathway	1.60E-03	1.20E-06	HMOX1;JUN;MCL1;SERPINE1;BHLHE40;ADM
DUSP1_smooth_muscle	63	PID	FRA pathway	1.80E-03	1.30E-06	FOSL2;HMOX1;JUN;JUNB;PLAUR
DUSP6_aorta	253	PID	FRA pathway	4.40E-06	3.30E-09	IL6;JUNB;LIF;MGP;MMP1;MMP2;PLAUR;CCL2;THBD;FOSL1
DUSP6_artery	50	PID	IL6 7pathway	1.00E-04	7.70E-08	FOXO1;JUN;JUNB;MCL1;TIMP1;CEBPD
DUSP6_artery	50	PID	Syndecan 4 pathway	2.00E-02	1.50E-05	FGFR1;SDCBP;TFPI;THBS1
DUSP6_cardiac_muscle	108	PID	AP1 pathway	5.10E-03	3.90E-06	CYR61;JUN;JUNB;BAG1;TCF7L2;TIMP1;DUSP1
DUSP6_cardiac_muscle	108	PID	IL6 7pathway	1.00E-01	7.50E-05	FOXO1;JUN;JUNB;TIMP1;CEBPD
DUSP6_smooth_muscle	17	REACTOME	MAPK targets nuclear events mediated by map kinases	8.90E-03	6.70E-06	DUSP6;JUN;DUSP4
DUSP6_smooth_muscle	17	PID	ERBB1 downstream pathway	9.80E-03	7.30E-06	DUSP6;EGR1;JUN;ZFP36
DUSP6_vascular_endothelium	122	PID	Il6 7pathway	2.90E-06	2.20E-09	FOXO1;FOS;IL6ST;JUN;JUNB;MCL1;PTPRE;TIMP1;CEBPD
EFEMP1_cardiac_muscle	63	NABA	Core matrisome	2.60E-06	1.90E-09	EFEMP1;EFEMP2;IGFBP3;CYR61;LTBP2;LUM;THBS1;SRPX;SLIT2;COL3A1;COL4A2;ECM2;FBLN2
EFEMP1_cardiac_muscle	63	NABA	ECM glycoproteins	1.20E-04	9.00E-08	EFEMP1;EFEMP2;IGFBP3;CYR61;LTBP2;THBS1;SRPX;SLIT2;ECM2;FBLN2
F2_adipose	49	KEGG	Complement and coagulation cascades	5.40E-13	7.20E-10	FGG;PLG;SERPINC1;SERPIND1;KNG1;MASP2;MBL2;F2;PROC
F2_adipose	49	BIOCARTA	Ami pathway	3.90E-09	5.10E-06	FGG;PLG;SERPINC1;F2;PROC
F2_adipose	49	KEGG	Complement and coagulation cascades	7.20E-10	5.40E-13	F2;FGG;KNG1;MASP2;MBL2;PROC;SERPINC1;SERPIND1;PLG
F2_muscle	47	KEGG	Complement and coagulation cascades	1.40E-12	1.90E-09	FGG;PLG;SERPIND1;F2;CFI;F9;MBL2;KLKB1;FGB
F2_muscle	47	BIOCARTA	Intrinsic pathway	1.40E-08	1.80E-05	FGG;F2;F9;KLKB1;FGB
FBLN2_PPI	22	PID	Integrin1 pathway	<1.0E-16	<1.0E-16	COL4A6;LAMA5;COL4A1;COL4A3;COL18A1;NID1;LAMA1;COL4A5;COL4A4;FN1;FBN1;LAMC2
FBLN2_PPI	22	NABA	Extracellular Matrix	<1.0E-16	<1.0E-16	COL4A6;BCAN;HSPG2;LAMA5;COL4A1;VCAN;PRELP;COL4A2;COL4A3;COL18A1;NID1;LAMA1;COL4A5;COL4A4;ACAN;FBLN2;FN1;FBN1;ELN;LAMC2
FBP1_muscle	23	REACTOME	Hdl mediated lipid transport	1.90E-06	2.60E-03	ALB;APOC3;LCAT
FBP1_muscle	23	REACTOME	Lipoprotein metabolism	1.40E-05	1.80E-02	ALB;APOC3;LCAT
FN1_kidney	16	PID	Integrin5 pathway	1.40E-04	1.90E-01	FN1;FBN1
FN1_kidney	16	NABA	Extracellular Matrix	1.40E-04	1.90E-01	WISP1;COL14A1;FN1;FBN1
FN1_PPI	75	KEGG	Focal adhesion	<1.0E-16	<1.0E-16	COL4A6;ITGA3;ITGA5;COL1A2;COL4A1;ITGA8;COL4A2;COL1A1;HGF;COL2A1;COL6A2;COL4A4;TNC;ITGB3;COMP;FN1;THBS1;ITGB1;ITGB6;ITGB7;ITGA4
FN1_PPI	75	KEGG	ECM receptor interaction	<1.0E-16	<1.0E-16	COL4A6;ITGA3;ITGA5;COL1A2;COL4A1;ITGA8;COL4A2;COL1A1;COL2A1;COL6A2;COL4A4;TNC;ITGB3;COMP;FN1;THBS1;ITGB1;ITGB6;SDC2;ITGB7;ITGA4
GBP1_adipose	25	REACTOME	Interferon gamma signaling	3.60E-08	4.80E-05	GBP2;GBP1;GBP4;STAT1;GBP5
GBP1_adipose	25	REACTOME	Interferon signaling	3.80E-06	5.00E-03	GBP2;GBP1;GBP4;STAT1;GBP5
GBP1_blood	18	REACTOME	Interferon signaling	3.40E-07	4.50E-04	GBP1;GBP4;UBE2L6;STAT1;GBP5
GBP1_blood	18	REACTOME	Interferon gamma signaling	4.00E-07	5.40E-04	GBP1;GBP4;STAT1;GBP5
GBP1_vascular_endothelium	92	REACTOME	Interferon alpha beta signaling	0.00E+00	0.00E+00	GBP2;HLA-A;HLA-B;HLA-C;HLA-F;HLA-G;IFI27;IFI35;IFIT1;IFIT3;IRF1;ISG20;MX1;OAS1;OAS2;STAT1;IFITM1;ISG15;ADAR;IRF9
GBP1_vascular_endothelium	92	REACTOME	Interferon signaling	0.00E+00	0.00E+00	GBP1;GBP2;HLA-A;HLA-B;HLA-C;HLA-F;HLA-G;IFI27;IFI35;IFIT1;IFIT3;IRF1;ISG20;MX1;OAS1;OAS2;B2M;STAT1;IFITM1;UBE2L6;ISG15;ADAR;IRF9;DDX58
GBP2_blood	20	REACTOME	Interferon gamma signaling	3.40E-06	4.50E-03	FCGR1A;GBP5;GBP2;IRF1
GBP2_blood	20	REACTOME	Interferon signaling	5.40E-06	7.10E-03	FCGR1A;UBE2L6;GBP5;GBP2;IRF1
GBP2_kidney	12	REACTOME	Interferon gamma signaling	4.50E-04	6.00E-01	GBP4;GBP2
GBP2_kidney	12	REACTOME	Interferon signaling	2.90E-03	1.00E+00	GBP4;GBP2
GEM_kidney	18	PID	Cmyb pathway	8.40E-05	1.10E-01	CEBPD;PTGS2;CEBPB
GEM_kidney	18	PID	P38alphabetadownstreampathway	7.30E-04	9.70E-01	PTGS2;CEBPB
HELZ_muscle	32	PID	Rb 1pathway	2.10E-03	1.00E+00	SMARCA4;UBTF
HELZ_muscle	32	KEGG	Long term depression	2.50E-03	1.00E+00	PRKCA;RYR1
HELZ_muscle	32	PID	Rb 1 pathway	1.00E+00	2.10E-03	SMARCA4;UBTF
HEMGN_muscle	21	REACTOME	Degradation of the extracellular matrix	7.30E-04	9.70E-01	CTSG;MMP13
HEMGN_muscle	21	REACTOME	Latent infection of homo sapiens with mycobacterium tuberculosis	9.50E-04	1.00E+00	LTF;CAMP
HEMGN_muscle	21	REACTOME	Degradation of the extracellular matrix	9.70E-01	7.30E-04	MMP13;CTSG
HGD_brain	40	KEGG	Ppar signaling pathway	1.20E-06	1.60E-03	APOA1;PCK1;APOA5;ACOX2;ACAA1
HGD_brain	40	REACTOME	Synthesis of bile acids and bile salts via 7alpha hydroxycholesterol	8.90E-06	1.20E-02	AKR1D1;ABCB11;ACOX2
HGD_brain	40	KEGG	PPAR signaling pathway	1.60E-03	1.20E-06	ACOX2;APOA5;PCK1;ACAA1;APOA1
HGD_muscle	48	KEGG	Complement and coagulation cascades	1.10E-07	1.50E-04	FGG;PLG;SERPINC1;F13B;F9;MBL2
HGD_muscle	48	REACTOME	Formation of fibrin clot clotting cascade	4.00E-06	5.30E-03	FGG;SERPINC1;F13B;F9
HGD_muscle	48	KEGG	Complement and coagulation cascades	1.50E-04	1.10E-07	F13B;F9;FGG;MBL2;PLG;SERPINC1
HLA-F_artery	50	REACTOME	Interferon gamma signaling	0.00E+00	0.00E+00	HLA-F;HLA-G;IFNGR1;OAS1;OAS2;B2M;STAT1;CD44;IRF9;HLA-A;HLA-B;HLA-C
HLA-F_artery	50	REACTOME	Interferon alpha beta signaling	0.00E+00	0.00E+00	HLA-F;HLA-G;IFI35;MX2;OAS1;OAS2;PSMB8;STAT1;IFITM1;ISG15;IRF9;HLA-A;HLA-B;HLA-C
IFI30_smooth_muscle	17	REACTOME	Interferon alpha beta signaling	3.60E-03	2.70E-06	IFIT3;PSMB8;ISG15;IFITM3
IFI30_smooth_muscle	17	KEGG	Antigen processing and presentation	1.40E-02	1.00E-05	IFI30;HLA-DMA;LGMN;PSME1
IFI35_artery	65	REACTOME	Interferon signaling	0.00E+00	0.00E+00	IFI35;IFIT2;IFIT1;IFIT3;IRF1;MX1;MX2;OAS1;PML;PSMB8;STAT1;STAT2;IFITM1;OASL;UBE2L6;ISG15;ADAR;IRF9;IFITM3;IFITM2;USP18;DDX58;IFI6;GBP1;HLA-A;HLA-B;HLA-C;HLA-F

IGFBP6_artery	45	PID	Integrin1 pathway	3.30E-04	2.50E-07	TGFBI;THBS1;COL6A1;COL6A2;FBN1;FN1
IGSF10_muscle	45	NABA	Extracellular Matrix	5.80E-09	7.70E-06	IGSF10;COL1A2;FNDC1;COL3A1;COL6A3;WISP1;TNC;SPON2;COL5A2
IGSF10_muscle	45	PID	Integrin1 pathway	3.90E-07	5.10E-04	COL1A2;COL3A1;COL6A3;TNC;COL5A2
IGSF10_muscle	45	NABA	Core matrisome	7.70E-06	5.80E-09	IGSF10;COL6A3;SPON2;TNC;WISP1;COL1A2;COL3A1;COL5A2;FNDC1
IL15RA_liver	20	BIOCARTA	G1 pathway	3.20E-04	4.20E-01	SMAD3;CDKN1A
IL15RA_liver	20	PID	Myc represspathway	1.60E-03	1.00E+00	SMAD3;CDKN1A
IRF1_artery	62	REACTOME	Interferon alpha beta signaling	5.90E-13	4.40E-16	IRF1;ISG20;PSMB8;STAT1;IFITM1;OASL;ISG15;ADAR;IRF9;GBP2;IFI35;IFIT3
IRF1_artery	62	REACTOME	Interferon signaling	3.20E-12	2.40E-15	IRF1;ISG20;PSMB8;STAT1;IFITM1;OASL;UBE2L6;CD44;ISG15;ADAR;IRF9;GBP2;ICAM1;IFI35;IFIT3
IRF7_adipose	24	REACTOME	Interferon alpha beta signaling	0.00E+00	0.00E+00	IRF7;ISG15;MX1;OAS2;USP18;ADAR;IFIT1;OAS1;OASL;STAT2
IRF7_adipose	24	REACTOME	Interferon signaling	0.00E+00	0.00E+00	IRF7;GBP4;ISG15;MX1;OAS2;USP18;ADAR;IFIT1;OAS1;OASL;STAT2
IRF7_vascular_endothelium	9	REACTOME	Interferon alpha beta signaling	3.80E-07	2.90E-10	IRF7;STAT1;ISG15;IFI35;IFIT3
IRF9_smooth_muscle	37	REACTOME	Interferon signaling	0.00E+00	0.00E+00	IRF9;DDX58;GBP1;HLA-B;HLA-G;IFI27;IFI35;IFIT3;IRF1;ISG20;MX1;MX2;SP100;STAT1;STAT2;IFITM1;UBE2L6;ISG15;ADAR
ISG15_cardiac_muscle	59	REACTOME	Interferon alpha beta signaling	0.00E+00	0.00E+00	ISG15;ADAR;IFITM3;IFITM2;HLA-A;HLA-B;HLA-C;HLA-F;HLA-G;IFI27;IFI35;MX1;STAT1;IFITM1
ISG15_cardiac_muscle	59	REACTOME	Interferon signaling	0.00E+00	0.00E+00	ISG15;ADAR;IFITM3;IFITM2;FLNB;GBP1;HLA-A;HLA-B;HLA-C;HLA-F;HLA-G;IFI27;IFI35;MX1;B2M;STAT1;UBA7;IFITM1;UBE2L6
ITGA7_adipose	37	KEGG	ECM receptor interaction	3.40E-05	4.50E-02	ITGA7;COL4A1;VTN;COL4A2
ITGA7_adipose	37	NABA	Basement membranes	9.50E-05	1.30E-01	NID2;COL4A1;COL4A2
ITGA7_adipose	37	KEGG	ECM receptor interaction	4.50E-02	3.40E-05	ITGA7;VTN;COL4A1;COL4A2
ITGB4_aorta	22	REACTOME	Interferon signaling	3.60E-01	2.70E-04	MX1;MX2;PML;HLA-B
JAG1_vascular_endothelium	25	PID	Integrin1 pathway	1.70E-02	1.30E-05	ITGA6;ITGAV;LAMB3;VEGFA
KCNK13_liver	45	PID	Tcr pathway	1.30E-05	1.70E-02	CD86;PLCG1;INPP5D;WAS
KCNK13_liver	45	PID	S1p s1p4 pathway	4.40E-04	5.90E-01	PLCG1;S1PR5
KL_brain	42	NABA	Collagens	4.90E-08	6.50E-05	COL9A3;COL8A2;COL8A1;COL4A4;COL23A1
KL_brain	42	NABA	Extracellular Matrix	1.30E-07	1.70E-04	COL9A3;COL8A2;LUM;COL8A1;COL4A4;COL23A1;FN1;IGFBP2
KL_brain	42	NABA	Collagens	6.50E-05	4.90E-08	COL4A4;COL8A1;COL8A2;COL9A3;COL23A1
KLF6_smooth_muscle	104	PID	AP1 pathway	5.30E-07	4.00E-10	DUSP1;EGR1;FOS;FOSL2;CYR61;JUN;MAFG;MYB;ATF3;TCF7L2
KLF6_smooth_muscle	104	PID	HIF1 tfpathway	6.50E-06	4.90E-09	FOS;HMOX1;ID2;JUN;SMAD3;MCL1;VEGFA;BHLHE40;CITED2
KNG1_brain	56	REACTOME	Lipoprotein metabolism	3.80E-10	5.10E-07	ALB;APOA1;APOC2;APOA5;APOC3;APOB
KNG1_brain	56	REACTOME	Chylomicron mediated lipid transport	1.60E-09	2.10E-06	APOA1;APOC2;APOA5;APOC3;APOB
KNG1_brain	56	REACTOME	Lipoprotein metabolism	5.10E-07	3.80E-10	APOA1;APOA5;APOB;APOC2;APOC3;ALB
KNG1_muscle	29	REACTOME	Chylomicron mediated lipid transport	1.10E-08	1.40E-05	APOA1;APOA5;APOC3;APOB
KNG1_muscle	29	KEGG	Ppar signaling pathway	8.30E-08	1.10E-04	APOA1;APOA5;APOC3;SLC27A2;ACOX2
LAMA2_adipose	33	PID	Integrin1 pathway	5.30E-06	7.10E-03	COL3A1;FN1;LAMA2;LAMC1
LAMA2_adipose	33	KEGG	ECM receptor interaction	1.40E-05	1.90E-02	COL3A1;FN1;LAMA2;LAMC1
LAMA2_adipose	33	PID	Integrin1 pathway	7.10E-03	5.30E-06	LAMA2;LAMC1;COL3A1;FN1
LARGE_liver	20	PID	Txa2pathway	1.60E-03	1.00E+00	VCAM1;PRKCA
LARGE_liver	20	PID	Integrin1 pathway	2.20E-03	1.00E+00	COL6A3;VCAM1
LDLR_PPI	11	REACTOME	Chylomicron mediated lipid transport	7.60E-10	1.00E-06	LDLR;APOE;LDLRAP1;APOB
LDLR_PPI	11	REACTOME	Lipoprotein metabolism	8.50E-09	1.10E-05	LDLR;APOE;LDLRAP1;APOB
LOXL1_muscle	30	REACTOME	Collagen formation	8.30E-10	1.10E-06	COL5A1;COL6A3;COL4A2;COL6A2;SERPINH1;PCOLCE
LOXL1_muscle	30	REACTOME	Extracellular Matrix	1.00E-08	1.30E-05	COL5A1;COL6A3;COL4A2;COL6A2;SERPINH1;PCOLCE
LOXL2_liver	28	REACTOME	Collagen formation	8.30E-10	1.10E-06	COL1A2;COL3A1;COL4A1;COL4A2;COL1A1;SERPINH1
LOXL2_liver	28	REACTOME	Ncam1 interactions	8.60E-09	1.10E-05	COL1A2;COL3A1;COL4A1;COL4A2;COL1A1
LUM_brain	45	NABA	Extracellular Matrix	1.90E-10	2.50E-07	DCN;COL3A1;LUM;COL13A1;COL8A1;SPOCK3;EFEMP1;OGN;PCOLCE;TGFBI;SMOC2
LUM_brain	45	NABA	Proteoglycans	3.30E-06	4.40E-03	DCN;LUM;SPOCK3;OGN
LY96_vascular_endothelium	15	REACTOME	Interferon signaling	5.00E-02	3.80E-05	HLA-G;IFITM1;UBE2L6;IFITM2
MAFF_liver	27	PID	P53downstreampathway	2.20E-07	3.00E-04	SERPINE1;EPHA2;MCL1;GDF15;DUSP5;ATF3
MAFF_liver	27	PID	Atf2 pathway	2.20E-04	3.00E-01	DUSP5;ATF3;IL8
MATN2_PPI	13	NABA	Extracellular Matrix	<1.0E-16	<1.0E-16	COL4A6;COL4A1;MATN4;COL1A1;COL4A2;COL4A3;MATN2;MATN1;COL4A5;FBN2;COL4A4;FN1
MATN2_PPI	13	BIOCARTA	Vitcb pathway	4.40E-16	5.90E-13	COL4A6;COL4A1;COL4A2;COL4A3;COL4A5;COL4A4
MMP9_PPI	31	REACTOME	Extracellular Matrix	<1.0E-16	<1.0E-16	COL4A6;PLG;COL1A2;PRSS2;COL4A1;COL4A2;COL1A1;COL4A3;MMP7;COL4A5;COL4A4;MMP10;MMP9
MMP9_PPI	31	BIOCARTA	Ami pathway	4.40E-16	5.90E-13	COL4A6;PLG;COL4A1;COL4A2;COL4A3;COL4A5;COL4A4;TFPI
MMT00002956_liver	36	REACTOME	Response to elevated platelet cytosolic ca2	4.40E-04	5.90E-01	TGFB3;SRGN;PLEK
MMT00002956_liver	36	BIOCARTA	Dc pathway	6.40E-04	8.50E-01	CD2;ITGAX
MMT00019644_adipose	37	REACTOME	Pyrimidine metabolism	7.60E-04	1.00E+00	TK1;UCK1
MMT00019644_adipose	37	PID	Vegfr1 pathway	9.00E-04	1.00E+00	VEGFA;PRKCA
MMT00081256_muscle	20	REACTOME	Interferon gamma signaling	1.70E-05	2.20E-02	GBP1;GBP4;STAT1
MMT00081256_muscle	20	REACTOME	Interferon signaling	2.60E-04	3.50E-01	GBP1;GBP4;STAT1
MSN_liver	56	KEGG	Fc gamma r mediated phagocytosis	1.90E-05	2.50E-02	PIK3CG;LIMK2;MARCKSL1;INPP5D;PTPRC
MSN_liver	56	PID	Cxcr4 pathway	4.00E-04	5.30E-01	ADRBK1;PIK3CG;INPP5D;PTPRC
MSN_vascular_endothelium	105	KEGG	Focal adhesion	7.40E-10	5.50E-13	MYLK;RAC2;SHC1;THBS1;ZYX;CAV2;ACTN1;MYL9;COL4A1;COL4A2;COL5A2;FLNA;FN1;FYN;BIRC3;ILK;ITGA5;LAMA4
MSN_vascular_endothelium	105	PID	Integrin1 pathway	3.80E-08	2.80E-11	NID1;PLAU;PLAUR;TGFBI;THBS1;COL4A1;COL5A2;FBN1;FN1;ITGA5;LAMA4
MTMR11_liver	80	PID	Avb3 integrin pathway	5.50E-04	7.40E-01	VCL;COL3A1;COL4A1;TGFBR2
MTMR11_liver	80	PID	Integrin3 pathway	1.30E-03	1.00E+00	COL4A1;PDGFRB;TGFBR2
MTMR11_liver	80	PID	AVB3 integrin pathway	7.40E-01	5.50E-04	COL4A1;TGFBR2;VCL;COL3A1
NCOR2_kidney	12	REACTOME	Transcriptional regulation of white adipocyte differentiation	8.80E-04	1.00E+00	NCOR2;MED13L
NCOR2_kidney	12	REACTOME	Fatty acid triacylglycerol and ketone body metabolism	4.70E-03	1.00E+00	NCOR2;MED13L
NGRN_liver	32	REACTOME	Transcriptional regulation of white adipocyte differentiation	8.80E-04	1.00E+00	NCOR2;MED13L
NGRN_liver	32	REACTOME	Fatty acid triacylglycerol and ketone body metabolism	4.70E-03	1.00E+00	NCOR2;MED13L
NM_009245_brain	26	REACTOME	Common pathway	2.40E-09	3.10E-06	SERPINC1;F13B;F2;FGB
NM_009245_brain	26	KEGG	Complement and coagulation cascades	2.50E-08	3.30E-05	SERPINC1;F13B;F2;CFI;FGB

NME6_kidney	10	REACTOME	Common pathway	2.40E-09	3.10E-06	SERPINC1;F13B;F2;FGB
NME6_kidney	10	KEGG	Complement and coagulation cascades	2.50E-08	3.30E-05	SERPINC1;F13B;F2;CFI;FGB
NOTCH1_PPI	46	KEGG	Notch signaling pathway	<1.0E-16	<1.0E-16	JAG2;MAML3;LFNG;NOTCH1;JAG1;MFNG;MAML2;DLL1;DTX1;EP300;DTX2;PSEN1;SNW1;KAT2B;DLL4;NUMB;MAML1;PSEN2;RBPJ;NUMBL;KAT2A;ADAM17
NOTCH1_PPI	46	PID	Notch pathway	<1.0E-16	<1.0E-16	YY1;JAG2;NOTCH1;JAG1;CNTN1;MAML2;DLL1;DTX1;EP300;PSEN1;DLL4;FURIN;NUMB;MAML1;CBL;FBXW7;RBPJ;ITCH
OAS2_kidney	12	REACTOME	Interferon signaling	1.70E-03	1.30E-06	OAS2;IRF7;IFIT1;OAS1
OSM_PPI	10	BIOCARTA	Vitcb pathway	1.10E-16	1.50E-13	COL4A6;COL4A1;COL4A2;COL4A3;COL4A5;COL4A4
OSM_PPI	10	BIOCARTA	Ace2 pathway	4.40E-16	5.90E-13	COL4A6;COL4A1;COL4A2;COL4A3;COL4A5;COL4A4
PAPSS2_cardiac_muscle	81	NABA	ECM glycoproteins	8.00E-05	6.00E-08	GAS6;EFEMP2;IGFBP7;CYR61;LAMB1;LAMB3;LAMC1;LTBP1;TGFBI;THBS1;SRPX
PAPSS2_cardiac_muscle	81	NABA	Core matrisome	3.00E-04	2.20E-07	COL4A1;GAS6;EFEMP2;IGFBP7;CYR61;LAMB1;LAMB3;LAMC1;LTBP1;TGFBI;THBS1;SRPX
PAPSS2_smooth_muscle	14	KEGG	Pathways in cancer	1.30E-01	9.80E-05	COL4A1;FGFR3;AR;VEGFA
PAPSS2_smooth_muscle	14	KEGG	Bladder cancer	7.40E-01	5.60E-04	FGFR3;VEGFA
PLG_adipose	46	KEGG	Complement and coagulation cascades	2.50E-11	3.30E-08	FGA;FGG;PLG;SERPINC1;C9;MBL2;F13B;F2
PLG_adipose	46	REACTOME	Common pathway	4.20E-10	5.60E-07	FGA;FGG;SERPINC1;F13B;F2
PLG_liver	43	NABA	ECM regulators	2.90E-07	2.20E-10	PLG;F2;HRG;ITIH2;KNG1;PZP;SERPINA11;SERPINC1;SERPIND1;SERPINF2;ITIH3
PTCHD1_adipose	104	BIOCARTA	Ccr5 pathway	1.80E-04	2.40E-01	FOS;CCR5;CCL4
PTCHD1_adipose	104	BIOCARTA	Igf1 pathway	2.10E-04	2.80E-01	FOS;PIK3CG;RASA1
PTCHD1_adipose	104	BIOCARTA	CCR5 pathway	2.40E-01	1.80E-04	CCL4;CCR5;FOS
PTPN11_PPI	109	KEGG	Focal adhesion	0.00E+00	0.00E+00	MAPK3;PDGFRB;SHC1;ACTN4;CRKL;PDGFRA;PRKCB;CAV1;GRB2;PIK3CG;KDR;PXN;SRC;IGF1R;PTK2;SOS1;EGFR;FLT1;FLT4;FYN;MET;ERBB2;PIK3R1;PRKCA
RAC2_cardiac_muscle	58	REACTOME	Interferon gamma signaling	6.00E-10	4.50E-13	STAT1;CD44;GBP1;HLA-A;HLA-B;HLA-DPA1;HLA-G;ICAM1;OAS2;B2M
RAC2_cardiac_muscle	58	REACTOME	Interferon signaling	1.90E-08	1.40E-11	STAT1;CD44;GBP1;HLA-A;HLA-B;HLA-DPA1;HLA-G;ICAM1;IFIT3;OAS2;B2M;PSMB8
RDH16_brain	43	KEGG	Complement and coagulation cascades	7.00E-09	9.30E-06	CFI;C8A;F10;KNG1;C9;KLKB1
RDH16_brain	43	REACTOME	Complement cascade	6.90E-07	9.10E-04	CRP;CFI;C8A;C9
RDH16_brain	43	KEGG	Complement and coagulation cascades	9.30E-06	7.00E-09	C8A;CFI;F10;KLKB1;C9;KNG1
RDH16_muscle	36	KEGG	Complement and coagulation cascades	3.80E-07	5.00E-04	PLG;SERPINC1;C8G;F2;KNG1
RDH16_muscle	36	BIOCARTA	Ami pathway	1.10E-05	1.50E-02	PLG;SERPINC1;F2
SCARA3_muscle	30	PID	Avb3 integrin pathway	1.40E-05	1.90E-02	TGFBR2;COL14A1;FN1;CSF1R
SCARA3_muscle	30	NABA	Matrisome associated	5.00E-04	6.60E-01	MMP2;GDF10;SFRP2;GPC6;TIMP2;CD109;SERPINF1
SDCBP_aorta	155	NABA	Core matrisome	3.70E-11	2.80E-14	THBS2;PXDN;SPARCL1;SRPX;FBLN5;POSTN;COL1A2;COL15A1;COL16A1;EPYC;FGG;NID2;MXRA5;TNC;IGFBP3;CYR61;LAMA3;LAMA4;LAMB1;LTBP2;LUM;MFAP4;OMD;PRELP
SDCBP_aorta	155	NABA	ECM glycoproteins	3.50E-07	2.60E-10	THBS2;PXDN;SPARCL1;SRPX;FBLN5;POSTN;FGG;NID2;MXRA5;TNC;IGFBP3;CYR61;LAMA3;LAMA4;LAMB1;LTBP2;MFAP4
SERPINC1_adipose	34	REACTOME	Common pathway	2.30E-10	3.10E-07	FGG;SERPINC1;F13B;F2;FGB
SERPINC1_adipose	34	KEGG	Complement and coagulation cascades	5.70E-10	7.50E-07	FGG;C4BPA;PLG;SERPINC1;F13B;F2;FGB
SERPINC1_adipose	34	REACTOME	Common pathway	3.10E-07	2.30E-10	SERPINC1;F13B;F2;FGG;FGB
SHC1_PPI	118	KEGG	Erbb signaling pathway	<1.0E-16	<1.0E-16	SHC1;ERBB4;PTK2;PIK3R1;MAPK1;SOS1;PRKCA;PAK1;CBLB;STAT5B;STAT5A;SOS2;PLCG1;MAPK8;EGFR;CBL;SRC;PIK3R2;CRK;PLCG2;GAB1;ERBB3;CRKL;ERBB2;GRB2
SHC1_PPI	118	KEGG	Focal adhesion	<1.0E-16	<1.0E-16	FLT4;SHC1;PTK2;PIK3R1;VAV3;MAPK1;SOS1;KDR;PRKCA;PAK1;PDGFRB;FLT1;VAV1;RAPGEF1;SOS2;MAPK8;EGFR;ITGB4;SRC;ITGB3;FYN;MET;PIK3R2;CRK;CRKL;ERBB2;GRB2
SHC1_PPI	118	KEGG	ERBB signaling pathway	0.00E+00	0.00E+00	SHC1;PAK1;SOS1;ERBB3;GRB2;SOS2;CBLB;CRKL;PLCG1;ERBB2;MAPK8;SRC;STAT5B;CBL;CRK;ERBB4;STAT5A;EGFR;GAB1;PIK3R2;PTK2;MAPK1;PIK3R1;PLCG2;PRKCA
SLC1A5_muscle	40	KEGG	Focal adhesion	0.00E+00	0.00E+00	SHC1;PAK1;SOS1;GRB2;SOS2;CRKL;FLT1;PDGFRB;ERBB2;KDR;MAPK8;RAPGEF1;SRC;ITGB3;MET;CRK;ITGB4;VAV1;VAV3;EGFR;FLT4;FYN;PIK3R2;PTK2;MAPK1;PIK3R1;PRKCA
SLC2A3_aorta	190	NABA	Core matrisome	5.20E-03	3.90E-06	SPOCK1;TNFAIP6;PXDN;COL18A1;POSTN;COL4A1;COL4A2;AEBP1;FMOD;IGFBP1;IGFBP3;IGFBP6;CYR61;LAMB1;LTBP2;NID1
SLC2A3_aorta	190	PID	P53 downstream pathway	9.20E-03	6.90E-06	SNAI2;TAP1;COL18A1;MAP4K4;DUSP5;EDN2;IGFBP3;JUN;MCL1;PML;S100A2
SLIT2_aorta	170	REACTOME	Cytokine signaling in immune system	1.80E-02	1.40E-05	MAP3K8;GBP2;GHR;HLA-B;HLA-F;IFIT2;IFNGR1;IL1B;IL6;SP100;VCAM1;IFITM1;IRS2
SLIT2_aorta	170	REACTOME	Interferon gamma signaling	1.10E-01	8.40E-05	GBP2;HLA-B;HLA-F;IFNGR1;SP100;VCAM1
SLIT3_muscle	28	NABA	ECM glycoproteins	2.90E-10	3.90E-07	SLIT3;THBS3;FNDC1;EMILIN2;NID1;SVEP1;FN1;EFEMP1;THBS2
SLIT3_muscle	28	NABA	Extracellular Matrix	5.80E-09	7.70E-06	SLIT3;THBS3;FNDC1;EMILIN2;NID1;SVEP1;FN1;EFEMP1;THBS2
SMAD1_PPI	111	KEGG	Tgf beta signaling pathway	2.70E-14	3.60E-11	SMAD1;BMPR1A;MAPK1;EP300;SMAD3;SMAD4;SMAD6;SMAD5;GDF6;TGFBR1;ACVR1;SMURF2;SMURF1
SMAD1_PPI	111	REACTOME	Tgf beta receptor signaling activates smads	9.20E-14	1.20E-10	XPO1;STUB1;SMAD3;SMAD4;UBA52;TGFBR1;SMURF2;RPS27A;SMURF1
SMAD1_PPI	111	KEGG	TGF beta signaling pathway	3.60E-11	2.70E-14	SMAD1;MAPK1;GDF6;SMAD5;SMAD6;SMURF1;TGFBR1;BMPR1A;EP300;SMAD4;SMURF2;ACVR1;SMAD3
SORL1_vascular_endothelium	14	KEGG	TGF beta signaling pathway	3.60E-11	2.70E-14	SMAD1;MAPK1;GDF6;SMAD5;SMAD6;SMURF1;TGFBR1;BMPR1A;EP300;SMAD4;SMURF2;ACVR1;SMAD3
SORL1_vascular_endothelium	14	REACTOME	TGF beta receptor signaling activates smads	1.20E-10	9.20E-14	XPO1;STUB1;UBA52;SMURF1;TGFBR1;RPS27A;SMAD4;SMURF2;SMAD3
SPARC_muscle	34	NABA	Extracellular Matrix	4.00E-13	5.30E-10	SPARC;COL5A1;COL1A2;COL3A1;COL4A1;COL4A2;COL1A1;MATN2;NID1;FN1;COL5A2;SRPX2
SPARC_muscle	34	REACTOME	Collagen formation	6.80E-13	9.00E-10	COL5A1;COL1A2;COL3A1;COL4A1;COL4A2;COL1A1;SERPINH1;COL5A2
STAT3_PPI	102	KEGG	Jak stat signaling pathway	<1.0E-16	<1.0E-16	IL6ST;IL7R;LEPR;IL2RB;JAK2;IL6R;STAT3;TSLP;IFNAR2;STAT5B;STAT1;EP300;PTPN11;IFNAR1;STAT5A;CSF2RB;GHR;CREBBP;STAT4;CCND1;IL2RA;PIAS3;IL23R;JAK3;JAK1;CSF3R
STAT3_PPI	102	KEGG	Pathways in cancer	<1.0E-16	<1.0E-16	HSP90AB1;FGFR3;MTOR;PDGFRA;STAT3;MAPK1;RELA;HIF1A;RAC1;STAT5B;STAT1;PDGFRB;EP300;RET;HDAC1;STAT5A;MAPK8;EGFR;NFKB1;PML;IGF1R;MET;CREBBP;JUN;CDKN1A;HSP90AA1;CCND1;MAPK3;PIAS3;JAK1;AR;CSF3R;HDAC2
TGFBI_PPI	10	PID	Integrin1 pathway	2.20E-16	3.00E-13	COL1A2;COL4A1;COL1A1;COL4A3;COL2A1;COL4A4;FN1

						;TGFBI
TGFBI_PPI	10	REACTOME	Integrin cell surface interactions	8.90E-16	1.20E-12	COL1A2;COL4A1;COL4A2;COL1A1;COL4A3;COL2A1;COL4A4;FN1
TNFAIP2_cardiac_muscle	95	REACTOME	Interferon signaling	4.80E-03	3.60E-06	CD44;IFITM3;HLA-A;HLA-B;HLA-F;ICAM1;IRF1;PML;STAT1
TRAPPC3_brain	40	KEGG	Proximal tubule bicarbonate reclamation	1.50E-03	1.00E+00	ATP1A2;ATP1A1
TRAPPC3_brain	40	REACTOME	Ion transport by p type atpases	3.20E-03	1.00E+00	ATP1A2;ATP1A1
TRAPPC3_brain	40	KEGG	Proximal tubule bicarbonate reclamation	1.00E+00	1.50E-03	ATP1A1;ATP1A2
TRIM22_vascular_endothelium	27	REACTOME	Interferon alpha beta signaling	3.00E-13	2.20E-16	IRF9;IFITM3;HLA-B;IFI35;IFIT1;IFIT3;MX1;STAT1;IFITM1;ISG15
TRIM8_smooth_muscle	7	PID	ATF2 pathway	5.30E-01	4.00E-04	DUSP5;PLAU
TRIM8_smooth_muscle	7	REACTOME	Interferon signaling	1.00E+00	2.90E-03	UBE2L6;HLA-C
VEGFA_adipose	36	PID	Il5 pathway	2.90E-04	3.80E-01	CISH;STAT5B
VEGFA_adipose	36	KEGG	Pantothenate and coa biosynthesis	3.80E-04	5.00E-01	ENPP1;VNN1
VPS33A_adipose	21	PID	VEGFR1 2 pathway	1.00E+00	1.50E-03	PTPN11;CAMKK2
WIPF1_liver	20	PID	Cdc42 reg pathway	5.50E-04	7.40E-01	DOCK10;DOCK11
WIPF1_liver	20	PID	Fcer1pathway	2.40E-03	1.00E+00	WIPF1;INPP5D
WWC2_aorta	30	REACTOME	Cell cell junction organization	3.00E-01	2.20E-04	CDH5;CDH11;CDH13
ZNF496_liver	39	REACTOME	Organic cation anion zwitterion transport	2.20E-04	2.90E-01	SLC22A4;SLC22A5
ZNF496_liver	39	REACTOME	Metabolism of non coding rna	3.20E-03	1.00E+00	GEMIN5;SMN2
ZYX_smooth_muscle	54	KEGG	Focal adhesion	4.00E-02	3.00E-05	ZYX;ACTN1;FLNA;ILK;ITGA5;LAMC1;VASP

Note:Fisher's exact test was performed for the enrichment of the KD subnetworks in MSigDB canonical pathway database. Only the top two functional terms are shown based on the p values with bonferroni corrections.

Supplementary Table VI. Data resources and references for tissue-specific Bayesian networks.

Tissue	Species	Dataset descriptions	References
Adipose tissue	Human	1,675 individuals from two Icelandic cohorts	(5)
	Mouse	C57BL/6J x A/J mouse cross	(6)
	Mouse	C57BL/6J x C3H ApoE -/- mouse cross	(7, 8)
	Mouse	C57BL/6J x C3H wildtype mouse cross	(9)
	Mouse	C57BL/6J x BTBR Lepob mouse cross	(10)
Blood	Human	1,675 individuals from two Icelandic cohorts	(5)
Brain	Mouse	C57BL/6J x A/J mouse cross	(6)
	Mouse	C57BL/6J x C3H ApoE -/- mouse cross	(7, 8)
	Mouse	C57BL/6J x BTBR Lepob mouse cross	(10)
Heart	Mouse	C57BL/6J x A/J mouse cross	(6)
Islet cells	Mouse	C57BL/6J x BTBR Lepob mouse cross	(10)
Kidney	Mouse	C57BL/6J x A/J mouse cross	(6)
Liver	Human	427 individuals	(9)
	Mouse	C57BL/6J x A/J mouse cross	(6)
	Mouse	C57BL/6J x C3H ApoE -/- mouse cross	(7, 8)
	Mouse	C57BL/6J x C3H wildtype mouse cross	(9)
	Mouse	C57BL/6J x BTBR Lepob mouse cross	(10)
Muscle	Mouse	C57BL/6J x A/J mouse cross	(6)
	Mouse	C57BL/6J x C3H ApoE -/- mouse cross	(7, 8)
	Mouse	C57BL/6J x C3H wildtype mouse cross	(9)
	Mouse	C57BL/6J x BTBR Lepob mouse cross	(10)
Cardiac Muscle	Human	GIANT tissue networks integrate 987 genome-scale datasets, encompassing ~38,000 conditions from ~14,000 publications and include both expression and interaction measurements.	(11)
Aorta	Human		
Artery	Human		
Smooth Muscle	Human		
Vascular Endothelium	Human		

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