

**Association between DNA methylation and coronary heart disease or other atherosclerotic events: a systematic review.**

Alba Fernández-Sanlés<sup>1,2</sup>, Sergi Sayols-Baixeras<sup>1,2,3</sup>, Isaac Subirana<sup>1,4</sup>, Irene R Degano<sup>1,3</sup>, Roberto Elosua<sup>1,3</sup>

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1.-Cardiovascular Epidemiology and Genetics Research Group, REGICOR Study group, IMIM (Hospital del Mar Medical Research Institute), Barcelona, Catalonia, Spain.

2.-Universitat Pompeu Fabra (UPF), Barcelona, Catalonia, Spain.

3.-CIBER Cardiovascular Diseases (CIBERCV), Barcelona, Catalonia, Spain.

4.-CIBER Epidemiology and Public Health (CIBERESP), Barcelona, Catalonia, Spain

**Author for correspondence:**

Roberto Elosua, MD, PhD

IMIM, Hospital del Mar Medical Research Institute

Dr Aiguader 88, 08003 Barcelona, Catalonia, Spain

Telephone: (+34) 933 160800; Email: [relosua@imim.es](mailto:relosua@imim.es)

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## ABSTRACT

**Background and aims:** The aim of this study was to perform a systematic review of the association between DNA methylation and coronary heart disease (CHD) or related atherosclerotic traits.

**Methods:** A systematic review was designed. The condition of interest was DNA methylation, and the outcome was CHD or other atherosclerosis-related traits. Three DNA methylation approaches were considered: global methylation, candidate-gene, and epigenome-wide association studies (EWAS). A functional analysis was undertaken using the Ingenuity Pathway Analysis software.

**Results:** In total, 51 articles were included in the analysis: 12 global methylation, 34 candidate-gene and 11 EWAS, with six studies using more than one approach. The results of the global methylation studies were inconsistent. The candidate-gene results were consistent for some genes, suggesting that hypermethylation in *ESRα*, *ABCG1* and *FOXP3* and hypomethylation in *IL-6* were associated with CHD. The EWAS identified 84 genes showing differential methylation associated with CHD in more than one study. The probability of these findings was  $<1.37 \cdot 10^{-5}$ . One third of these genes have been related to obesity in genome-wide association studies. The functional analysis identified several diseases and functions related to these set of genes: inflammatory, metabolic and cardiovascular disease.

**Conclusions:** Global DNA methylation seems to be not associated with CHD. The evidence from candidate-gene studies was limited. The EWAS identified a set of 84 genes highlighting the relevance of obesity, inflammation, lipid and carbohydrate metabolism in CHD. This set of genes could be prioritized in future studies assessing the role of DNA methylation in CHD.

**Keywords:** DNA methylation, myocardial infarction, coronary heart disease, atherosclerosis, systematic review.

## **1. INTRODUCTION**

Cardiovascular diseases (CVDs) are the leading cause of mortality and morbidity, being responsible of 31% of global deaths in 2012 and 14% of all-age disability-adjusted life-years (DALY) in 2015 [1,2]. Coronary heart disease (CHD) is the leading individual cause of morbidity and mortality, and atherosclerosis is its main underlying mechanism.

Although the pathogenesis of CHD and its underlying atherosclerosis is not completely understood, a growing body of evidence suggests an important role for epigenetics in the development of atherosclerosis [3]. Epigenetic modifications can alter the expression of genes without changing their sequences. Deciphering the epigenomic signatures linked to CHD and atherosclerosis could contribute to better understanding of their mechanisms and to the definition of new therapeutic targets and preventive strategies.

DNA methylation, one of the most well-known epigenetic signatures, consists of the covalent methylation of the C5 position of cytosine residues when they are followed by guanine residues (CpG dinucleotides) [4]. It is heritable but it is also a dynamic process related to environmental stimuli. Both global methylation status of the genome and differentially methylated specific loci have been studied in several atherosclerotic conditions.

The aim of this study was to perform a systematic review to summarize all available evidence related to the association between DNA methylation and CHD. We selected studies that analyzed DNA methylation at either a global or gene-specific level, the latter using either a candidate-gene or epigenome-wide association approach.

## **2. MATERIALS AND METHODS**

### Data sources and searches

A systematic review of the articles included in PubMed database ([www.ncbi.nlm.nih.gov/pubmed](http://www.ncbi.nlm.nih.gov/pubmed)) until December 7<sup>th</sup> 2016 was designed. The search terms were as follows: “DNA methylation” AND (“Coronary heart disease” OR

“Ischemic heart disease” OR “Myocardial infarction” OR “Cardiovascular risk” OR “Vascular age”). No limits were defined on the basis of language, country or publication date. The reference lists of all relevant original research and review articles were also manually scanned to identify potentially missed studies (AF-S). (Figure 1).

### Study selection

The condition of interest was the differential DNA methylation, and the outcome was CHD (myocardial infarction or angina), atherosclerosis or other CVD diseases related to atherosclerosis. DNA methylation was considered either global or at specific CpGs or at CpG islands (CGIs) as defined by each study, with no restriction regarding laboratory method or gene panel.

Studies were considered as eligible if they: a) were full-length original studies published in peer-reviewed journals; b) investigated the DNA methylation patterns in relationship with CHD or atherosclerosis traits, by using epidemiological observational designs or other experimental studies in human cell culture; c) the study was published in English. Those studies undertaken in specific populations of patients, such as familiar hypercholesterolemia or chronic kidney disease, were excluded. No restriction criteria were imposed with regard to: a) the type or size of the population studied; b) the tissue or anatomical site analyzed; c) the length of follow-up. Animal studies or non-human cell culture studies were excluded from the review.

The selection of eligible studies was performed in two phases. In the first one, studies that were not relevant for the aim of the review according to the content summary in the title or the abstract were excluded (AF-S). In the second phase, the articles were fully read for their eligibility according to the pre-defined inclusion/exclusion criteria (AF-S). In case of doubt, the inclusion of that study was discussed with a second reviewer (RE).

### Data extraction and quality assessment

Studies were classified according to the DNA methylation approach as: (i) global methylation studies, (ii) candidate-gene methylation studies, and (iii) epigenome-wide

association studies (EWAS). In case of doubt, the classification of that study was discussed with a second reviewer. Some of the eligible studies included data obtained from more than a single approach. For each of them, the following data were collected: surname of first author, year of publication, journal, PMID, country, study design, population sample size, type of tissue analyzed, molecular technique used to assess DNA methylation, clinical outcome, adjustment of the measures of association and conclusions of the study. In the case of EWAS, population size of both discovery and validation phase were recorded. Data were extracted initially by one author (AF-S), followed by re-extraction of each paper by the co-author (RE). Discrepancies were resolved by discussion and consensus.

Two of the authors (AF-S, RE) conducted a quality assessment of the selected studies using the STrengthening the REporting of Genetic Association studies (STREGA) recommendations for reporting results of genetic association studies [5]. We considered all the questions in the checklist if applicable to each specific study. The final score for each study was the total number of checklist questions addressed divided by the total number of applicable questions.

#### Data synthesis and analysis

Due to the large heterogeneity in study aims, study designs, molecular techniques used to assess DNA methylation, analyzed tissues and evaluated outcomes, no quantitative meta-analysis of the results of the eligible studies was performed. The results are shown as a narrative synthesis and as summary tables according to the three defined DNA methylation approaches.

In the case of EWAS, we identified those CpGs that were reported in more than one study and we assessed whether the direction of the association was consistent across studies (set 1). We also identified those genes showing at least one CpG/CGI associated with CHD in more than one study, and also assessed whether the direction of the association was consistent (set 2) or not (set 3). Finally, we estimated the probability of finding a certain CpG and gene showing differential methylation associated with the traits of interest in at least two or three studies by chance. To calculate this probability we used a binomial approach and we made the following assumptions: 1) the arrays analyze 400,000 CpGs per individual, and there are

20,000 genes in the human genome, and 2) the different arrays include 10 CpGs by gene. We used the following equation:

$$B(x, n, P) = \binom{n}{x} p^x (1 - p)^{n-x}, \text{ where}$$

- $b(x, n, P)$  = probability that a  $n$ -trial binomial experiment results in  $x$  successes, assuming the probability of success to be  $p$ ;
- $x$  = the number of successes that result from the binomial experiment. In our case two and three studies;
- $n$  = the number of trials in the binomial experiment. In our study corresponds to the number of EWAS studies;
- $p$  = probability of success on an individual trial. In our case was stated as  $2.5 \cdot 10^{-6}$  (1/400.000 CpGs) per CpGs and  $5.0 \cdot 10^{-4}$  [(1/20.000 genes)\*10 CpGs per gene] per genes.

### Functional studies and pathway analysis

We performed functional analyses of the genes identified as differentially methylated in more than one of the EWAS. On one hand, we searched in the Genome-wide Association Studies (GWAS) Catalog (<https://www.ebi.ac.uk/gwas/>) if any of those genes had previously been related to a cardiovascular or atherosclerotic trait in a GWAS. If such was the case, the traits were recorded.

On the other hand, we performed a pathway and network analysis of three sets of genes found in more than one of the EWAS: set 1, genes including the same CpG methylation direction; set 2, genes with the same methylation direction at gene level; and set 3, differentially methylated genes independently of the methylation consistency. In that purpose, we used the Ingenuity Pathway Analysis (IPA) software (<http://www.ingenuity.com/>; QIAGEN, Redwood City, CA, USA). We uploaded the Gene symbol identifiers of those genes. The database underlying IPA is referred to as the Ingenuity Knowledge Base (Genes only). Only human annotations were considered. Pathway analyses were performed with IPA's Core Analysis module. "Canonical pathways" and "Diseases and functions" terms with a  $p < 0.05$  in the Fisher's exact test or after Benjamini-Hochberg multiple testing correction were defined as a statistically significant overrepresentation of input genes in a given process.

In the “Canonical pathway” analysis, we selected all “Metabolic pathways” and “Signalling pathways” related to “Cardiovascular signalling”, “Cell cycle regulation”, “Cellular growth, proliferation and development”, “Cellular immune response”, “Cellular stress and injury”, “Humoral immune response”, “Intracellular and second messenger signalling”, “Nuclear receptor signalling” and “Transcription regulation”. In the “Diseases and functions” analysis, we selected CHD and atherosclerosis-relevant terms to create functional networks linking the input genes to functions or diseases. These networks are based on the information contained in the IPA database.

### 3. RESULTS

We identified 96 potentially relevant publications in the PubMed database ([www.ncbi.nlm.nih.gov/pubmed](http://www.ncbi.nlm.nih.gov/pubmed)) (Supplementary Figure 1). Based on the titles and abstracts, full texts of 43 articles were selected for further evaluation. Of those, 31 were original studies, while the remaining 12 articles were reviews. The examination of their reference lists allowed us to identify 20 additional original studies. In total, 51 articles met our eligibility criteria (Supplementary Table 1) and were included in the analysis.

#### 3.1. Characteristics of the included studies

Detailed characteristics of the eligible studies are summarized in Tables 2-4. The outcomes of interest ranged widely, from CHD clinical events to atherosclerosis-related traits such as smooth muscle cell phenotype (proliferative vs contractile), carotid intima-media thickness, arterial stiffness, atherosclerotic plaque and cardiovascular risk, cardiac fibrosis induced by ischemia, endothelial progenitor cells function, and T regulatory cells function.

Of the 51 selected studies, 17 included participants from Europe [6–22] 14 from China [23–36], six from USA [37–42], three from India [43–45], two from Canada [46,47], and one each from Japan[48], Malaysia [49], Iran [50], Russia [51], Brazil [52] and Mexico [53]. One article did not clearly specify the origin of the samples [54] and two studies used commercial samples [55,56].

Seven studies analyzed global DNA methylation [6,7,23,34,36,42,52], 31 followed a candidate-gene approach [8–14,20,22,24–33,35,38–41,45,46,49,50,54–56], seven were epigenome-wide association studies (EWAS) [16,18,19,21,44,48,53], two used both global DNA methylation and candidate-gene approaches [37,43], three used EWAS and global DNA methylation approaches [15,17,51], and one used EWAS and candidate-gene approaches [47]. Most of the studies had a case-control design (n=29) [6,8,15,18,20,21,24–26,28–36,44–51,53,54,56]; the remaining study designs were case-control nested in a cohort (n=5) [9–11,17,43], cohort (n=3) [13,22,41], cross-sectional (n=3) [16,40,52], case-control and *in vitro* (n=3) [27,38,39], case-control in a survey (n=2) [12,19], *in vitro* (n=2) [37,55], case-cohort (n=1) [14], cross-sectional in a cohort (n=1) [42], cross-sectional and *in vitro* (n=1) [7] and cohort and case-control in a survey (n=1) [23].

### 3.2 Global methylation studies

Twelve studies analyzing the association between global methylation and CHD or atherosclerosis were selected. High heterogeneity was observed among the molecular techniques used to assess global DNA methylation. Almost half of the studies used the methylation measurement of repetitive elements (LINE-1 or Alu) as a proxy for assessing global methylation [17,23,34,36,42] and the remaining studies used other methods [6,7,15,37,43,51,52] (Supplementary Table 2a).

Most of the eligible global methylation studies analyzed this feature in blood samples (n=8) [6,17,23,34,36,42,43,52] and the rest used vascular tissues [7,15,37,51] (Supplementary Table 2a). Six of the studies included a sample larger than 100 individuals [17,23,34,36,42,43], two studies analyzed samples from fewer than 10 individuals [15,51] and one study used a cell line derived from the aorta but the number of aortas isolated was not mentioned [37] (Supplementary Table 2a).

The results of the 12 eligible global DNA methylation studies were inconsistent, with hypomethylation associated to CHD or atherosclerosis in six studies [6,17,34,36,42,52], and hypermethylation associated to those same traits in four studies [15,23,43,51] and to cardiac fibrotic burden in another [7]. The remaining study found no association between global DNA methylation and the phenotype of

smooth muscle cell (proliferative vs differentiated) [37] (Table 1, Supplementary Table 2a).

### 3.3. Candidate-gene methylation studies

Thirty-four studies analyzing the association between DNA methylation in candidate-genes and CHD or atherosclerosis were selected (Table 2). In the analyzed studies, several molecular techniques were used to assess DNA methylation at the gene level (Supplementary Table 2b).

The vast majority of the selected candidate-gene methylation studies analyzed blood samples (n=28) [8–12,14,20,22,24–32,35,40,41,43,46,47,49,50,56]. The other tissues isolated were aortic [37,39,55] or other vascular tissues [13,38,54] (Supplementary Table 2b). Five of the studies included more than 1,000 participants [12,14,22,31,41], and 13 studies included a sample size between 100 and 999 [9–11,13,25,27,30,32,33,40,45,49,50]. One study analyzed a commercial cell line derived from one individual [55] (Supplementary Table 2b).

Four studies analyzed *ESRα* [8,24,37,38], while *ABCA1* [9,46], *ABCG1* [12,30], *APOE* [11,43], *FOXP3* [27,33], *IL-6* [31,32], *MTHFR* [11,49], and *PON1* [11,20] were analyzed in two studies. Two studies analyzed the association between epigenetic aging and mortality due to CHD [41] or CVD [14]. The full list of candidate-genes and the reported results are shown in Supplementary Table 3.

We found consistent results for *ESRα*, *ABCG1*, *APOE*, *FOXP3* and *IL-6*.

Hypermethylation in the promoters of *ESRα* [8,24,37,38] and *ABCG1* [12,30] and in *FOXP3* [27,33], and hypomethylation in the promoter of *IL-6* [31,32] were associated with CHD, whereas *APOE* methylation was not [11,43]. However, a discrepancy was observed between studies that found an association between CHD or atherosclerosis and DNA methylation in the promoter of *ABCA1* [46], *MTHFR* [49] and *PON1* [11] and others that found no association [9,11,20], respectively.

### 3.4. Epigenome-wide association studies

Eleven EWAS analyzing the association between DNA methylation and CHD or atherosclerosis were selected (Table 3, Supplementary Table 2c). The Infinium Human Methylation 450 BeadChip Array (Illumina) was the most commonly used

array (Supplementary Table 2c) [15–17,19,47,48]. Most of the selected EWAS analyzed blood samples (n=7) [16–19,21,43,47], and the others analyzed vascular tissues [15,48,53] (Supplementary Table 2c).

Four EWAS only showed results of the discovery cohort without any validation of the main findings [18,19,47,48]. Samples from more than 100 individuals were analyzed in the discovery phase of three EWAS [16,17,19] and in the validation phase of three EWAS [16,17,21]. Two EWAS included samples from fewer than 10 individuals in the discovery phase [18,51]. Some studies discovered differentially methylated CpG sites, while others found regions (“islands”) with a high frequency of CpG sites (Supplementary Table 4).

Not all studies provided the full list of CpGs identified in the discovery phase. From the available information, we identified 2,625 CpGs and 111 CpG islands (CGIs) showing differential methylation associated with CHD or atherosclerosis (Supplementary Table 4). The reported CpG sites or CGIs were located within 1,540 different genes (n=2,057) and hundreds of intergenic regions (n=673) (Supplementary Table 5). Six CGIs did not match any pairwise sequence. Of the 2,625 reported CpGs, 14 were identified in more than one of the EWAS, and 8 of these were located in different genes, showing a consistent direction of the association (set 1). Of the 1,540 genes identified in those sequences, 75 were found in two studies and only one gene was identified by three studies. Moreover, 8 additional genes were reported in two of the EWAS when considering genes located upstream or downstream of intergenic CpGs/CGIs. These 84 genes (set 3) and the direction of the association between methylation at gene level and CHD are shown in table 4. Of those 84 genes, 52 have shown consistency in the direction of the association between methylation and atherosclerosis-related traits (set 2). The probability of finding the same gene or CpG in two of the 11 studies was  $1.37 \cdot 10^{-5}$  and  $3.44 \cdot 10^{-10}$ , and in three studies was  $2.05 \cdot 10^{-8}$  and  $2.58 \cdot 10^{-15}$ , respectively.

### 3.5. Functional studies and pathway analysis

We analyzed the biological function of the genes identified as differentially methylated in more than one of the EWAS (n=84). First, we reviewed the Genome-Wide Association Studies catalog and found none of the listed traits identified in 9 of the genes and no CVD- or atherosclerosis-related trait in 19 other genes. The CVD-

or atherosclerosis-related traits associated with the remaining 56 genes are shown in Supplementary Table 6. Most of these genes showed several associations, the most common being obesity-related traits (33%).

We next used the IPA software to identify enriched canonical pathways and the “diseases and functions” terms related to the three sets of genes established according to the consistency on the direction of the association between methylation and CHD: set 1, 8 genes with consistency on CpG methylation status; set 2, 52 genes with consistent methylation at gene level; and set 3, 84 differentially methylated genes. The main results are shown in table 5. The top canonical pathway related to CHD or atherosclerosis, consistently identified by Fisher’s exact test in all three sets, was RhoA signaling (Supplementary Figure 2). Statistical significance declined when adjusting by Benjamini-Hochberg. Using this multiple comparison adjustment, we observed five consistent cardiovascular-related terms in all three sets: endocrine system disorders, cardiovascular system development and function, inflammatory response, immune cell trafficking, and inflammatory disease. Assessment of the more extended sets of genes (set 2 and 3) also identified the following: cardiovascular and nutritional diseases; lipid, carbohydrate and vitamin and mineral metabolism; connective tissue development and function or disorders, and cell-mediated immune response (Supplementary Figures 3 and 4). As an example, the defined cardiovascular disease network is shown in Figure 1.

#### 4. DISCUSSION

In this review, we systematically analyzed the currently available evidence on the association between DNA methylation and CHD and its underlying atherosclerosis. Overall, the scarce evidence suggests no consistent association between global DNA methylation and CHD. On the other hand, several studies have shown a relationship between differential methylation at specific loci and CHD or atherosclerosis outcomes, suggesting a role of epigenetics in the etiopathogenesis of CHD. In total, 84 genes were found in more than one of the EWAS, and this set was enriched in genes related to obesity and metabolism.

The 12 studies that examined the association between global methylation and CHD reported contradictory results. These findings are consistent with other reviews of DNA methylation and CVD studies [57]. Inconsistencies among the results were also reported in systematic reviews examining the relationship between DNA methylation and type 2 diabetes [58], and dyslipidaemia [59]. There are several explanations for this inconsistency: first, methodological issues related to differences in sample size and heterogeneous outcomes; second, the applied assay, the DNA source and the DNA isolation method are critical in the interpretation of global DNA methylation patterns but the analyzed studies had applied heterogeneous methods [60,61]; and third, global methylation refers to the overall level of methylated cytosines within CpG sites in the genome but does not take into account differential methylation at specific loci. The effect of DNA methylation on gene expression is known to be dependent on the location within the genomic sequence where it occurs. Consequently, gene- and loci-specific methylation may be a more informative measure to determine the association between DNA methylation and gene expression and health-related outcomes [62].

Most of the selected studies analyzed DNA methylation using either a candidate gene or an EWAS approach. Although the overall results are more consistent than those from global methylation studies, the outcomes, sample sizes, methylation assays, and DNA sources and isolation methods are diverse across studies, limiting the interpretation of the overall results. The majority of the reviewed studies used a candidate-gene approach. These genes were selected based on previous genetic studies or their biological function. Only eight genes were examined in more than one study; therefore, most of the findings must still be replicated. Considering the replicated candidate-genes, hypermethylation in gene promoters of *ESRα* and *ABCG1* and in the first intron of *FOXP3* and hypomethylation in the promoter of *IL-6* were associated with CHD.

*ESRα* acts dually on cardiovascular cells and tissues: if this receptor bonds to estrogen, the result is vascular protective effects, while the unligated form promotes an inflammatory phenotype in vascular cells [63]. If hypermethylation of its gene promoter inactivates its expression, it could be that no estrogen will bind the receptor and thus, its protective effects would be lost. *ABCG1* encodes a transporter involved

in reverse cholesterol transport [64]. Thus, if hypermethylation in its promoter led to its downregulated expression, this would be expected to influence atherosclerosis through a lower reverse cholesterol transport capacity. On the other hand, *IL-6*, which encodes a pro-inflammatory cytokine, is related to CHD [65]. Therefore, under atherosclerotic conditions, hypomethylation in its promoter could entail the upregulation of its expression, leading to a higher production of the cytokine by macrophages. Finally, *FOXP3* encodes a transcriptional regulator crucial for the regulatory T-cells (Tregs), which modulate inflammation and immunity, and their dysregulation was associated with CVD and atherosclerosis [66]. Demethylation at a highly conserved CpG-enriched element within *FOXP3* intron 1 (*FOXP3-i-1*) has been found to be restricted specifically to this type of Tregs [67]. A final consideration is the important role of *Apo E* in the clearance of triglyceride- and cholesterol-rich lipoproteins from the circulation, slowing down the process of atherosclerosis [68]. The results of four studies support the lack of association between DNA methylation in *APOE* and CHD, suggesting that this relationship may be not influenced through this epigenetic mechanism.

EWAS also examine gene-specific DNA methylation. They have increasingly replaced the candidate-gene approach as they are useful to identify novel CpG sites related to disease phenotypes. Large sample sizes are required and the results obtained must be validated in a replication cohort [69]. Most of the reviewed EWAS validated the obtained results in a replication cohort, but the sample size was relatively small in all of them. Among the differentially methylated translating loci, 84 were identified in more than one of the EWAS, suggesting an epigenetic regulation of those genes in CHD or atherosclerotic conditions. However, the direction of the association between methylation at the gene level and CHD or atherosclerosis is difficult to ascertain, as the effects of methylation on gene expression depend on where the methylation occurs in the genomic sequence [62]. Using three distinct approaches, we analyzed this issue first at the CpG level (8 CpGs showing consistent association); second, at the gene level (52 genes); and third, selecting all the genes showing differential methylation (84 genes).

Among the 84 genes found in more than one of the EWAS, differential methylation of *MCL1* was observed in three independent EWAS. It encodes isoforms of a member

of the Bcl-2 family involved in the regulation of apoptosis, both those maintaining cell viability and inducing apoptosis [70,71]. Apoptosis is associated with the progression of atherosclerosis, with opposing roles depending on the cell type, plaque stage and apoptotic cell localization [72]. Interestingly, anti-inflammatory *IL-10* was shown to enhance both lipid accumulation in macrophages from ACS patients and *MCL1* expression with an anti-apoptotic effect [73]. Thus, *MCL1* may have an important role in atherosclerosis development and it could be regulated differently in each stage through a different mechanism, including DNA methylation.

From the 8 genes showing consistency in the direction of the association between methylation at CpG level and CHD or atherosclerosis, *CRELD2* and *KCNJ14* (a potassium channel) have not been related to any atherosclerotic trait. *AIM2* encodes a cytoplasmic DNA sensor that triggers the inflammasome in macrophages and is upregulated in advanced coronary plaques [74]. *TNS1* is differentially expressed in atherosclerotic plaques [75,76]. *NGEF* is associated with abdominal visceral fat and overall adiposity [77,78]. *PKD2* has a role in monocyte migration and atherosclerosis development [79]. *HRH2* encodes an histamine receptor and is involved in hyperlipidemia-induced atherosclerosis [80]. Finally, *GRIP1* has been shown to play a role in platelet function and thrombosis [81].

In addition, from the other 75 genes found in at least two EWAS, *HOXA3*, whose expression is associated with high abdominal adiposity [82], has been recently identified as differentially methylated in relationship with HDL functionality. Its hypomethylation is associated with a high cholesterol efflux capacity and, thus, a lower atherosclerosis burden [83].

A significant proportion of the genes identified as differentially methylated in more than one of the EWAS were previously identified in genome-wide association studies as associated with CVD or its risk factors and related conditions. The most frequent one was obesity, which is a well-known coronary risk factor [84]. Similarly, in the IPA for “diseases and functions” terms overrepresented among those genes, endocrine system disorders, metabolic disease, and carbohydrate and lipid metabolism were some of the most significant terms. These risk factors for atherosclerotic CVD have obesity as a major driver [85].

In conclusion, the present systematic review suggests that differential DNA methylation at specific genes is associated with CHD or atherosclerosis. The findings describe a set of genes that could be prioritized in future EWAS analysis. The EWAS identify a set of genes highlighting the importance of obesity, lipid and carbohydrate metabolism, inflammation and other pathways in CHD. Further studies are needed to validate the reported results in larger sample sizes. In addition, a consensus method for DNA methylation analysis could be useful to allow data comparisons, especially regarding the type of tissue examined, the molecular technique used and the confounder adjustment for statistical analysis. Finally, functional assays are required to understand the molecular mechanisms that relate DNA methylation to CHD or atherosclerosis and determine its causal, mediating or reversal of causality role.

### **Conflict of interest**

The authors declare they do not have any conflict of interest.

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### **Author contributions**

A.F-S., R.E., I.S., S.S-B. participated in the conception or design of the work. A.F-S. and R.E. were responsible of the review of the manuscripts included in this systematic review and the extraction of the data. S.S-B. and I.S. performed the analysis of the data. All the authors participated in the interpretation of data for the work. A.F-S. and R.E. wrote the draft of the manuscript and the rest of authors revised it critically for important intellectual content. All authors have approved the final version of the manuscript. All authors agree to be accountable for all aspects of

the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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## **FIGURES AND TABLES**

**Figure 1.** Downstream effect analysis of specific differentially methylated genes associated with Cardiovascular disease (CVD), using the set 2 of genes (those reported as methylated in the same direction by more than one of the EWAS, independently of the CpG). Gene products (in the upper part) and CVDs (in yellow) are represented as nodes, and the biological relationship between two nodes is represented as an edge. Edge arrows indicate causation, while simple edges indicate correlation. All edges are supported by at least one publication in the Ingenuity Knowledge Database.

**Table 1.** Main results of the studies using a global methylation approach.

Reference	Conclusion
Ying 2000 <sup>37</sup>	Non-significant increase in global DNA hypermethylation in proliferating SMCs vs differentiated SMCs.
Castro 2003 <sup>6</sup>	Global DNA hypomethylation was associated with CHD.
Sharma 2008 <sup>43</sup>	Global DNA hypermethylation was associated with CHD, especially in aged patients.
Kim 2010 <sup>23</sup>	Global DNA hypermethylation was associated with prevalence and incidence of CHD and its risk factors (MI, stroke, hypertension, diabetes) in males.
Baccarelli 2010 <sup>42</sup>	Global DNA hypomethylation assessed in LINE-1 was associated with CHD and stroke.
Lin 2014 <sup>36</sup>	Global DNA hypomethylation assessed in LINE-1 was associated with ischemic stroke in men.
Watson 2014 <sup>7</sup>	Global DNA hypermethylation in hypoxic cardiac fibroblast was associated to the fibrotic burden in hypoxia.
Wei 2014 <sup>34</sup>	Global DNA hypomethylation measured in LINE-1 repeats was associated with CHD in the Chinese population.
Zaina 2014 <sup>15</sup>	Global DNA hypermethylation was associated with atherosclerosis.
Nazarenko 2015 <sup>51</sup>	Global DNA hypermethylation was associated with coronary atherosclerosis.
Guarrera 2015 <sup>17</sup>	Global DNA hypomethylation measured in LINE-1 repeats was associated with CHD and MI risk in men, being more pronounced in cases with shorter time to disease.
Ramos 2016 <sup>52</sup>	Global DNA hypomethylation was associated with higher cardiovascular risk in postmenopausal women.

CHD: coronary heart disease; CVD: cardiovascular disease. MI: myocardial infarction. SMCs: smooth muscle cells.

**Table 2.** Main results of the studies using a candidate-gene approach.

Reference	Conclusion
Post 1999 <sup>38</sup>	Hypermethylation in <i>ESRα</i> promoter was associated with atherosclerosis and aging of the vascular system.
Ying 2000 <sup>37</sup>	Hypermethylation in <i>ESRα</i> promoter was associated with proliferating SMCs.
Zhu 2005 <sup>39</sup>	Hypermethylation in exon 2 of <i>MTC3</i> was associated with atherosclerosis burden.
Kim 2007 <sup>54</sup>	Hypermethylation in <i>ESRβ</i> promoter was associated with atherosclerosis.
Sharma 2008 <sup>43</sup>	No significant differences in methylation in <i>APOE</i> promoter between patients and controls.
Huang 2009 <sup>24</sup>	Hypermethylation in <i>ESRα</i> promoter was associated with atherosclerosis.
Huica 2011 <sup>8</sup>	Hypermethylation of <i>TIMP1</i> and <i>ESRα</i> was associated with CVD and aging.
Talens 2012 <sup>9</sup>	Hypermethylation of <i>INS</i> and <i>GNASAS</i> was associated with the incidence in MI in women.
Friso 2012 <sup>10</sup>	Hypomethylation in <i>F7</i> promoter was associated with CHD in wild-type A1A1 genotypes.
Zhuang 2012 <sup>25</sup>	Hypermethylation of <i>p15<sup>INK4b</sup></i> was associated with CHD and may have been mediated by altered expression of <i>ANRIL</i> .
Zhao 2012 <sup>40</sup>	Hypermethylation in <i>MAOA</i> promoter was associated with decreased carotid intima-media thickness when twins were analyzed as individuals, but in match pair analysis no association was observed.
Lakshmi 2013 <sup>45</sup>	Hypomethylation in <i>BNIP3</i> promoter and hypermethylation in <i>EC-SOD</i> promoter were associated with CHD.
Jiang 2013 <sup>26</sup>	Hypermethylation in <i>PLA2G7</i> promoter was associated with CHD and aging in women independently of classical risk factors.
Jia 2013 <sup>33</sup>	Epigenetic suppression of <i>FOXP3</i> might have led to downregulation of Treg cells and, in turn, increased the risk of CHD.

Afzali 2013 <sup>50</sup>	Hypermethylation in <i>NPC1</i> promoter was associated with CHD independently of other parameters.
Lü 2013 <sup>27</sup>	Hypomethylation of <i>FOXP3</i> , which is a characteristic of Treg cells, was associated with non-CHD.
Connelly 2013 <sup>55</sup>	Hypomethylation of <i>COL15A1</i> occurs during SMC proliferation and the subsequent increased gene expression may impact SMC phenotype and atherosclerosis formation.
Fiorito 2014 <sup>11</sup>	Hypermethylation in <i>TCN2</i> promoter and <i>AMT</i> gene body in males, <i>PON1</i> gene body in females, and <i>CBS</i> 5'UTR in both genders was associated with CHD.
Gómez-Úriz 2014 <sup>20</sup>	Hypomethylation in <i>TNF-α</i> promoter was associated with stroke.
Zhang 2014 <sup>22</sup>	Hypomethylation of <i>F2RL3</i> was associated with higher CVD mortality, as well as all-cause and other mortality.
Xu 2014 <sup>28</sup>	Hypomethylation in <i>GCK</i> gene-body was associated with high risk of CHD, while its hypermethylation is associated with aging in healthy individuals.
Niu 2014 <sup>29</sup>	Hypermethylation in <i>DDAH2</i> promoter was associated with CHD and with the dysfunction of endothelial progenitor cells in CHD patients.
Peng 2014 <sup>30</sup>	Hypermethylation in <i>ABCG1</i> and <i>GALNT2</i> promoters was associated with an increased risk of CHD.
Guay 2014 <sup>46</sup>	Hypermethylation in <i>ABCA1</i> promoter was associated with CHD and aging in men.
Pfeiffer 2015 <sup>12</sup>	Hypermethylation in <i>ABCG1</i> was associated with CHD.
Wei 2015 <sup>49</sup>	Hypermethylation in <i>MTHFR</i> was associated with ischemic stroke.
Baccarelli 2015 <sup>56</sup>	Hypermethylation of <i>MT-CO1</i> , <i>MT-CO2</i> , <i>MT-CO3</i> and <i>MT-TL1</i> was associated with CVD.
Yang 2016 <sup>31</sup>	Hypomethylation in <i>IL-6</i> promoter was associated with increased risk of CHD.
Nguyen 2016 <sup>47</sup>	Hypomethylation in <i>ANGPTL2</i> promoter was associated with the pro-inflammatory environment in post-ACS patients.

Perna 2016 <sup>14</sup>	Epigenetic age acceleration was associated with higher CVD mortality.
Horvath 2016 <sup>41</sup>	Epigenetic aging rates were not associated with incident CHD outcomes.
Zuo 2016 <sup>32</sup>	Hypomethylation in <i>IL-6</i> promoter was associated with increased risk of CHD, especially MI.
Murray 2016 <sup>13</sup>	Hypermethylation in <i>ANRIL</i> promoter was associated with increased arterial stiffness, which indicated greater cardiovascular risk.
Zhong 2016 <sup>35</sup>	Hypomethylation in <i>COMT</i> promoter was associated with CHD in males and with aging in controls.

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CHD: coronary heart disease; CVD: cardiovascular disease. MI: myocardial infarction. ACS: acute coronary syndrome. SMCs: smooth muscle cells.

**Table 3.** Main results of the studies using an epigenome-wide approach.

Reference	Conclusion
Castillo-Díaz 2010 <sup>53</sup>	Hypomethylation at 142 CGIs and hypermethylation at 17 CGIs were associated with atherosclerosis.
Sharma 2014 <sup>44</sup>	Hypermethylation at 72 DMRs was associated with CHD.
Yamada 2014 <sup>48</sup>	Hypomethylation at 15 CpGs in 14 genes and hypermethylation at 30 CpGs in 22 genes were associated with atherosclerosis.
Zaina 2014 <sup>15</sup>	1858 dm-CpGs were associated with atherosclerosis.
Gómez-Úriz 2015 <sup>21</sup>	80 dm-CpGs and hypermethylation in the promoter of <i>PM20D1</i> were associated with stroke.
Nazarenko 2015 <sup>51</sup>	Hypomethylated CpGs in atherosclerotic samples were located within genes involved in inflammation, immune processes and development.
Ek 2015 <sup>16</sup>	16 CpGs at 11 genes out of 31 discovered and 66 CpGs identified by meta-analysis were associated with CHD.
Guarrera 2015 <sup>17</sup>	Hypomethylation at a DMR within <i>ZBTB12</i> gene body was associated with CHD, being more pronounced in cases with shorter time to disease.
Oudejans 2016 <sup>18</sup>	12 DMRs were identified in the twin sisters at risk of CVD.
Nguyen 2016 <sup>47</sup>	No statistical difference in methylation between controls and CHD patients.
Rask-Andersen 2016 <sup>19</sup>	211 dm-CpGs in 196 genes were associated with MI, of which 42 had been related to cardiac function and development, CVD and recovery after ischemic episode.

CHD: coronary heart disease; CVD: cardiovascular disease. MI: myocardial infarction. CGI: CpG island. dm-CpG: differentially methylated CpG. DMR: differentially methylated region.

**Table 4.** Differentially methylated genes identified in more than one epigenome-wide association study (EWAS).

<b>(A) Set 1, genes with one CpG reported as methylated in the same direction by two EWAS (n=8)</b>			
<b>Hypermethylated</b>		<b>Hypo-methylated</b>	
<i>GRIP1</i> <sup>15,51</sup>	<i>KCNJ14</i> <sup>15,51</sup>	<i>PKD2</i> <sup>15,51</sup>	<i>AIM2</i> <sup>16,51</sup>
<i>HRH2</i> <sup>15,51</sup>	<i>NGEF</i> <sup>15,51</sup>	<i>TNS1</i> <sup>15,51</sup>	<i>CRELD2</i> <sup>16,48,a.</sup>
<b>(B) Set 2, genes reported as methylated in the same direction by more than one EWAS, independently of the CpG (n=52)</b>			
<b>Hypermethylated</b>			<b>Hypo-methylated</b>
<i>ABCB4</i> <sup>15,51</sup>	<i>DLC1</i> <sup>19,48</sup>	<i>KCNJ14</i> <sup>15,51</sup>	<i>SFRP4</i> <sup>15,19</sup>
<i>ACOT2</i> <sup>15,51</sup>	<i>DLG2</i> <sup>15,51</sup>	<i>MECOM</i> <sup>15,19</sup>	<i>SH2D4B</i> <sup>15,51</sup>
<i>AR</i> <sup>44,51,a.</sup>	<i>DOCK5</i> <sup>15,19</sup>	<i>NGEF</i> <sup>15,51</sup>	<i>SLC6A6</i> <sup>15,51</sup>
<i>C1QTNF7</i> <sup>15,51</sup>	<i>DSCAML1</i> <sup>15,44</sup>	<i>OLFML3</i> <sup>15,51</sup>	<i>SMOC2</i> <sup>15,19</sup>
<i>C4orf48</i> <sup>18,19</sup>	<i>DYSF</i> <sup>15,19</sup>	<i>PART1</i> <sup>15,51</sup>	<i>SYTL3</i> <sup>15,19</sup>
<i>CALD1</i> <sup>15,51</sup>	<i>FOXJ3</i> <sup>15,16</sup>	<i>PDZD2</i> <sup>15,19</sup>	<i>THSD4</i> <sup>15,51</sup>
<i>CAMTA1</i> <sup>15,48</sup>	<i>FYN</i> <sup>15,48</sup>	<i>PHACTR2</i> <sup>15,19</sup>	<i>TNS1</i> <sup>15,51</sup>
<i>CBFA2T3</i> <sup>15,17</sup>	<i>GATA3-</i> <i>AS1</i> <sup>44,51</sup>	<i>PKD2</i> <sup>15,51</sup>	<i>TRANK1</i> <sup>15,19</sup>
<i>CORT</i> <sup>15,51</sup>	<i>GRIP1</i> <sup>15,51</sup>	<i>PKNOX2</i> <sup>15,44</sup>	<i>VWC2</i> <sup>15,19</sup>
<i>CTNNA3</i> <sup>15,44</sup>	<i>HAND2</i> <sup>19,44</sup>	<i>RASGRF1</i> <sup>15,19</sup>	<i>ZBTB16</i> <sup>15,16</sup>
<i>DFNA5</i> <sup>15,19</sup>	<i>HMCN1</i> <sup>15,19</sup>	<i>RNF216</i> <sup>15,48</sup>	
<i>DIP2C</i> <sup>15,19</sup>	<i>HRH2</i> <sup>15,51</sup>	<i>SEPT9</i> <sup>15,48</sup>	
<b>(C) Set 3, genes reported as differentially methylated by more than one EWAS, independently of the CpG or the methylation direction (Set 2 + 32 additional genes)</b>			
<i>ABCC1</i> <sup>15,51</sup>	<i>CARS</i> <sup>15,16</sup>	<i>GSC</i> <sup>19,53</sup>	<i>PNLIP</i> <sup>15,51,b.</sup>
<i>ABR</i> <sup>15,48</sup>	<i>CLIC4</i> <sup>15,53,a.</sup>	<i>HOXA3</i> <sup>15,51</sup>	<i>PNLIPRP1</i> <sup>15,5 1,b.</sup>
<i>ALX4</i> <sup>19,51</sup>	<i>ESRRG</i> <sup>19,53,a.</sup>	<i>HOXC11</i> <sup>15,53,a.</sup>	<i>SCEL</i> <sup>15,51</sup>
<i>ARHGEF10</i> <sup>15,16</sup>	<i>FAM109B</i> <sup>19,53</sup>	<i>HOXD4</i> <sup>51,53,a.</sup>	<i>TAS2R9</i> <sup>15,51,b.</sup>
<i>ARID1B</i> <sup>15,48</sup>	<i>FMNL2</i> <sup>15,19</sup>	<i>IL5RA</i> <sup>15,51</sup>	<i>TEAD1</i> <sup>15,51</sup>
<i>ART4</i> <sup>15,19,b.</sup>	<i>FOXP1</i> <sup>15,53</sup>	<i>MIR2054</i> <sup>15,19</sup>	<i>TGFBR3</i> <sup>15,44</sup>
<i>BEND6</i> <sup>15,19</sup>	<i>GCNT2</i> <sup>15,51</sup>	<i>MRPS9</i> <sup>15,53,a.</sup>	<i>TICAM1</i> <sup>15,53,a.</sup>
<i>CAPZB</i> <sup>16,53</sup>	<i>GDF6</i> <sup>15,19</sup>	<i>NRG1</i> <sup>16,19</sup>	<i>WT1</i> <sup>19,51</sup>

<sup>a</sup>genes that are upstream or downstream of one of the reported CpGs; <sup>b</sup>genes within which one CpG/CGI was reported by two EWAS.

**Table 5.** Ingenuity pathway analysis: functional classification of the three sets of genes identified as differentially methylated in more than one independent EWAS. Set 1 includes the 8 genes with methylation consistency at CpG level. Set 2 contains the 52 genes with methylation consistency at gene level. Set 3 comprises the 84 genes found as differentially methylated genes in more than one EWAS, independently of the consistency of the methylation direction. **(A)** Ingenuity pathway analysis of “Canonical pathways” using Fisher’s exact test. **(B)** Ingenuity pathway analysis of “Diseases and functions” using Fisher’s exact test and Benjamini-Hochberg multiple testing correction. Note that those “Diseases and functions” terms in italic separated by a dash line are only significant when using Fisher’s exact test. Terms in bold are those found as enriched for the three sets of genes.

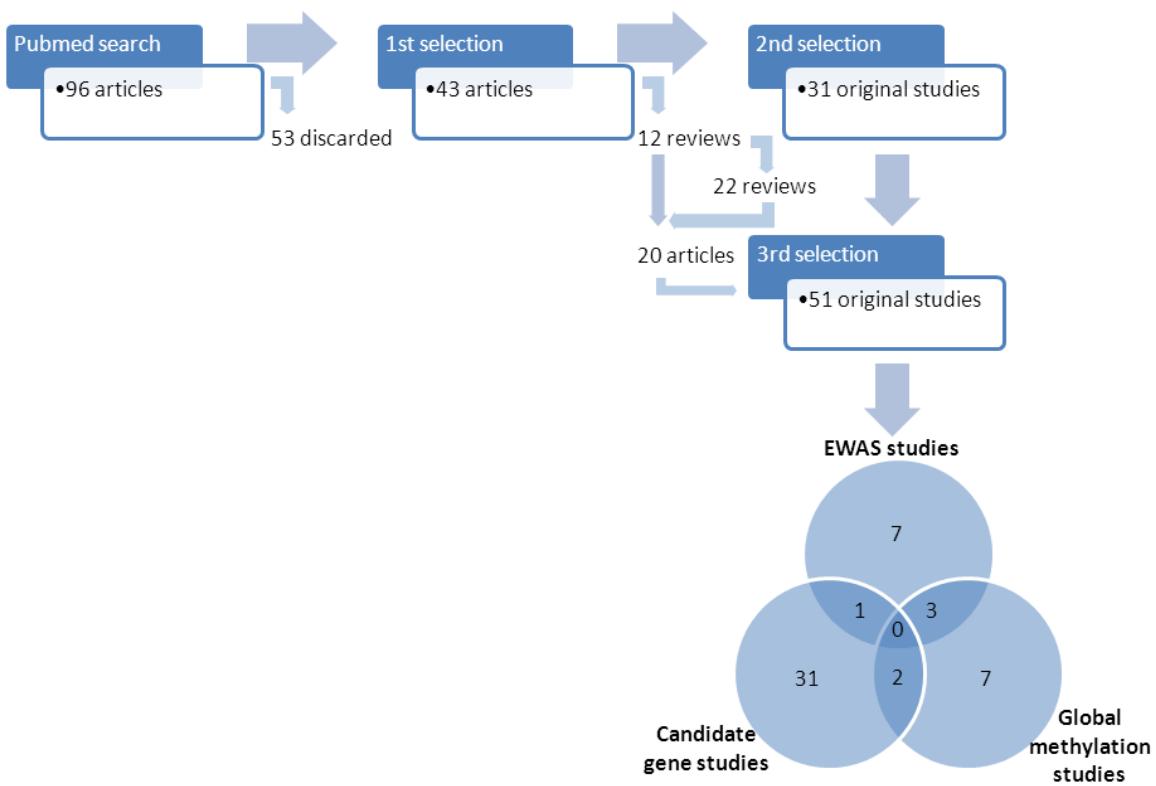
Set 1	Set 2	Set 3
<b>(A) Canonical pathways</b>		
<ul style="list-style-type: none"> <li>- Inflamasome pathway           <ul style="list-style-type: none"> <li>- FAK Signaling</li> <li>- Gas Signaling</li> <li><b>- RhoA Signaling</b></li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>- <b>RhoA Signaling</b> <ul style="list-style-type: none"> <li>- FAK Signaling</li> <li>- Acyl-CoA Hydrolysis</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>- Retinol Biosynthesis           <ul style="list-style-type: none"> <li>- Triacylglycerol Degradation</li> </ul> </li> <li><b>- RhoA Signaling</b></li> <li>- Ephrin A Signaling</li> <li>- RhoGDI Signaling</li> <li>- Acyl-CoA Hydrolysis</li> </ul>
<b>(B) Diseases and functions</b>		
<ul style="list-style-type: none"> <li>- <b>Endocrine System Disorders</b></li> <li>- <b>Inflammatory Disease</b></li> <li>- <b>Cardiovascular System Development and Function</b></li> <li>- <b>Inflammatory Response</b></li> <li>- <b>Immune Cell Trafficking</b></li> </ul>	<ul style="list-style-type: none"> <li>- <b>Endocrine System Disorders</b></li> <li>- <b>Cardiovascular Disease</b> <ul style="list-style-type: none"> <li>- Carbohydrate Metabolism</li> </ul> </li> <li>- Connective Tissue Disorders</li> <li>- <b>Inflammatory Disease</b> <ul style="list-style-type: none"> <li>- Lipid Metabolism</li> <li>- Metabolic Disease</li> <li>- Nutritional Disease</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>- <b>Endocrine System Disorders</b></li> <li>- Metabolic Disease</li> <li>- Carbohydrate Metabolism</li> <li>- <b>Cardiovascular Disease</b></li> <li>- <b>Cardiovascular System Development and Function</b></li> <li>- Connective Tissue Disorders</li> <li>- <b>Inflammatory Disease</b> <ul style="list-style-type: none"> <li>- Lipid Metabolism</li> <li>- Nutritional Disease</li> </ul> </li> <li><b>- Vitamin and Mineral Metabolism</b></li> <li>- Connective Tissue Development and Function</li> </ul>

<ul style="list-style-type: none"> <li>- <b>Vitamin and Mineral Metabolism</b></li> <li>- <b>Cardiovascular Disease</b></li> </ul>	<ul style="list-style-type: none"> <li>- <i>Cell-mediated Immune Response</i></li> <li>- <i>Immune Cell Trafficking</i></li> <li>- <i>Inflammatory Response</i></li> <li>- <b>Connective Tissue Development and Function</b></li> <li>- <b>Cardiovascular System Development and Function</b></li> <li>- <b>Vitamin and Mineral Metabolism</b></li> </ul>	<ul style="list-style-type: none"> <li>- <i>Cell-mediated Immune Response</i></li> <li>- <b>Immune Cell Trafficking</b></li> <li>- <b>Inflammatory Response</b></li> </ul>
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## **SUPPLEMENTAL MATERIAL**

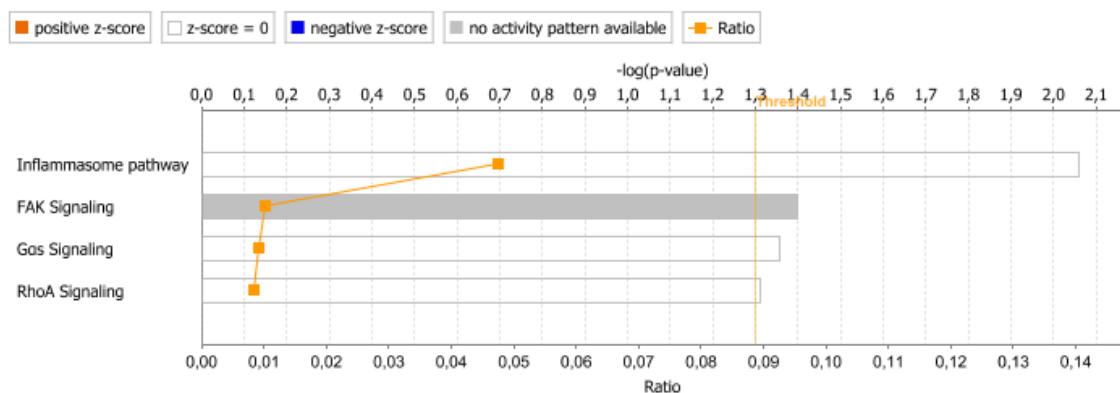
### **Supplemental Figures**

Figure 1. Flowchart of the systematic selection process for the included and excluded studies.

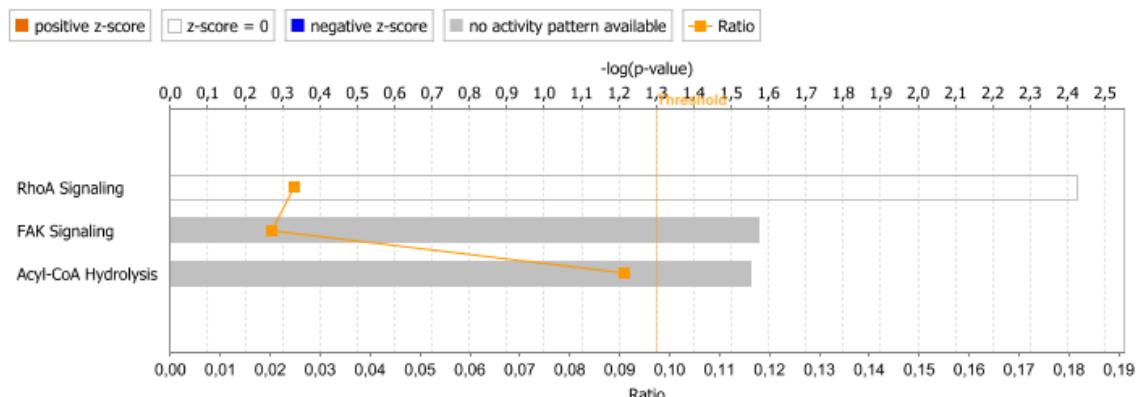


**Figure 2.** Ingenuity pathway analysis of “Canonical Pathways”. Functional classification of: (A) set 1, genes with one CpG reported as methylated in the same direction by two EWAS; (B) set 2, genes reported as methylated in the same direction by more than one of the EWAS, independently of the CpG; and (C) set 3, genes identified as differentially methylated in more than one of the EWAS, independently of the methylation direction. Fisher’s exact test was applied. The orange dots connected by a line indicate the ratio (lower axis) between the number of genes from our dataset that map to one pathway and the total number of genes from the Ingenuity database mapping to the same pathway.

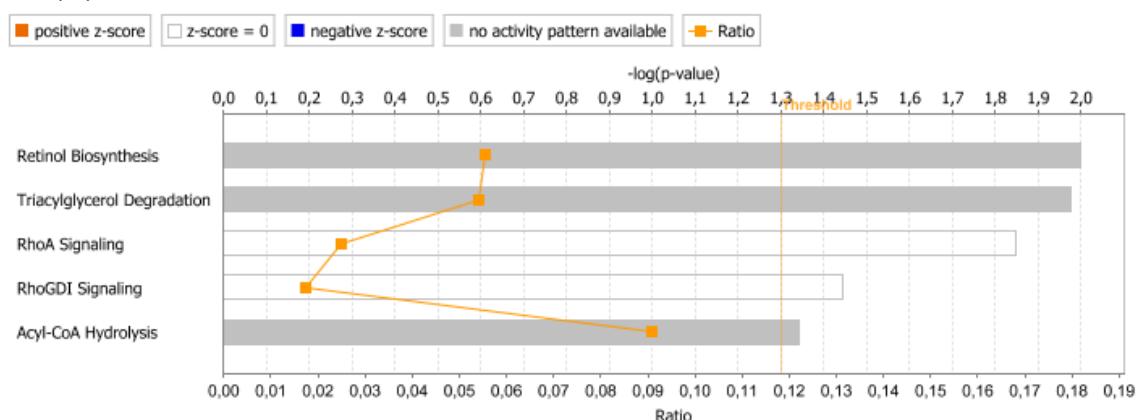
(A) Set 1



(B) Set 2

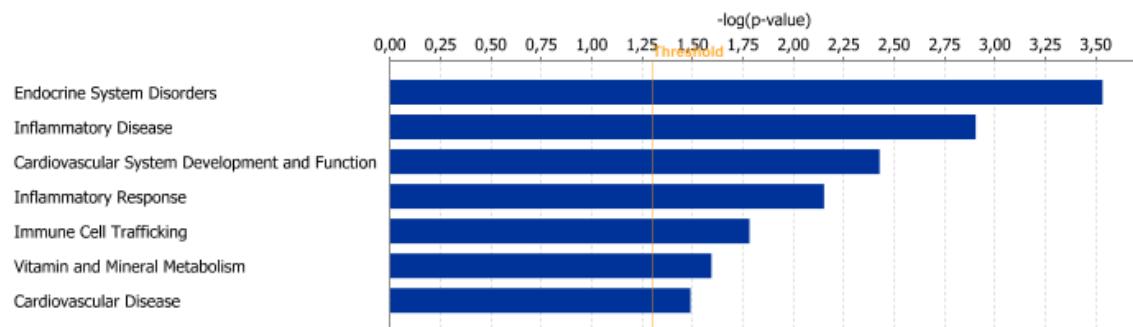


(C) Set 3

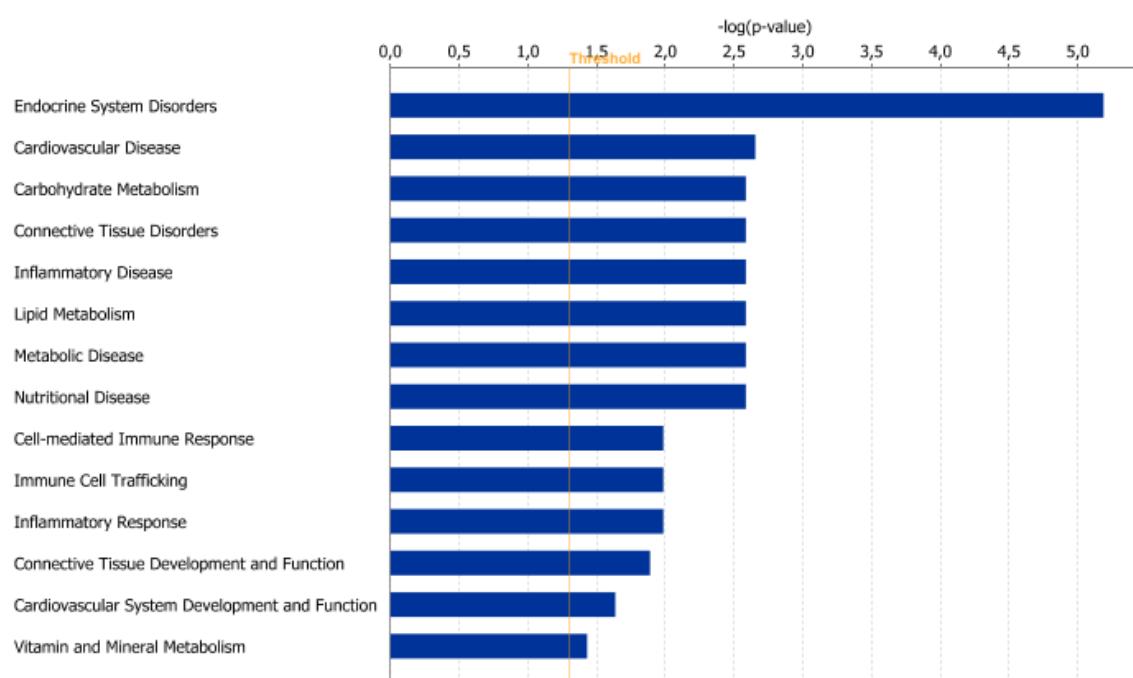


**Figure 3.** Ingenuity pathway analysis of “Diseases and functions”. Functional classification of: set 1, genes with one CpG reported as methylated in the same direction by two EWAS; set 2, genes reported as methylated in the same direction by more than one of the EWAS, independently of the CpG; and set 3, genes identified as differentially methylated in more than one of the EWAS, independently of the methylation direction, using Fisher’s exact test (A) or Benjamini-Hochberg (B-H) multiple testing correction (B).

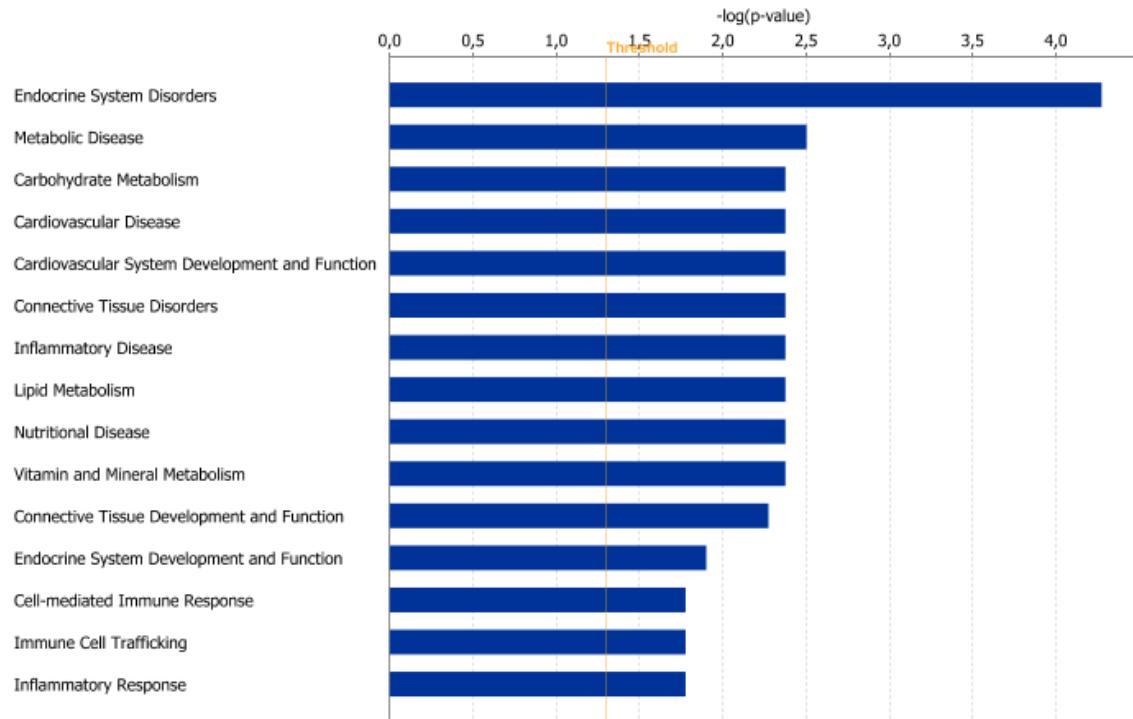
(A-Set 1)



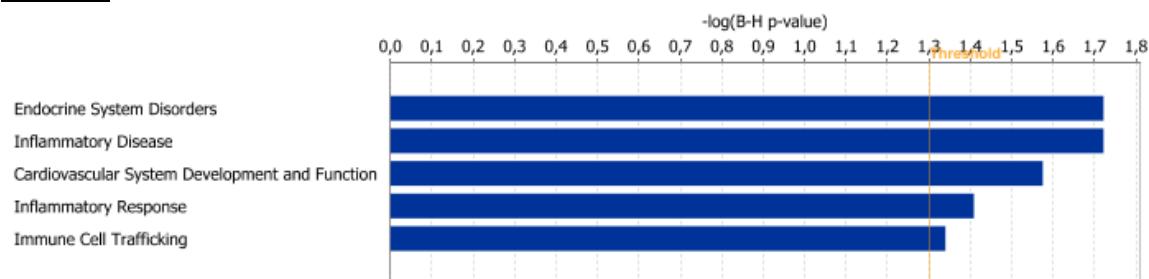
(A-Set 2)



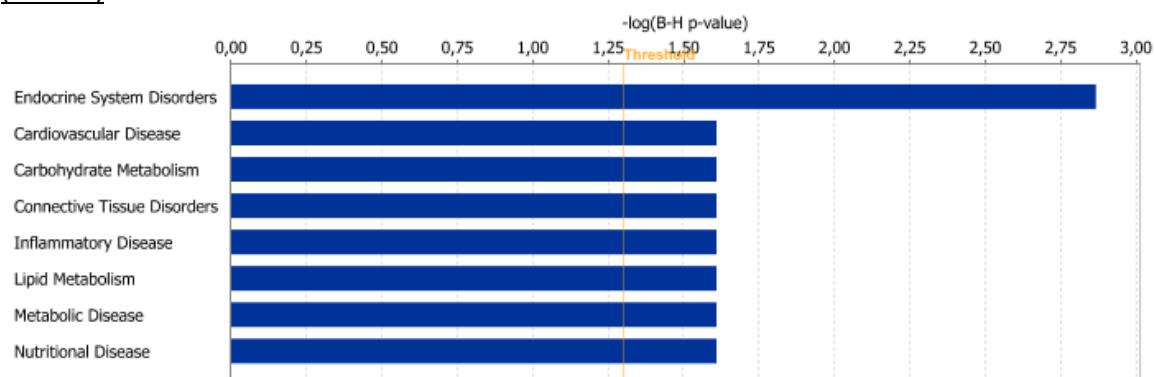
**(A-Set 3)**



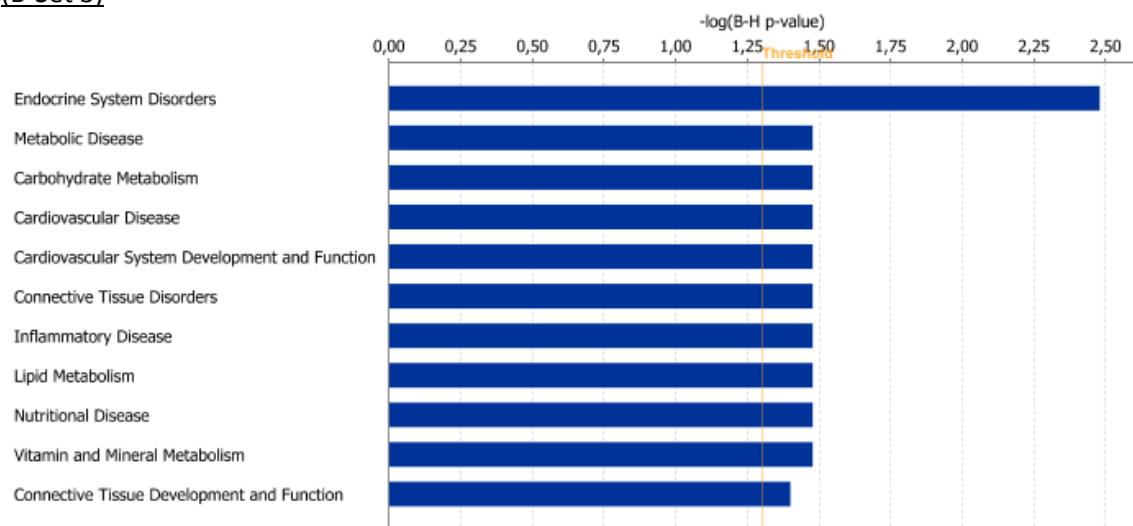
**(B-Set 1)**



**(B-Set 2)**

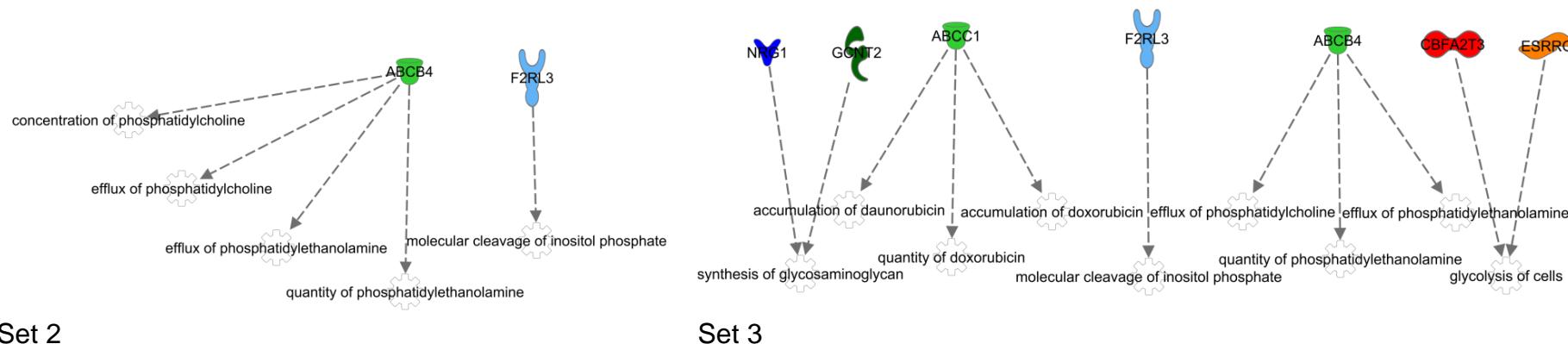


**(B-Set 3)**

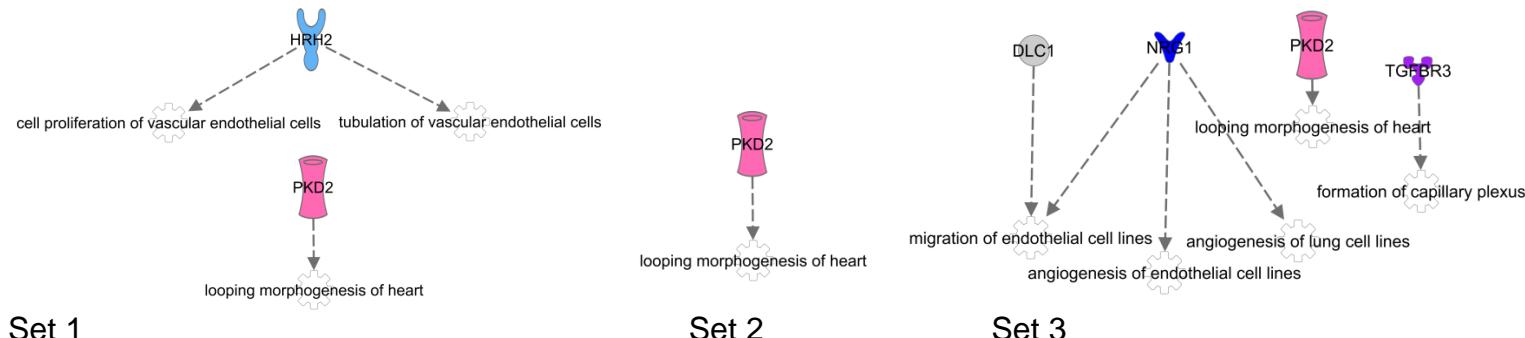


**Figure 4.** Downstream effect analysis of specific differentially methylated genes associated with cardiovascular-related “Diseases and Functions”, using: genes with one CpG reported as methylated in the same direction by two EWAS (Set 1), genes reported as methylated in the same direction by more than one of the EWAS, independently of the CpG (Set 2), and genes identified as differentially methylated in more than one of the EWAS, independently of the methylation direction (Set 3). For these networks, gene products and diseases or functions are represented as nodes, and the biological relationship between two nodes is represented as an edge. Edge arrows indicate causation, while simple edges indicate correlation. All edges are supported by at least one publication in the Ingenuity Knowledge Database. The legend of the interaction networks is also summarized.

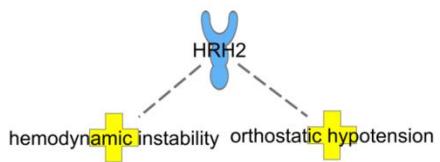
#### (A) Carbohydrate metabolism



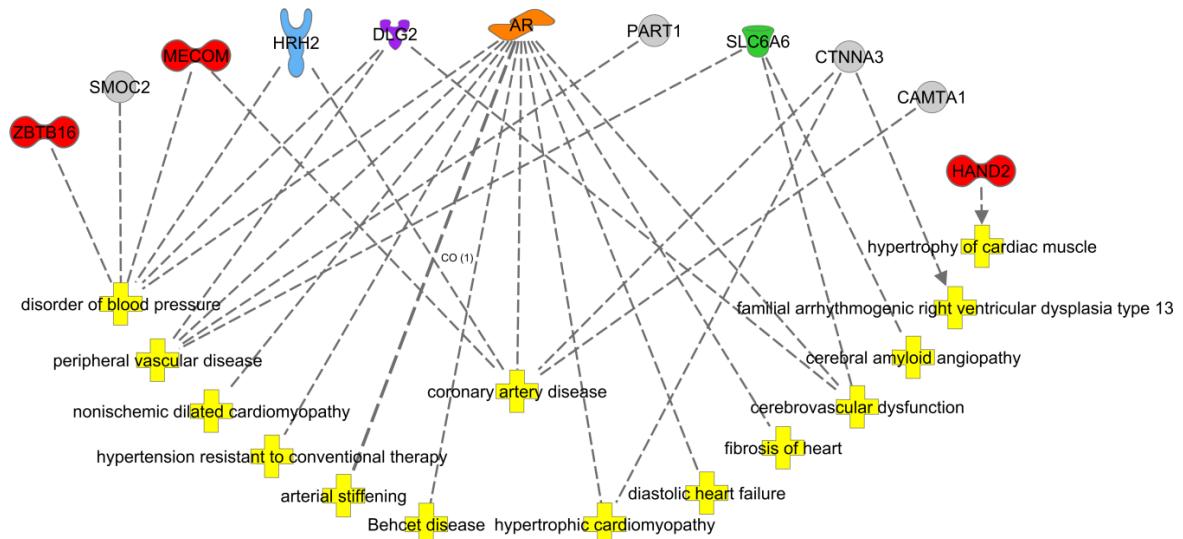
#### (B) Cardiovascular development and function



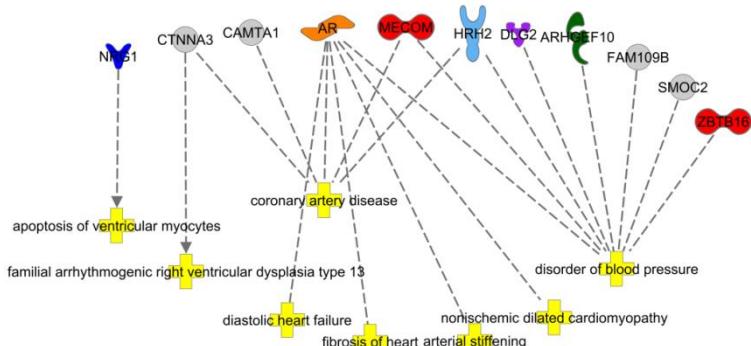
### (C) Cardiovascular disease



Set 1



Set 2



Set 3

### (D) Cell-mediated immune response and Immune cell trafficking

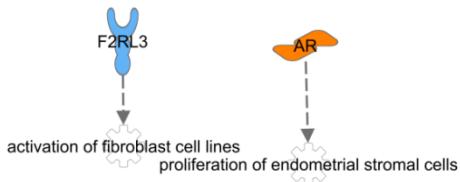


Set 1

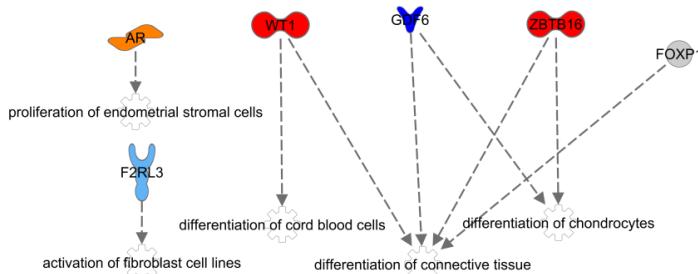
(only Immune cell trafficking)

Set 2 and 3

### (E) Connective tissue development and function

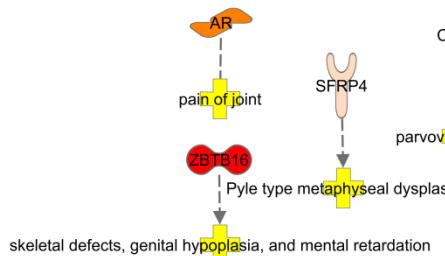


Set 2

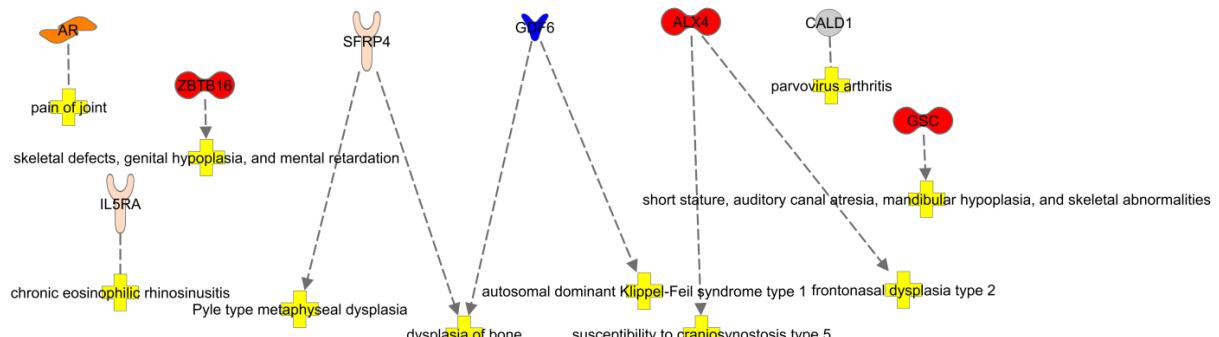


Set 3

### (F) Connective tissue disorders

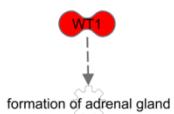


Set 2



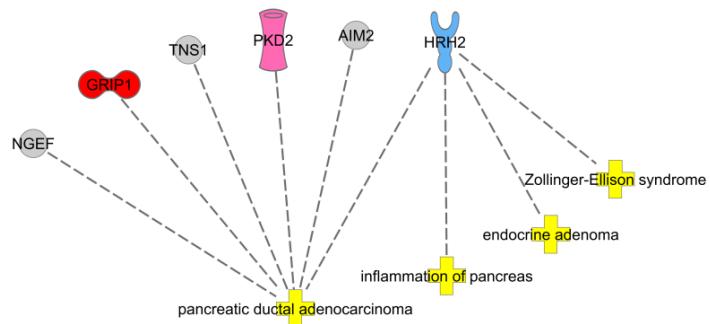
Set 3

### (G) Endocrine system development

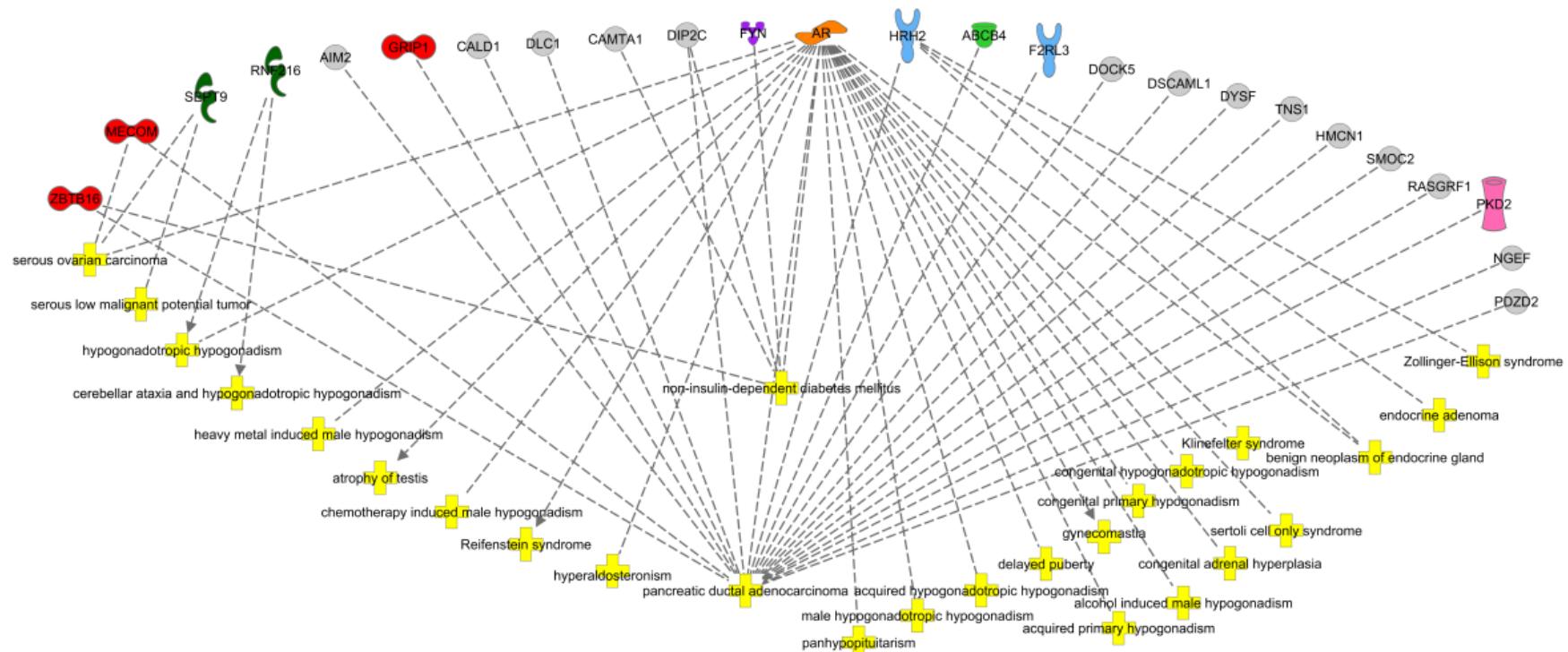


Set 3

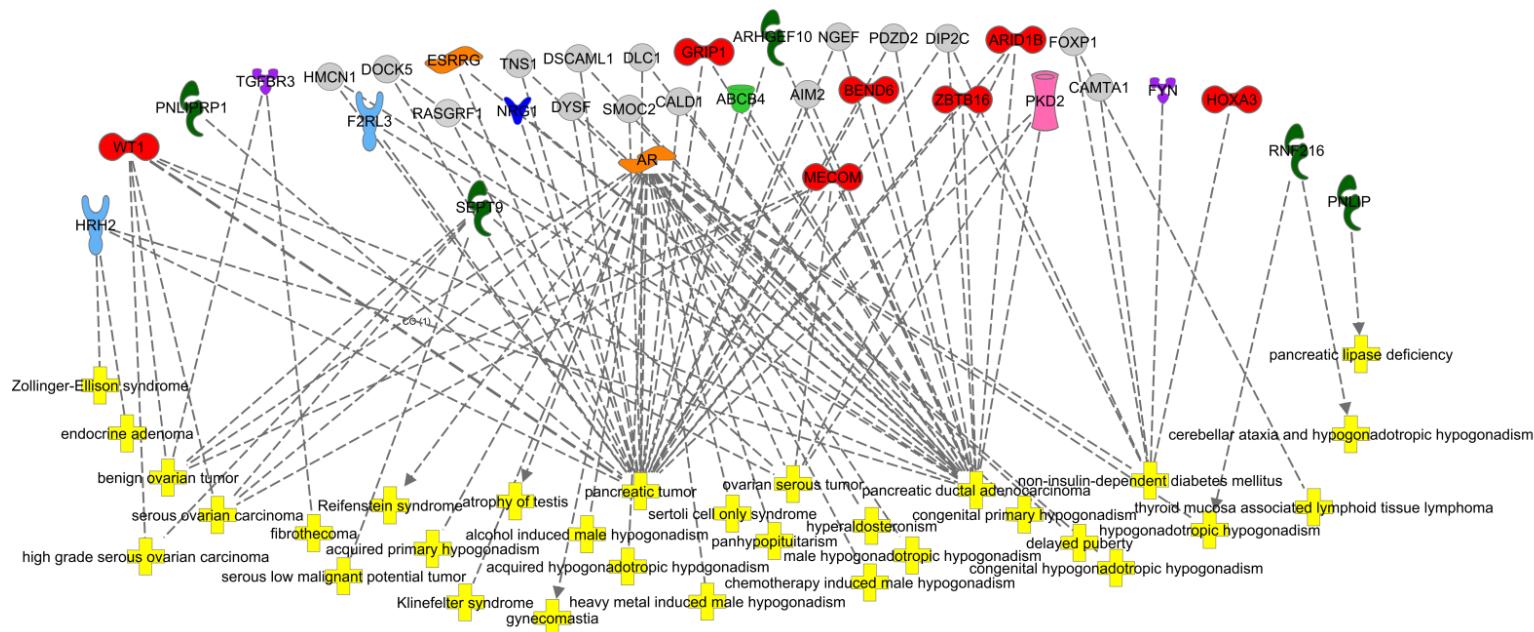
## (H) Endocrine system disorders



Set 1

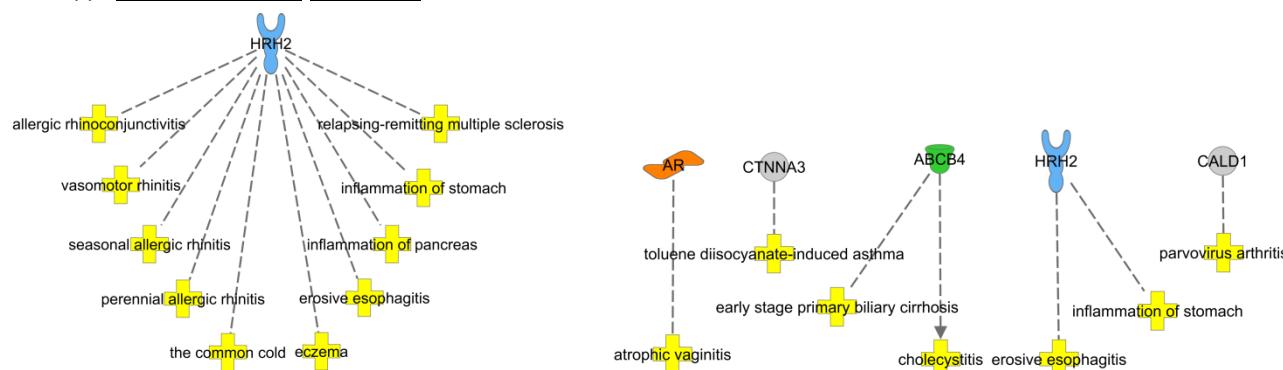


Set 2



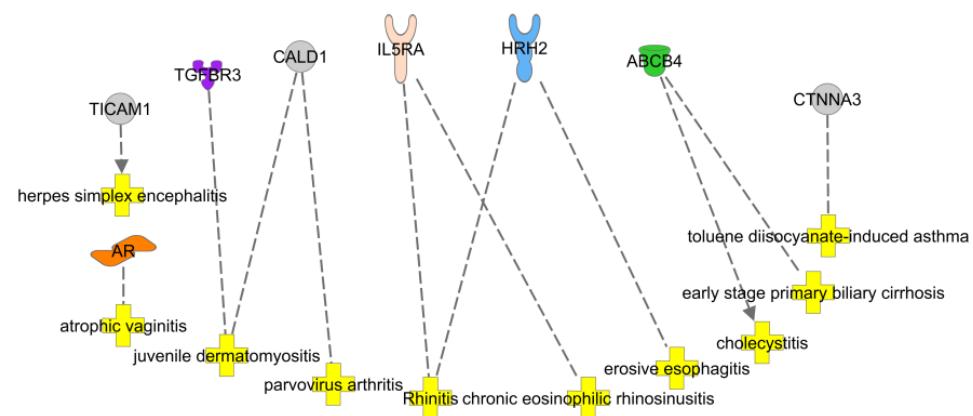
Set 3

(I) Inflammatory disease



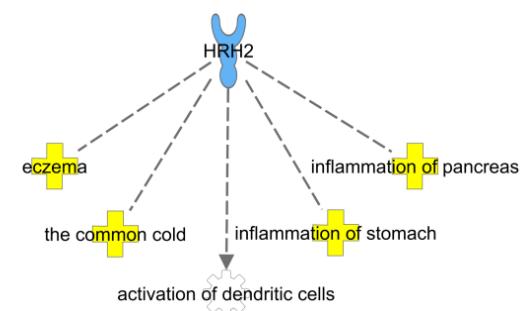
Set 1

Set 2

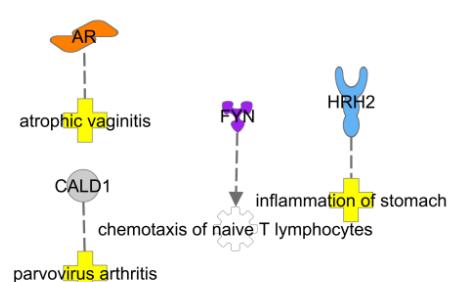


Set 3

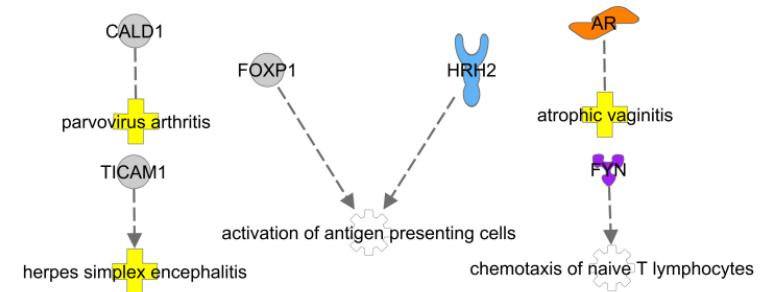
#### (J) Inflammatory response



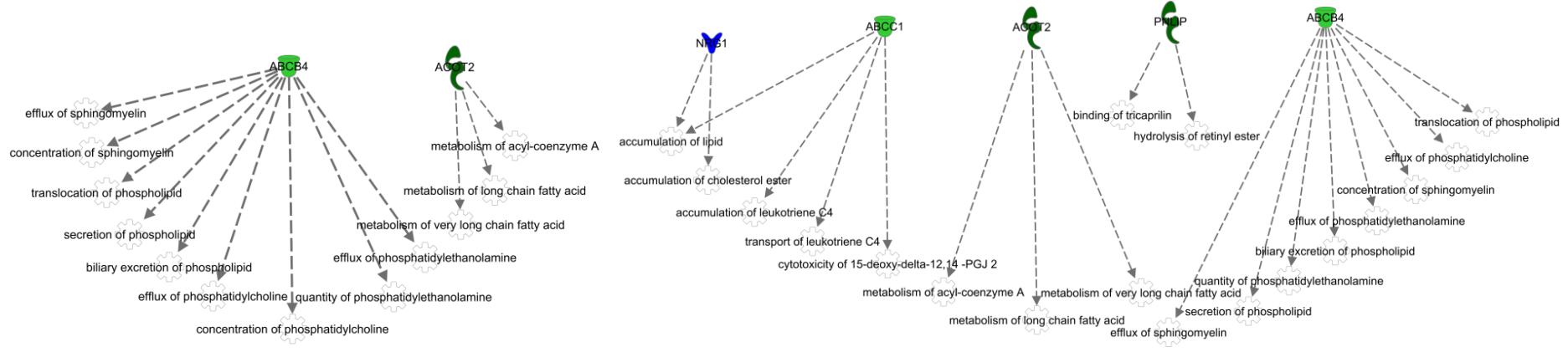
Set 2



Set 3



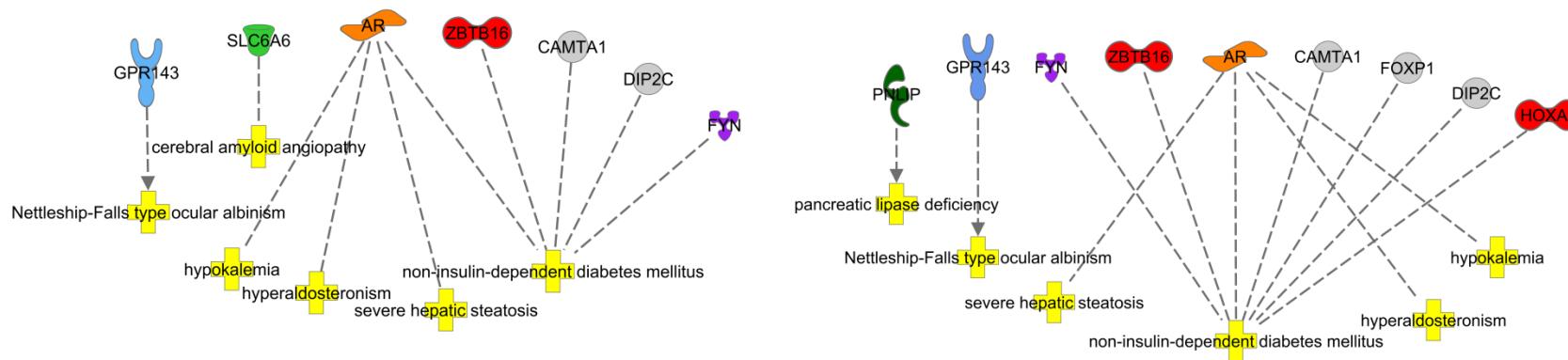
## (K) Lipid metabolism



Set 2

Set 3

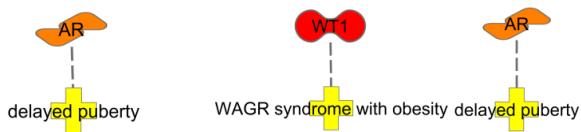
## (L) Metabolic disease



Set 2

Set 3

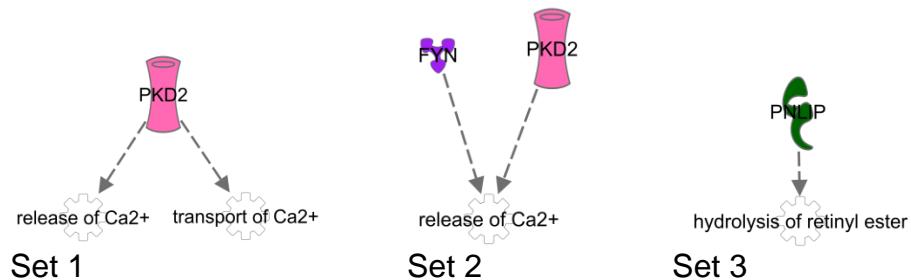
### (M) Nutritional disease



Set 2

Set 3

### (N) Vitamin and mineral metabolism



Set 1

Set 2

Set 3

### Legend

- Enzyme
- G-protein Coupled Receptor
- Transmembrane receptor
- Growth factor
- Ion Channel
- Kinase
- Ligand-dependent Nuclear Receptor
- Transcription Regulator
- Transporter
- Other
- Function
- Disease
- Relationship

### **Supplemental Tables**

Supplementary tables (1-6) are available in the Excel file.

**Table 1. Study eligibility criteria.**

Study eligibility criteria	
Differential DNA methylation	CpG or CGI methylation as defined by each study (no restriction regarding laboratory method, gene panel or marker threshold value)
Outcome measure	MI, CVD, CHD or atherosclerosis
Study design	Epidemiological designs and <i>in vitro</i> in humans
Population size/type	Any/General population, excluding specific subgroups of patients, such as those with familiar hypercholesterolemia or chronic kidney disease
Anatomical site	Any
Study tissue	Any
Length of follow-up	Any

CGI: CpG islands; MI: myocardial infarction; CVD: cardiovascular disease; CHD: coronary heart disease.

Table 2a. Summary of the selected studies using a global methylation approach with all the extracted information

Reference	First author, year and journal	Country	Study Design	Reference population	Sample size	Tissue	Methylation strategy	Outcome	Conclusion	Quality assessment
					n=?					
Ying 2000 Cardiovasc Res	10727665	USA	<i>In vitro</i>	Organ donors		Non-atherosclerotic aorta (derived SMCs)	RLGS-M	SMC phenotype	Non-significant increase in global DNA hypermethylation in proliferating SMCs vs differentiated SMCs.	10/31
Castro 2003 Clin Chem	12881445	Portugal/The Netherlands?	Case-control	Male atherosclerotic vascular patients (stroke or MI) and healthy controls	17 CHD cases (8 stroke + 9 MI) + 15 controls	Blood (leukocytes)	Cytosine extension assay	Stroke or MI	Global DNA hypomethylation was associated with CHD.	17/37
Sharma 2008 DNA Cell Biol	18613790	India	Case-control nested in a cohort	CHD patients and healthy controls	137 CHD cases + 150 controls	Blood	Cytosine extension assay	CHD	Global DNA hypermethylation was associated with CHD, especially in aged patients.	17/35
Kim 2010 PLoS One	20300621	China	Case-control nested in a cross-sectional and cohort	Singapore Chinese Health Study	286 (101 prevalent CHD cases + 52 incident CHD cases)	Blood (leukocytes)	MethylLight assay of ALU and SAT	MI, stroke, hypertension or diabetes	Global DNA hypermethylation was associated with prevalence and incidence of CHD and its risk factors (MI, stroke, hypertension, diabetes) in males but not in females.	30/37
Baccarelli 2010 Epidemiology	20805753	USA	Cross-sectional in a cohort and cohort	Elderly men from the Normative Aging Study	712 (242 prevalent CVD cases; 470 CVD free at baseline: 44 incident CVD cases + 86 deaths)	Blood	LINE-1, pyrosequencing	CHD, stroke, and CHD and stroke mortality	Global DNA hypomethylation assessed in LINE-1 was associated with CHD and stroke.	32/37
Lin 2014 Curr Neurovasc Res	24295503	China	Case-control	Ischemic stroke patients and healthy controls	280 ischemic stroke cases + 280 matched controls	Blood	LINE-1, pyrosequencing	Ischemic stroke	Global DNA hypomethylation assessed in LINE-1 was associated with ischemic stroke in men.	29/36
Watson 2014 Hum Mol Genet	24301681	Ireland	Cross-sectional and <i>in vitro</i>	Stable patients undergoing elective cardiac-bypass surgery	26 CHD cases (13 with high hypoxia markers and 13 with low hypoxia markers)	Right atrial appendages	Flow cytometry based on an antibody specific to methylated DNA	Cardiac fibrosis induced by ischemia	Global DNA hypermethylation in hypoxic cardiac fibroblast was associated to the fibrotic burden in hypoxia.	15/33
Wei 2013 Arq Bras Cardiol	24918913	China	Case-control	CHD patients and healthy controls	334 CHD cases + 788 controls	Blood (leukocytes)	LINE-1, pyrosequencing	CHD	Global DNA hypomethylation measured in LINE-1 repeats was associated with CHD in the Chinese population.	29/37
Zaina 2014 Circ Cardiovasc Genet	25091541	Spain & Sweden	Case-control	Deceased Spanish woman	1 donor-matched pair of atherosclerotic/ normal aorta	Aorta (donor-matched atherosclerotic/ non-atherosclerotic)	Bisulfite sequencing	Atherosclerotic plaque	Genome-wide DNA hypermethylation was associated with atherosclerosis.	21/37
Nazarenko 2015 PLoS One	25856389	Russia	Case-control	Russian men undergoing surgery for severe coronary artery stenosis	4 donor-matched samples of the 3 tissues from 6 individuals	Atherosclerotic right coronary artery, internal mammary arteries and great saphenous veins (donor-matched)	Infinium HM27 BeadChip (Illumina)	Coronary atherosclerosis	Genome-wide DNA hypermethylation was associated with coronary atherosclerosis.	25/36
Guarrera 2015 Clin Epigenetics	26705428	Italy	Case-control nested in a cohort	MI cases and healthy controls from Italian EPICOR and Dutch EPIC (EPIC-NL)	292 prevalent CHD cases + 247 matched controls (EPICOR), 317 incident CHD cases + 262 controls (EPIC-NL)	Blood (leukocytes)	LINE-1, Infinium HM450 BeadChip (Illumina) in EPICOR samples, MALDI-TOF mass spectrometry methylation assay in EPIC-NL	CHD and MI risk	Global DNA hypomethylation measured in LINE-1 repeats was associated with CHD and MI risk in men, being more pronounced in cases with shorter time to disease.	31/37
Ramos 2016 BMC Med Genet	27724854	Brazil	Cross-sectional	Postmenopausal women	90	Blood (leukocytes)	MDQ1 Imprint kit (ELISA-based kit)	Cardiovascular risk	Global DNA hypomethylation was associated with higher risk of cardiovascular risk in postmenopausal women.	25/34

MI: myocardial infarction. CVD: cardiovascular disease. ACS: acute coronary syndrome. CHD: coronary heart disease.RLGS-M: restriction landmark genome scanning. MALDI-TOF: Matrix-Assisted Laser Desorption/Ionization - Time Of Flight. MDQ1: Methylated DNA Quantification Kit.

Table 2b. Summary of the selected studies using a candidate-gene methylation approach with all the extracted information

Reference	Country	Study Design	Reference population	Sample size	Tissue	Methylation strategy	Gene(s)	Outcome	Conclusion	Quality assessment	
Post 1999 Cardiovasc Res	10615426	USA	Case-control and <i>in vitro</i>	Patients undergoing coronary artery bypass grafting	19 internal mammary, 21 saphenous vein, 17 aorta, 31 right atrium	Methylation sensitive enzyme analysis by Southern blot	<i>ESRα</i>	Atherosclerotic plaque	Hypermethylation in <i>ESRα</i> promoter was associated with atherosclerosis and aging of the vascular system.	15/35	
Ying 2000 Cardiovasc Res	10727665	USA	<i>In vitro</i>	Organ donors	n=?	Methylation sensitive enzyme analysis by Southern blot and COBRA	<i>ESRα</i>	SMC phenotype	Hypermethylation at <i>ESRα</i> promoter was associated with proliferating SMCs.	10/31	
Zhu 2005 Circulation	16116050	USA	Case-control and <i>in vitro</i>	Organ donors	SMC from 10 aorta; Vascular tissue: 23 aorta + 12 coronary artery with different atherosclerosis burden	Bisulfite sequencing	<i>MCT3</i>	SMC phenotype	Hypermethylation at CCG in exon 2 of <i>MTC3</i> was associated with atherosclerosis burden. <i>MTC3</i> expression downregulation was associated with proliferating SMCs vs differentiated SMCs.	13/35	
Kim 2007 Biochim Biophys Acta	17110088	Korea/USA?	Case-control	Patients undergoing directional coronary atherectomy and surgical carotid endarterectomy, coronary artery bypass grafting	15-20 CHD patients	MSP and COBRA	<i>ESRβ</i>	Atherosclerotic plaque	Hypermethylation in <i>ESRβ</i> promoter was associated with atherosclerosis.	14/35	
Sharma 2008 DNA Cell Biol	19813790	India	Case-control nested in a cohort	CHD patients and healthy controls	15 CHD cases + 15 controls	Blood	Bisulfite sequencing	<i>ApoE</i>	CHD	No significant differences in methylation in <i>ApoE</i> promoter between patients and controls.	17/35
Huang 2009 Pathophysiology	19285843	China	Case-control	Patients with atherosclerosis approved by carotid calcified ultrasound examination and healthy	54 CHD cases + 28 controls	Blood	Nested-MSP	<i>ESRα</i>	Atheromatosis	Hypermethylation in <i>ESRα</i> promoter was associated with atherosclerosis and homocysteine increased serum levels.	17/32
Huica 2011 Romanian Biotechnological Letters	-	Romania	Case-control	CVD patients and healthy controls	37 CHD cases + 25 controls	Blood	MSP	<i>TIMP-1, ESRα</i>	CVD	Hypermethylation of <i>TIMP-1</i> and <i>ESRα</i> was associated with CVD and aging.	9/34
Talens 2012 Int J Epidemiol	22101166	The Netherlands, USA & UK	Case-control nested in a cohort	European PROSPER trial	122 MI cases + 126 controls	Blood (Leukocytes)	Mass spectrometry	<i>IL10, LEP, ABCA1, IGF2, INS (INSIGF), GNASAS (NESPAS)</i>	MI	Hypermethylation of <i>INS</i> (and 4 CpGs within) and <i>GNASAS</i> (and at 10 CpGs within) was associated with the incidence in MI in women, suggesting a development of atherosclerosis in women. There were shown to be associated to prevalent coronary artery disease.	26/32
Frisco 2012 J Med Genet	22315437	Italy	Case-control nested in a cohort	CHD patients from the Verona Heart Project Cohort	165 CHD cases + 88 controls	Blood (PBMCs)	Bisulfite sequencing	Plasma factor VII gene (F7)	CHD	Hypermethylation in <i>F7</i> promoter corresponded to higher FVIIa concentrations and was associated with CHD in wild-type A1A1 genotypes but not in mutant polymorphism A2A2 (323)	24/32
Zhuang 2012 Plos One	23091611	China	Case-control	CHD patients and healthy controls	95 CHD cases + 110 controls	Blood	MethylLight assay and bisulfite pyrosequencing	Apoptosis-related genes ( <i>LOX-1, CASP3, BCL-2, BAX, TIMP3, ANXA5, cFLIP-3</i> ) and INK4/ARF tumor suppressor genes ( <i>p14(ARF), p15(INK4b), p15(INK4a)</i> )	CHD (neither MI nor severe heart failure)	Hypermethylation of <i>p15(INK4b)</i> was associated with CHD and may have been mediated by altered expression of <i>ANRL</i> .	26/35
Zhao 2012 BMC Med Genet	23116433	USA	Cross-sectional, twins register	Monzygotic twin pairs from the Emory Twin Studies in USA	84 twin pairs	Blood (Leukocytes)	Bisulfite pyrosequencing	<i>MAOA</i>	Carotid intima-media thickness	Hypermethylation in <i>MAOA</i> promoter was associated with decreased carotid intima-media thickness at mean level and at 4 of 7 CpGs when twins were analyzed as individuals, but in match pair analysis no association was observed.	29/34
Lakshmi 2013 Mol Cell Biochem	23160801	India	Case-control	CHD patients and healthy controls	94 CHD cases + 83 controls	Blood	COBRA and MSP	<i>BNIP3, EC-SOD, GSTP1</i>	CHD	Hypermethylation of <i>BNIP3</i> and <i>EC-SOD</i> was associated with CHD. Hypermethylation in <i>GSTP1</i> promoter was not significant.	16/35
Jiang 2013 Plos One	23556769	China	Case-control	CHD patients and healthy controls	36 CHD cases + 36 controls	Blood	Bisulfite pyrosequencing	<i>PLA2G7</i>	CHD	Hypermethylation of <i>PLA2G7</i> promoter was associated with CHD and aging in women independently of classical risk factors.	23/34
Jia 2013 Atherosclerosis	23566804	China	Case-control	ACS patients with stenosis and healthy controls	188 CHD cases + 68 controls	PBMCs and CD4+CD25+Tregs	Bisulfite sequencing	<i>FOXP3</i>	Tregs function	Eigenetic suppression of <i>FOXP3</i> might have led to down-regulation of Tregs cells and, in turn, increased the risk of CHD.	20/33
Alzali 2013 Iranian Biomed Journal	23567849	Iran	Case-control	CVD patients and healthy controls	50 CHD cases + 50 controls	Blood (Leukocytes)	Nested-MSP	<i>NPC1</i>	MI and coronary insufficiency	Hypermethylation in <i>NPC1</i> promoter was associated with CHD independently of other parameters.	23/33
Lü 2013 Atherosclerosis	23735638	China	Case-control and <i>in vitro</i>	ACS patients before thrombolytic or coronary revascularization	89 CHD cases + 35 controls	Blood (CD4+CD25+ Tregs) and cultured CD4+CD25+ Tregs	Bisulfite pyrosequencing	<i>FOXP3</i>	Tregs function and CHD	Hypermethylation of <i>FOXP3</i> , which is a characteristic of Treg cells, was associated with CHD.	18/33
Connelly 2013 Hum Mol Genet	23912340	Commercial sample	<i>In vitro</i>	Cell culture	SMC from a 22-year-old individual	Aorta-derived SMCs	Bisulfite pyrosequencing	<i>COL15A1</i>	SMC phenotype	Hypermethylation of <i>COL15A1</i> markers during SMC proliferation and the subsequent increased gene expression may impact SMC phenotype and atherosclerosis formation.	15/20
Florio 2014 Nutr Metab Cardiovasc Dis	24418380	Italy	Case-control nested in a cohort	MI patients from EPIC cohort	206 CHD cases + 206 matched controls	Blood	Infinium HM450 BeadChip (Illumina)	One Carbon Metabolism and homocysteine pathway genes: <i>ANCR, ALDH1A1, AMT, APOE, ATC, BHMT, CBL, CBS, CTH, DHFR, DMT1, FOLH1, FOLR2, FTO, GART, MAT1A, MAT2B, MTHFD1, MTHFD1L, MTHFD2, MTHFD2L, MTHFS, MTHFR, MTR, MTRN, PON1, PON2, SLC1, SNAT1, SNAT2, TCN2, TYMS</i>	CHD	5 DMRs were identified with hypermethylation in CHD cases than in controls ( <i>TCN2</i> and <i>AMT</i> gene body, <i>dhfr</i> in males, <i>PON1</i> gene body) and only in females, and <i>CBS</i> 5UTR in both genders). Four methylation clusters associated with CHD were also identified.	26/37
Gómez-Uriza 2014 J Physiol Biochem	24500802	Spain	Case-control	Stroke patients and healthy controls	12 stroke cases + 12 matched-controls	Blood	EpiTYPER assay (Sequenom)	<i>TNF-α</i> and <i>PON</i>	Stroke	Hypermethylation in <i>TNF-α</i> promoter was associated with stroke.	26/38
Zhang 2014 Int J Epidemiol	24510982	Germany	Cohort	ESTHER cohort	3,588 participants (151 CVD-deaths)	Blood	MALDI-TOF	<i>F2RL3</i>	CVD mortality	Hypermethylation of <i>F2RL3</i> was associated with higher CVD mortality, as well as all-cause and other mortality.	30/35
Xu 2014 Biomed Res Int	24696842	China	Case-control	CHD patients and healthy controls	36 CHD cases + 36 matched controls	Blood	Bisulfite sequencing	<i>GCK</i>	CHD	Hypermethylation in <i>GCK</i> gene-body was associated with high risk of CHD, while its hypermethylation is associated with aging in healthy individuals.	19/35
Niu 2014 J Transl Med	24934151	China	Case-control	CHD patients and healthy controls	25 CHD cases + 15 controls	Blood (endothelial progenitor cells)	Bisulfite pyrosequencing	<i>DDAH2</i>	Endothelial progenitor cells function	Hypermethylation in <i>DDAH2</i> promoter was associated with CHD, and with the cytotoxicity of endothelial progenitor cells in CHD patients.	21/34
Peng 2014 Plos One	25084356	China	Case-control	Patients with at least one major coronary artery with more than 50% occlusion	85 CHD cases + 54 controls	Blood	MSP	<i>ABCG1, GALNT2, HMGCR</i>	CHD	Hypermethylation in <i>ABCG1</i> and <i>GALNT2</i> promoters was associated with an increased risk of CHD.	20/34
Guay 2014 Clin Epigenetics	25093045	Canada	Case-control	Men with CHD undergoing heart surgery	38 CHD cases + 50 controls	Blood (leukocytes)	Bisulfite pyrosequencing	<i>ABC1</i>	CHD	Hypermethylation in <i>ABC1</i> promoter was associated with both CHD (especially in older patients) and aging in men.	26/32
Pfeiffer 2015 Circ Cardiovasc Genet	25583993	Germany	Case-control in a cross-sectional survey	MI patients from the KORA F4 cohort	60 CHD prevalent cases + 1771 controls	Blood	Infinium HM450 BeadChip (Illumina)	Lipid-related CpGs identified in the same study in <i>CPT1A, ABCG1, SREBF1, MR33B</i> and <i>TNP1</i>	CHD	Hypermethylation in <i>ABC1</i> (cg06500161) was associated with CHD.	21/35
Wei 2015 Biomed Res Int	25705649	Malaysia	Case-control	Ischemic stroke patients and healthy controls	297 ischemic stroke cases + 110 controls	Blood	Bisulfite pyrosequencing	<i>MTHFR</i>	Ischemic stroke	Hypermethylation at CpGA within <i>MTHFR</i> was associated with ischemic stroke.	21/33
Baccarelli 2015 Clin Epigenetics	25901185	Commercial samples	Case-control	CVD patients (samples purchased from Bioreclamation/VT, USA)	10 CHD cases + 17 controls	Blood (platelets)	Bisulfite pyrosequencing	ATP synthesis related genes: <i>MT-CO1, MT-CO2, MT-CO3, MT-ATP6, MT-ATP8, MT-AD5</i> , and mitochondrial rRNA gene <i>MT-TL1</i>	CVD	Hypermethylation of cytosine-c guanine-rich <i>MT-CO1, MT-CO2, MT-CO3</i> and rRNA nucleotide 1 gene <i>MT-TL1</i> was associated with CVD, while methylation in ATP synthase genes <i>MT-ATP6, MT-ATP8</i> or NADH dehydrogenase <i>MT-ND5</i> was not.	19/33
Yang 2016 Scand J Clin Lab Invest	26986049	China	Case-control	CHD patients and healthy controls	582 CHD cases + 673 controls	Blood (leukocytes)	Bisulfite pyrosequencing	<i>IL-6</i>	CHD	Hypermethylation in <i>IL-6</i> promoter (irrespective of the two CpG sites) was associated with increased risk of CHD.	27/36
Nguyen 2016 Plos One	27101308	Canada	Case-control	Post-ACS patients	28 CHD cases + 16 young controls and 13 aged controls	Blood (leukocytes)	EpiTYPER assay (Sequenom)	<i>ANGPTL2</i>	ACS	Hypermethylation at CpGs within <i>ANGPTL2</i> promoter was associated with the pro-inflammation environment in post-ACS patients.	22/36
Perna 2016 Clin Epigenetics	27274774	Germany	Case-cohort	Subsample of the ESTHER cohort	605 deaths + 1546 subcohorts (268 deaths in the subcohorts)	Blood	Infinium HM450 BeadChip (Illumina)	Epigenetic aging*	CVD death	Epigenetic age acceleration was associated with higher CVD mortality.	28/36
Horvath 2016 Genome Biology	27511193	USA	Cohort	Women from the Women's Health Initiative study	1462	Blood, saliva, lymphoblastoid cell lines and brain	Infinium HM450 BeadChip (Illumina)	Epigenetic aging*	CHD	Epigenetic aging rates were not associated with incident CHD outcomes.	20/35
Zuo 2016 Arq Bras Cardiol	27594927	China	Case-control	CHD patients and healthy controls	212 CHD cases + 218 controls	Blood (leukocytes)	Bisulfite pyrosequencing	<i>IL-6</i>	AMI, MI and unstable angina	Hypermethylation in <i>IL-6</i> promoter was associated with increased risk of CHD, specifically AMI. Hypermethylation of <i>CpG1</i> may have had a stronger association than <i>CpG2</i> . Hypermethylation at CpGs within <i>ANGPTL2</i> promoter was associated with epigenetic aging in controls that indicated greater cardiovascular risk.	27/35
Murray 2016 Clin Epigenetics	27627640	UK	Cohort (subcohort)	Children in a mother-offspring cohort	144	Umbilical cord (methylation)	Bisulfite pyrosequencing at birth	<i>ANRIL</i>	Arterial stiffness	Hypermethylation at CpGs within <i>ANRIL</i> promoter was associated with arterial stiffness.	22/36
Zhong 2016 Exp Ther Med	27882177	China	Case-control	CHD patients and non-CHD controls	48 CHD cases + 48 gender-matched controls	Blood	Bisulfite pyrosequencing	<i>COMT</i>	CHD	Hypermethylation at CpG within <i>COMT</i> promoter was associated with CHD in males and with aging in controls.	19/35

CHD: coronary heart disease; CVD: cardiovascular diseases; MI: myocardial infarction; ACS: acute coronary syndrome; SMCs: smooth muscle cells; ECs: endothelial cells; PBMCs: peripheral blood mononuclear cells; Tregs: regulatory T cells; HTN: hypertension; MSP: methylation-specific PCR; COBRA: combined bisulfite restriction analysis; MALDI-TOF: Matrix-Assisted Laser Desorption/Ionization - Time Of Flight; CpG: CpG island; DMR: differentially methylated region. (\*)Epigenetic aging instead of a candidate-gene.

Table 2c. Summary of the selected studies using a genome-wide approach with all the extracted information

Reference	PMID	Country	Study Design	Reference population	Sample size	Tissue	Methylation strategy	Validation (sample size)	Outcome	Conclusion	Observations	Quality assessment
Castillo-Diaz 2010 Int J Mol Med	20878091	Mexico	Case-control	Non-smoking coronary artery patients undergoing revascularization surgery and non-CHD patients undergoing angiography	45 CHD cases + 16 controls	Aorta (atherosclerotic/non-atherosclerotic)	Microarray HCG115K (UHN Microarray Centre) for discovery and MSP for validation	10 CHD cases + 10 controls	Ischemic cardiopathy	Hypomethylation at 47 CpGs (42 CpGs in the discovery phase and hypermethylation at 10 CpGs (17 CpGs in the discovery phase) were associated with atherosclerosis.	No list with all identified CpGs	13/36
Sharma 2014 Gene	24582973	India	Case-control	-50-year-old men with and without CHD from an Indian study of ~900 individuals	18 CHD cases + 18 controls	Blood	Microarray HCG112K (UHN Microarray Centre) for discovery and bisulfite 454 sequencing for validation	48 CHD cases + 48 controls	CHD	Hypermethylation at 12 DMRs (72 DMRs in the discovery phase) and at 6 CpGs in 3 of the validated DMRs was associated with CHD.		20/35
Yamada 2014 IJ Mol Med	2462634	Japan	Case-control	Deceased Japanese patients	24 donor-matched samples of atherosclerotic/normal Aorta	Aorta (donor-matched atherosclerotic/ non-atherosclerotic)	Infinium HM450 BeadChip (Illumina)	—	Atherosclerotic plaque	Hypomethylation at 15 CpGs, 14 genes and hypermethylation at 30 CpGs in 22 genes were associated with atherosclerosis.		22/35
Zaina 2014 Circ Cardiovasc Genet	25091541	Spain & Sweden	Case-control	Post-mortem human aortas from Spain and carotid plaque samples from Sweden	15 donor-matched samples of atherosclerotic/ normal Aorta + 19 atherosclerotic carotid	Aorta (donor-matched atherosclerotic/ non-atherosclerotic) and atherosclerotic carotid	Bisulfite sequencing and Infinium HM450 BeadChip (Illumina) for discovery and pyrosequencing and bisulfite sequencing for validation	25 donor-matched pairs (1 from discovery)	Atherosclerotic plaque	16 out of 1858 discovered dm-CpGs were validated and mapped to vascular-wall specific, atherosclerosis-specific genes.		21/37
Gómez-Uriz 2015 Hum Mol Genet	25429063	Spain	Case-control	Ischemic stroke patients and healthy controls	12 ischemic stroke cases + 12 controls	Blood (leukocytes)	Infinium HM27 BeadChip (Illumina) for discovery	60 ischemic stroke cases + 55 controls	Ischemic stroke	80 dm-CpGs were discovered to be associated with stroke, and hypermethylation in the promoter of <i>PM20D1</i> was validated.	No list with all identified CpGs	26/38
Nazarenko 2015 Plos One	25856389	Russia	Case-control	Russian men undergoing surgery for severe coronary artery stenosis	6 donor-matched samples of the 3 tissues	Atherosclerotic right coronary artery, internal mammary arteries and great saphenous veins (donor-matched)	Infinium HM27 BeadChip (Illumina) for discovery and pyrosequencing for validation	21 donor-matched samples	Atherosclerotic plaque	Hypomethylated CpGs in atherosclerotic samples were located within genes involved in inflammation, immune processes and development, such as <i>HOXD4</i> , within whose promoter 4 CpGs are hypomethylated.		25/36
Ek 2015 Hum Mol Genet	26681806	Sweden & UK	Cross-sectional	Swedish cohorts, NSPHS for discovery and PVUS for validation	717 (47 incident CHD cases)	Blood (leukocytes)	Infinium HM450 BeadChip (Illumina)	963	Cardiovascular biomarker GDF-15	16 CpGs at 11 genes out of 31 discovered and 66 CpGs identified by meta-analysis were associated with CHD.		33/38
Guarneri 2015 Clin Epigenetics	26705428	Italy	Case-control nested in a cohort	MI cases and healthy controls from Italian EPICOR for discovery and Dutch EPIC for validation	292 CHD cases + 247 matched controls	Blood (leukocytes)	Infinium HM450 BeadChip (Illumina) for discovery and MALDI-TOF mass spectrometry methylation assay for validation	317 CHD cases + 262 controls	MI	Hypermethylation at a DMR within <i>ZBTB12</i> gene body and in LINE-1 was associated with CHD, being more pronounced in cases with shorter time to disease.		31/37
Oudejans 2016 Plos One	26870946	The Netherlands	Case-control	Two monozygous twin sister pairs discordant for hypertensive pregnancy disorders	2 matched pairs	Blood	Bisulfite sequencing	—	CVD risk	12 DMRs were identified in the twin sisters at risk of CVD.		23/36
Nguyen 2016 Plos One	27101308	Canada	Case-control	Post-ACS Canadian patients, and young and aged healthy controls	5 CHD cases + 4 young controls + 7 aged controls	Blood	Infinium HM450 BeadChip (Illumina)	—	ACS	No statistical difference in methylation between controls and CHD patients.	No list with all identified CpGs	22/36
Rask-Andersen 2016 Hum Mol Genet	27634651	Sweden	Case-control nested in a survey	Swedish NSPHS cross-sectional cohort	249 CVD cases (147 HTN + 48 MI + 27 Stroke + 22 Thrombosis + 5 Arrhythmia) + 729 cohort	Blood	Infinium HM450 BeadChip (Illumina)	—	HTN, MI, stroke, diabetics, thrombosis, Arrhythmia	211 dm-CpGs in 196 genes were associated with MI, of which 42 had been related to cardiac function and development, CVD and recovery after ischemic episode.		26/34

**Table 3. List of genes analyzed in the candidate-gene approach classified according to the number of studies assessing them and their methylation status.**

Gene	Reference
<i>Genes studied in several articles (n=8)</i>	
<i>Hypermethylated</i>	
ABCG1	Peng 2014 PLoS One Pfeiffer 2015 Circ Cardiovasc Genet Post 1999 Cardiovasc Res Ying 2000 Cardiovasc Res 2000 Cardiovasc Res
ESR $\alpha$	Huang 2009 Pathophysiology Huica 2011 Romanian Biotechnological Letters Jia 2013 Atherosclerosis Lu 2013 Atherosclerosis
FOXP3	
<i>Hypomethylated</i>	
IL-6	Yang 2016 Scand J Clin Lab Invest Zuo 2016 Arq Bras Cardiol
<i>Non-differential methylation status</i>	
APOE	Sharma 2008 DNA Cell Biol Fiorito 2014 Nutr Metab Cardiovasc Dis
<i>Inconsistent methylation status</i>	
ABCA1	Guay 2014 Clin Epigenetics Talens 2012 Int J Epidemiol
MTHFR	Wei 2015 BioMed Res Int Fiorito 2014 Nutr Metab Cardiovasc Dis
PON1	Gómez-Úriz 2014 J Physiol Biochem Fiorito 2014 Nutr Metab Cardiovasc Dis
<i>Genes studied in one article (n=75)</i>	
<i>Hypermethylated</i>	
AMT	Fiorito 2014 Nutr Metab Cardiovasc Dis
ANRIL	Murray 2016 Clin Epigenetics
CBS	Fiorito 2014 Nutr Metab Cardiovasc Dis
DDAH2	Niu 2014 J Transl Med
EC-SOD	Lakshmi 2013 Mol Cell Biochem
ESR $\beta$	Kim 2007 Biochim Biophys Acta
GALNT2	Peng 2014 PLoS One
GNASAS	Talens 2012 Int J Epidemiol
INS	Talens 2012 Int J Epidemiol
MCT3	Zhu 2005 Circulation
MT-CO1	Baccarelli 2015 Clin Epigenetics
MT-CO2	Baccarelli 2015 Clin Epigenetics
MT-CO3	Baccarelli 2015 Clin Epigenetics
MT-TL1	Baccarelli 2015 Clin Epigenetics
NPC1	Afzali 2013 Iranian Biomed Journal
p15INK4b	Zhuang 2012 PLoS One
PLA2G7	Jia 2013 Atherosclerosis
TCN2	Fiorito 2014 Nutr Metab Cardiovasc Dis
TIMP1	Huica 2011 Romanian Biotechnological Letters
<i>Hypomethylated</i>	
ANGPTL2	Nguyen 2016 PLoS One
BNIP3	Lakshmi 2013 Mol Cell Biochem
COL15A1	Connelly 2013 Hum Mol Genet
COMT	Zhong 2016 Exp Ther Med
F7	Friso 2012 J Med Genet
F2RL3	Zhang 2014 Int J Epidemiol
GCK	Xu 2014 Biomed Res Int
TNF- $\alpha$	Gómez-Úriz 2014 J Physiol Biochem
<i>Non-differential methylation status</i>	
AHCY	Fiorito 2014 Nutr Metab Cardiovasc Dis
ALDH1L1	Fiorito 2014 Nutr Metab Cardiovasc Dis
ANXA5	Zhuang 2012 PLoS One
ATIC	Fiorito 2014 Nutr Metab Cardiovasc Dis
BAX	Zhuang 2012 PLoS One
BCL-2	Zhuang 2012 PLoS One
BHMT	Fiorito 2014 Nutr Metab Cardiovasc Dis
CASP3	Zhuang 2012 PLoS One
CBL	Fiorito 2014 Nutr Metab Cardiovasc Dis
cIAP3	Zhuang 2012 PLoS One
CPT1A	Pfeiffer 2015 Circ Cardiovasc Genet
CTH	Fiorito 2014 Nutr Metab Cardiovasc Dis
DHFR	Fiorito 2014 Nutr Metab Cardiovasc Dis
DNMT1	Fiorito 2014 Nutr Metab Cardiovasc Dis
FOLH1	Fiorito 2014 Nutr Metab Cardiovasc Dis
FOLR2	Fiorito 2014 Nutr Metab Cardiovasc Dis
FTCD	Fiorito 2014 Nutr Metab Cardiovasc Dis
GART	Fiorito 2014 Nutr Metab Cardiovasc Dis
GSTP1	Lakshmi 2013 Mol Cell Biochem
HMGCR	Peng 2014 PLoS One
IGF2	Talens 2012 Int J Epidemiol
IL-10	Talens 2012 Int J Epidemiol
LEP	Talens 2012 Int J Epidemiol
LOX-1	Zhuang 2012 PLoS One
MAOA	Zhao 2012 BMC Med Genet
MAT1A	Fiorito 2014 Nutr Metab Cardiovasc Dis
MAT2B	Fiorito 2014 Nutr Metab Cardiovasc Dis
MIR338	Pfeiffer 2015 Circ Cardiovasc Genet
MT-ATP6	Baccarelli 2015 Clin Epigenetics
MT-ATP8	Baccarelli 2015 Clin Epigenetics
MTHFD1	Fiorito 2014 Nutr Metab Cardiovasc Dis
MTHFD1L	Fiorito 2014 Nutr Metab Cardiovasc Dis
MTHFD2	Fiorito 2014 Nutr Metab Cardiovasc Dis
MTHFD2L	Fiorito 2014 Nutr Metab Cardiovasc Dis
MTHFS	Fiorito 2014 Nutr Metab Cardiovasc Dis
MT-ND5	Baccarelli 2015 Clin Epigenetics
MTR	Fiorito 2014 Nutr Metab Cardiovasc Dis
MTRR	Fiorito 2014 Nutr Metab Cardiovasc Dis
NNMT	Fiorito 2014 Nutr Metab Cardiovasc Dis
p14ARF	Zhuang 2012 PLoS One
p15INK4a	Zhuang 2012 PLoS One
RFC1	Fiorito 2014 Nutr Metab Cardiovasc Dis
SHMT1	Fiorito 2014 Nutr Metab Cardiovasc Dis
SHMT2	Fiorito 2014 Nutr Metab Cardiovasc Dis
SREBF1	Pfeiffer 2015 Circ Cardiovasc Genet
TIMP3	Zhuang 2012 PLoS One
TNIP-1	Pfeiffer 2015 Circ Cardiovasc Genet
TYMS	Fiorito 2014 Nutr Metab Cardiovasc Dis





























1	RGSL1	1	Nazarenko 2014 PLoS One Nazarenko 2014 PLoS One
1	RIMS3	1	Zaina 2014 Circ Cardiovasc Genet
1	RNF220	1	Zaina 2014 Circ Cardiovasc Genet
1	ROR1	1	Castillo-Diaz 2014 J Mol Med
1	RPS6KC1	1	Castillo-Diaz 2014 J Mol Med
1	RUNX3	1	Rask-Andersen 2016 Hum Mol Genet
1	RYR2	1	Nazarenko 2014 PLoS One
1	S100A10	1	Nazarenko 2014 PLoS One
1	S100A8	2	Ek 2016 Hum Mol Genet
1	SARS	1	Zaina 2014 Circ Cardiovasc Genet
1	SCNM1	1 (with LYSMD1)	Sharma 2014 Gene
1	SCP2	1	Nazarenko 2014 PLoS One
1	SH2D2A	2	Nazarenko 2014 PLoS One
1	SLAMF1	1	Yamada 2014 J Mol Med
1	SLC2A1	1	Rask-Andersen 2016 Hum Mol Genet
1	SLC30A2	1	Zaina 2014 Circ Cardiovasc Genet
1	SLC35D1	1	Zaina 2014 Circ Cardiovasc Genet
1	SLC35F3	2	Zaina 2014 Circ Cardiovasc Genet
1	SLC41A1	1	Zaina 2014 Circ Cardiovasc Genet
1	SLC6A1	1	Zaina 2014 Circ Cardiovasc Genet
1	SLC6A11	1	Zaina 2014 Circ Cardiovasc Genet
1	SNX7	1	Zaina 2014 Circ Cardiovasc Genet
1	SOAT1	1	Zaina 2014 Circ Cardiovasc Genet
1	SPRR2D	1	Nazarenko 2014 PLoS One
1	ST3GAL3	1	Zaina 2014 Circ Cardiovasc Genet
1	ST6GALNAC5	1	Rask-Andersen 2016 Hum Mol Genet
1	ST7L	1	Zaina 2014 Circ Cardiovasc Genet
1	SV2A	1	Zaina 2014 Circ Cardiovasc Genet
1	TCEA3	1	Ek 2016 Hum Mol Genet
1	TCTEX1D1	1	Nazarenko 2014 PLoS One
1	TGFBR2	1	Rask-Andersen 2016 Hum Mol Genet
1	TGFBR3	1 (1 CGI, 2 CpGs)	Sharma 2014 Gene, Zaina 2014 Circ Cardiovasc Genet
1	TNFRSF25	1	Zaina 2014 Circ Cardiovasc Genet
1	TRAF5	1	Zaina 2014 Circ Cardiovasc Genet
1	TSPAN1	1	Zaina 2014 Circ Cardiovasc Genet
1	UBR4	1	Zaina 2014 Circ Cardiovasc Genet
1	USH2A	1	Nazarenko 2014 PLoS One
1	UTS2	1	Nazarenko 2014 PLoS One
1	VASH2	1	Castillo-Diaz 2014 J Mol Med
1	VTCN1	1	Nazarenko 2014 PLoS One
1	WDR64	1	Ek 2016 Hum Mol Genet
1	WNT2B	1	Zaina 2014 Circ Cardiovasc Genet
1	ZBTB40	2	Zaina 2014 Circ Cardiovasc Genet
1	ZNF683	1	Nazarenko 2014 PLoS One
1	ZNF697	2	Nazarenko 2014 PLoS One
2	SEPT2	1	Rask-Andersen 2016 Hum Mol Genet
2	ABC B1	1	Zaina 2014 Circ Cardiovasc Genet
2	ABCG5	1	Nazarenko 2014 PLoS One
2	ACP1	1	Rask-Andersen 2016 Hum Mol Genet
2	ACTG2	1	Zaina 2014 Circ Cardiovasc Genet
2	AFF3	2	Zaina 2014 Circ Cardiovasc Genet
2	ARHgap15	2	Rask-Andersen 2016 Hum Mol Genet
2	ASB3	1 (downstream, upstream: NRXN1)	Zaina 2014 Circ Cardiovasc Genet
2	ATG12B	1	Zaina 2014 Circ Cardiovasc Genet
2	ATG16L1	1	Zaina 2014 Circ Cardiovasc Genet
2	C2orf43	1	Zaina 2014 Circ Cardiovasc Genet
2	C2orf59	1	Zaina 2014 Circ Cardiovasc Genet
2	C2orf84	3	Zaina 2014 Circ Cardiovasc Genet
2	C2orf88	1	Zaina 2014 Circ Cardiovasc Genet
2	CAPN10	4	Zaina 2014 Circ Cardiovasc Genet
2	CCDC140	1	Rask-Andersen 2016 Hum Mol Genet
2	CD28	1	Zaina 2014 Circ Cardiovasc Genet
2	CD8A	1	Nazarenko 2014 PLoS One
2	CNTNAP5	1	Zaina 2014 Circ Cardiovasc Genet
2	CR936735	1 (upstream, downstream: MRPS9)	Zaina 2014 Circ Cardiovasc Genet
2	CTNNA2	1	Zaina 2014 Circ Cardiovasc Genet
2	CXCR7	1	Zaina 2014 Circ Cardiovasc Genet
2	CYP27C1	2	Zaina 2014 Circ Cardiovasc Genet
2	DAPL1	1	Zaina 2014 Circ Cardiovasc Genet
2	DARS	1	Zaina 2014 Circ Cardiovasc Genet
2	DGKD	1	Zaina 2014 Circ Cardiovasc Genet
2	DNAH6	1	Zaina 2014 Circ Cardiovasc Genet
2	DNAH7	1	Zaina 2014 Circ Cardiovasc Genet
2	DOK1	1 (with LOXL3)	Rask-Andersen 2016 Hum Mol Genet, Zaina 2014 Circ Cardiovasc Genet
2	DPP4	1	Rask-Andersen 2016 Hum Mol Genet, Zaina 2014 Circ Cardiovasc Genet
2	DYSF	4	Rask-Andersen 2016 Hum Mol Genet, Zaina 2014 Circ Cardiovasc Genet
2	EMX1	1	Rask-Andersen 2016 Hum Mol Genet, Zaina 2014 Circ Cardiovasc Genet
2	EN1	1	Rask-Andersen 2016 Hum Mol Genet, Zaina 2014 Circ Cardiovasc Genet
2	ERBB4	1	Nazarenko 2014 PLoS One
2	FABP1	1	Rask-Andersen 2016 Hum Mol Genet, Zaina 2014 Circ Cardiovasc Genet
2	FAM150B	1	Rask-Andersen 2016 Hum Mol Genet, Zaina 2014 Circ Cardiovasc Genet
2	FAM168B	1	Rask-Andersen 2016 Hum Mol Genet, Zaina 2014 Circ Cardiovasc Genet
2	FAM178B	1	Rask-Andersen 2016 Hum Mol Genet, Zaina 2014 Circ Cardiovasc Genet
2	FLJ30294	1	Nazarenko 2014 PLoS One
2	FLML2	1	Rask-Andersen 2016 Hum Mol Genet, Zaina 2014 Circ Cardiovasc Genet
2	FSHR	2	Nazarenko 2014 PLoS One
2	GCKR	1	Nazarenko 2014 PLoS One
2	GDF7	1	Zaina 2014 Circ Cardiovasc Genet
2	GLS	1	Zaina 2014 Circ Cardiovasc Genet
2	HDAC4	1	Zaina 2014 Circ Cardiovasc Genet
2	HDLBP	1	Zaina 2014 Circ Cardiovasc Genet
2	HK2	1	Zaina 2014 Circ Cardiovasc Genet
2	HOXD3	1	Ek 2016 Hum Mol Genet
2	HOXD4	6 (1 downstream, upstream: HOXD9)	Zaina 2014 Circ Cardiovasc Genet
2	HOXD9	1 (upstream, downstream: HOXD4)	Zaina 2014 Circ Cardiovasc Genet
2	IMMT	1	Nazarenko 2014 PLoS One
2	LOC100130691	1	Castillo-Diaz 2014 J Mol Med, Nazarenko 2014 PLoS One
2	LOC100132215	1	Castillo-Diaz 2014 J Mol Med, Nazarenko 2014 PLoS One
2	LOC150622	3	Zaina 2014 Circ Cardiovasc Genet
2	LOXL3	1 (with DOK1)	Yamada 2014 J Mol Med
2	LRP2	1	Zaina 2014 Circ Cardiovasc Genet
2	LRRKIP1	1	Zaina 2014 Circ Cardiovasc Genet
2	MAP4K3	1	Zaina 2014 Circ Cardiovasc Genet
2	MAP4K4	1	Zaina 2014 Circ Cardiovasc Genet
2	MARCH4	2	Zaina 2014 Circ Cardiovasc Genet
2	MEIS1	1	Yamada 2014 J Mol Med
2	MIR128-1	1	Rask-Andersen 2016 Hum Mol Genet
2	MRPS9	4 (1 downstream, upstream: CR936735)	Rask-Andersen 2016 Hum Mol Genet, Castillo-Diaz 2014 J Mol Med, Nazarenko 2014 PLoS One
2	MYL1	1	Castillo-Diaz 2014 J Mol Med, Nazarenko 2014 PLoS One
2	MYO1B	1	Zaina 2014 Circ Cardiovasc Genet
2	NAT8	1	Zaina 2014 Circ Cardiovasc Genet
2	NCK2	1	Zaina 2014 Circ Cardiovasc Genet
2	NCKAP5	1	Zaina 2014 Circ Cardiovasc Genet
2	NGEF	1	Zaina 2014 Circ Cardiovasc Genet
2	NHEJ1	1	Zaina 2014 Circ Cardiovasc Genet
2	NPAS2	2	Zaina 2014 Circ Cardiovasc Genet
2	NRNWH1	1 (upstream, downstream: ASB3)	Zaina 2014 Circ Cardiovasc Genet, Castillo-Diaz 2014 J Mol Med, Nazarenko 2014 PLoS One
2	NTSR2	1	Zaina 2014 Circ Cardiovasc Genet
2	OSR1	5	Zaina 2014 Circ Cardiovasc Genet
2	PDCD1	1	Rask-Andersen 2016 Hum Mol Genet
2	PRK4	1	Zaina 2014 Circ Cardiovasc Genet
2	PLEKHM3	1	Nazarenko 2014 PLoS One
2	PREPL	1	Zaina 2014 Circ Cardiovasc Genet
2	PRKCE	2	Zaina 2014 Circ Cardiovasc Genet
2	PTCD3	1	Zaina 2014 Circ Cardiovasc Genet
2	PXDN	4	Zaina 2014 Circ Cardiovasc Genet
2	RAB11Fip5	3	Zaina 2014 Circ Cardiovasc Genet
2	RAPGEF4	1	Zaina 2014 Circ Cardiovasc Genet
2	RFX8	1	Zaina 2014 Circ Cardiovasc Genet
2	RPL31	1	Rask-Andersen 2016 Hum Mol Genet
2	SCN9A	1	Zaina 2014 Circ Cardiovasc Genet
2	SFTPB	1	Nazarenko 2014 PLoS One
2	SH3RF3	1	Zaina 2014 Circ Cardiovasc Genet
2	SLC40A1	1	Zaina 2014 Circ Cardiovasc Genet
2	SP140	1	Nazarenko 2014 PLoS One
2	SPATS2L	1	Zaina 2014 Circ Cardiovasc Genet
2	SPEG	1	Zaina 2014 Circ Cardiovasc Genet
2	SPRED2	1	Zaina 2014 Circ Cardiovasc Genet
2	SPTBN1	1	EK 2016 Hum Mol Genet
2	STK39	3	Nazarenko 2014 PLoS One
2	STON1-GTF2A1L	1	Zaina 2014 Circ Cardiovasc Genet
2	TANC1	1	EK 2016 Hum Mol Genet
2	TET3	1	Zaina 2014 Circ Cardiovasc Genet

2	<i>TFPI</i>	1	Zaina 2014 Circ Cardiovasc Genet
2	<i>TNP1</i>	1	Nazarenko 2014 PLoS One
2	<b><i>TNS1</i></b>	1	Zaina 2014 Circ Cardiovasc Genet, Nazarenko 2014 PLoS One
2	<i>TTN</i>	1	Nazarenko 2014 PLoS One
2	<i>UGP2</i>	1	Zaina 2014 Circ Cardiovasc Genet
2	<i>VAX2</i>	1	Rask-Andersen 2016 Hum Mol Genet
2	<i>VRK2</i>	1	Zaina 2014 Circ Cardiovasc Genet
2	<i>WDR69</i>	1	Zaina 2014 Circ Cardiovasc Genet
2	<i>WIPF1</i>	1	Zaina 2014 Circ Cardiovasc Genet
2	<i>ZDBF2</i>	2	Rask-Andersen 2016 Hum Mol Genet
2	<i>ZEB2</i>	1	Ek 2016 Hum Mol Genet
2	<i>ZNF804A</i>	1	Rask-Andersen 2016 Hum Mol Genet
2	<i>ZSWIM2</i>	1	Rask-Andersen 2016 Hum Mol Genet
3	<i>ALCAM</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>AMT</i>	1	Nazarenko 2014 PLoS One
3	<i>ARF4</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>ARHGEF3</i>	1	Ek 2016 Hum Mol Genet
3	<i>ARLB8</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>ATG7</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>ATP2B2</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>AUDL</i>	1	Nazarenko 2014 PLoS One
3	<i>B3GNA1NT1</i>	1	Rask-Andersen 2016 Hum Mol Genet
3	<i>C3orf15</i>	1	Rask-Andersen 2016 Hum Mol Genet
3	<i>C3orf26</i>	4 (with <i>MIR546G</i> and <i>FILIP1L</i> )	Zaina 2014 Circ Cardiovasc Genet
3	<i>C3orf35</i>	1	Nazarenko 2014 PLoS One
3	<i>C3orf42</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>C3orf62</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<b><i>CACNA2D3</i></b>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>CADPS</i>	2	Rask-Andersen 2016 Hum Mol Genet
3	<i>CAMK1</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>CCDC50</i>	1 (with <i>UTS2D</i> )	Nazarenko 2014 PLoS One
3	<i>CCDC52</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>CCDC80</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>CCR3</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>CCLR2</i>	5	Rask-Andersen 2016 Hum Mol Genet
3	<i>CD96</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>CELSR3</i>	1	Rask-Andersen 2016 Hum Mol Genet
3	<i>CHCHD6</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>CIDE6</i>	1	Nazarenko 2014 PLoS One
3	<i>CNTN6</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>CRTAP</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>CSTA</i>	1	Nazarenko 2014 PLoS One
3	<i>DLEC1</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>EEFSEC</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>EPHB3</i>	1	Rask-Andersen 2016 Hum Mol Genet
3	<i>FEZ2</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>FHT</i>	1	Rask-Andersen 2016 Hum Mol Genet
3	<i>FILIP1L</i>	3 (with <i>C3orf26</i> and <i>MIR546G</i> )	Zaina 2014 Circ Cardiovasc Genet
3	<i>FLNB</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>FNDC3B</i>	2	Zaina 2014 Circ Cardiovasc Genet
3	<i>FOXP1</i>	3	Castillo-Diaz 2014 J Mol Med, Zaina 2014 Circ Cardiovasc Genet
3	<i>GALNT2</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>GDF1</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>GOLGB1</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>GORASP1</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>GPR62</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>GRM7</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>HEG1</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>HRASLS</i>	1 (with <i>MGC2889</i> )	Nazarenko 2014 PLoS One, Zaina 2014 Circ Cardiovasc Genet
3	<i>IL5RA</i>	2	Zaina 2014 Circ Cardiovasc Genet
3	<i>ITGA9</i>	2	Zaina 2014 Circ Cardiovasc Genet
3	<i>ITGB5</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>KAT2B</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>KCNMB3</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>LEPREL1</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>LMD1</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>LOC100129550</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>LPP</i>	2	Zaina 2014 Circ Cardiovasc Genet
3	<i>LRTM1</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>MAP4</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>MBNL1</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>MECOM</i>	3	Zaina 2014 Circ Cardiovasc Genet
3	<i>MGC2889</i>	1 (with <i>HRASLS</i> )	Rask-Andersen 2016 Hum Mol Genet, Zaina 2014 Circ Cardiovasc Genet
3	<i>MIR546G</i>	3 (with <i>C3orf26</i> and <i>FILIP1L</i> )	Zaina 2014 Circ Cardiovasc Genet
3	<i>MRPL47</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>NAALADL2</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>OPA1</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>OSBP10</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>OXSR1</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>PLCH1</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>POLQ</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>POPOC2</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>PROS1</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>RAB43</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>RBM33</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>RBPF1</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>RIO1</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>SELT</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>SGMA5B</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>SGOL1</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>SIDT1</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>SLC12A8</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>SLC15A2</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>SLC22A14</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>SLC6A6</i>	2	Nazarenko 2014 PLoS One, Zaina 2014 Circ Cardiovasc Genet
3	<i>SLC9A9</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>SLMAP</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>SOX2</i>	1	Rask-Andersen 2016 Hum Mol Genet
3	<i>SPTSSB</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>SST</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>TBC1D5</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>TDGF1</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>TGFBR2</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>TIGIT</i>	1	Nazarenko 2014 PLoS One
3	<i>TMEM108</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>TMEM39A</i>	2	Zaina 2014 Circ Cardiovasc Genet
3	<i>TNFSF10</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>TRAK1</i>	2	Zaina 2014 Circ Cardiovasc Genet
3	<i>TRANK1</i>	3	Rask-Andersen 2016 Hum Mol Genet
3	<i>UCN2</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>USP19</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>UTS2D</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>UZPLD1</i>	1 (upstream)	Rask-Andersen 2016 Hum Mol Genet, Zaina 2014 Circ Cardiovasc Genet
3	<i>VGLL4</i>	2	Zaina 2014 Circ Cardiovasc Genet
3	<i>WNT7A</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>ZBTB38</i>	1	Rask-Andersen 2016 Hum Mol Genet
3	<i>ZCT1</i>	1	Zaina 2014 Circ Cardiovasc Genet
3	<i>ZDC4</i>	1	Nazarenko 2014 PLoS One
4	<i>ACOY3</i>	1	Zaina 2014 Circ Cardiovasc Genet
4	<i>AFAP1</i>	1	Ek 2016 Hum Mol Genet
4	<i>AFP</i>	1	Zaina 2014 Circ Cardiovasc Genet
4	<i>ACXT2L1</i>	1	Guerrera 2015 Clin Epigenet
4	<i>ANTXR2</i>	3	Ek 2016 Hum Mol Genet
4	<i>ARAP2</i>	1	Zaina 2014 Circ Cardiovasc Genet
4	<i>BC131768</i>	1	Zaina 2014 Circ Cardiovasc Genet
4	<i>C10TNF7</i>	2	Rask-Andersen 2016 Hum Mol Genet
4	<i>C4orf23</i>	1	Zaina 2014 Circ Cardiovasc Genet
4	<i>C4orf36</i>	1	Zaina 2014 Circ Cardiovasc Genet
4	<i>C4orf44</i>	1	Rask-Andersen 2016 Hum Mol Genet
4	<i>C4orf48</i>	2 (CpG and CGI)	Zaina 2014 Circ Cardiovasc Genet
4	<i>CLCN3</i>	1	Nazarenko 2014 PLoS One, Rask-Andersen 2016 Hum Mol Genet
4	<i>CRMP1</i>	1	Zaina 2014 Circ Cardiovasc Genet
4	<i>CTBP1</i>	1	Nazarenko 2014 PLoS One
4	<i>CXL5</i>	1	Zaina 2014 Circ Cardiovasc Genet
4	<i>DCLK2</i>	1	Nazarenko 2014 PLoS One
4	<i>FGF2</i>	1	Zaina 2014 Circ Cardiovasc Genet
4	<i>FIP1L1</i>	1	Nazarenko 2014 PLoS One
4	<i>FLJ20184</i>	1	Zaina 2014 Circ Cardiovasc Genet
4	<i>FLJ20273</i>	1	Nazarenko 2014 PLoS One
4	<i>FLJ23235</i>	1	Nazarenko 2014 PLoS One
4	<i>FLJ23657</i>	1	Nazarenko 2014 PLoS One
4	<i>FRAS1</i>	1	Zaina 2014 Circ Cardiovasc Genet
4	<i>GALNT7</i>	1	Ek 2016 Hum Mol Genet

4	GALNTL6	1	Rask-Andersen 2016 Hum Mol Genet
4	HAND2	2	Rask-Andersen 2016 Hum Mol Genet, Sharma 2014 Gene
4	HERC5	1	Castillo-Diaz 2014 J Mol Med
4	HOP	1	Nazarenko 2014 PLoS One
4	IGFBP7	1	Zaina 2014 Circ Cardiovasc Genet
4	IL21	1	Zaina 2014 Circ Cardiovasc Genet
4	INPP4B	2	Zaina 2014 Circ Cardiovasc Genet
4	LIMCH1	1	EK 2016 Hum Mol Genet
4	MAB21L2	1	Nazarenko 2014 PLoS One
4	MAPK10	1	Rask-Andersen 2016 Hum Mol Genet
4	MARCH1	1	Zaina 2014 Circ Cardiovasc Genet
4	MGST2	1	Zaina 2014 Circ Cardiovasc Genet
4	MIR2054	2	Rask-Andersen 2016 Hum Mol Genet, Zaina 2014 Circ Cardiovasc Genet
4	NDST4	1	Zaina 2014 Circ Cardiovasc Genet
4	NEIL3	1	Zaina 2014 Circ Cardiovasc Genet
4	PDE6B	1	Zaina 2014 Circ Cardiovasc Genet
4	PDGFRα	1	Zaina 2014 Circ Cardiovasc Genet
4	<b>PKD2</b>	1	<b>Zaina 2014 Circ Cardiovasc Genet, Nazarenko 2014 PLoS One</b>
4	RGS12	1	Zaina 2014 Circ Cardiovasc Genet
4	RPLP1	1	Zaina 2014 Circ Cardiovasc Genet
4	SCOC	1	Nazarenko 2014 PLoS One
4	SH3D19	1	Yamada 2014 J Mol Med
4	SU3TC1	1	Zaina 2014 Circ Cardiovasc Genet
4	SHROOM3	3	Zaina 2014 Circ Cardiovasc Genet
4	SNX26	1	Zaina 2014 Circ Cardiovasc Genet
4	SOD3	1	Gómez-Urte 2015 Human Mol Genet
4	SORCS2	1	Zaina 2014 Circ Cardiovasc Genet
4	SPARCL1	2	Zaina 2014 Circ Cardiovasc Genet
4	SPP1	1	Nazarenko 2014 PLoS One
4	TADA2B	1	Zaina 2014 Circ Cardiovasc Genet
4	TBC1D1	1	Nazarenko 2014 PLoS One
4	TBC1D14	1	Zaina 2014 Circ Cardiovasc Genet
4	TMPRSS1B	1	Zaina 2014 Circ Cardiovasc Genet
4	TNIP2	1	EK 2016 Hum Mol Genet
4	TSPAN5	1	Zaina 2014 Circ Cardiovasc Genet
4	U6	1	Rask-Andersen 2016 Hum Mol Genet
4	UCHL1	1	Zaina 2014 Circ Cardiovasc Genet
4	UGT2B7	2	Zaina 2014 Circ Cardiovasc Genet
4	ZNF827	1	Rask-Andersen 2016 Hum Mol Genet
5	ADAMTS16	1	EK 2016 Hum Mol Genet
5	AHRR	1	Zaina 2014 Circ Cardiovasc Genet
5	ANKRD33B	1	Rask-Andersen 2016 Hum Mol Genet
5	AP3S1	1	Zaina 2014 Circ Cardiovasc Genet
5	APC	1	Rask-Andersen 2016 Hum Mol Genet
5	ARL15	1	Zaina 2014 Circ Cardiovasc Genet
5	ARSB	1	Zaina 2014 Circ Cardiovasc Genet
5	C1QTNF3	1	Rask-Andersen 2016 Hum Mol Genet
5	C5orf28	1	EK 2016 Hum Mol Genet
5	C5orf36	1	Zaina 2014 Circ Cardiovasc Genet
5	CAMK2A	1	Rask-Andersen 2016 Hum Mol Genet
5	CCL28	1	Zaina 2014 Circ Cardiovasc Genet
5	CDH10	1	Rask-Andersen 2016 Hum Mol Genet
5	CDY1	2	Zaina 2014 Circ Cardiovasc Genet
5	CSF2	1	Zaina 2014 Circ Cardiovasc Genet
5	CTXN3	1	Zaina 2014 Circ Cardiovasc Genet
5	DCTN4	1	Zaina 2014 Circ Cardiovasc Genet
5	DOS96041	1	Zaina 2014 Circ Cardiovasc Genet
5	EBF1	1	Yamada 2014 J Mol Med
5	EIF4EBP3	1	Rask-Andersen 2016 Hum Mol Genet
5	EPB41L4A	1	Castillo-Diaz 2014 J Mol Med
5	ERGIC1	2	Zaina 2014 Circ Cardiovasc Genet
5	ESM1	1	Rask-Andersen 2016 Hum Mol Genet
5	F2RL1	1	Zaina 2014 Circ Cardiovasc Genet
5	FAM172A	1	Rask-Andersen 2016 Hum Mol Genet
5	FBN2	3	Zaina 2014 Circ Cardiovasc Genet
5	FGF18	1	Rask-Andersen 2016 Hum Mol Genet
5	GABRA6	1	Zaina 2014 Circ Cardiovasc Genet
5	GALNT10	1	Rask-Andersen 2016 Hum Mol Genet
5	GDNF	1	Zaina 2014 Circ Cardiovasc Genet
5	GEMIN5	1	Rask-Andersen 2016 Hum Mol Genet
5	GHR	2	Zaina 2014 Circ Cardiovasc Genet
5	GLRX	1	Rask-Andersen 2016 Hum Mol Genet
5	GPR98	1	Zaina 2014 Circ Cardiovasc Genet
5	HAPLN1	2	Zaina 2014 Circ Cardiovasc Genet
5	<b>HRH2</b>	1	<b>Zaina 2014 Circ Cardiovasc Genet, Nazarenko 2014 PLoS One</b>
5	HSPB3	1	Zaina 2014 Circ Cardiovasc Genet
5	IQGAP2	1	Rask-Andersen 2016 Hum Mol Genet
5	IRX2	2	Zaina 2014 Circ Cardiovasc Genet
5	ITGA2	1	Rask-Andersen 2016 Hum Mol Genet
5	KCNN2	1	Zaina 2014 Circ Cardiovasc Genet
5	KCTD16	1	Zaina 2014 Circ Cardiovasc Genet
5	LEAP2	1	Zaina 2014 Circ Cardiovasc Genet
5	LHFPL2	1	Zaina 2014 Circ Cardiovasc Genet
5	LOC10133050	1	Zhana 2014 Gene
5	LRRK2B	1	Zaina 2014 Circ Cardiovasc Genet
5	MAP1B	2	Zaina 2014 Circ Cardiovasc Genet
5	MARCH11	1	Rask-Andersen 2016 Hum Mol Genet
5	MAT2B	1	Zaina 2014 Circ Cardiovasc Genet
5	MCC	1	Zaina 2014 Circ Cardiovasc Genet
5	MRPS27	1	Zaina 2014 Circ Cardiovasc Genet
5	MYO10	2	Zaina 2014 Circ Cardiovasc Genet
5	NEURL1B	2	Rask-Andersen 2016 Hum Mol Genet
5	NK2D	1	Zaina 2014 Circ Cardiovasc Genet
5	NRG2	1	Zaina 2014 Circ Cardiovasc Genet
5	ODZ2	1	Zaina 2014 Circ Cardiovasc Genet
5	PART1	2	Rask-Andersen 2016 Hum Mol Genet
5	PCDH41	1	Nazarenko 2014 PLoS One, Zaina 2014 Circ Cardiovasc Genet
5	PDE8B	1	Oudejans 2016 PLoS One
5	PDLM4	1	Zaina 2014 Circ Cardiovasc Genet
5	PDLM7	1	Nazarenko 2014 PLoS One
5	PDZD2	3	Zaina 2014 Circ Cardiovasc Genet
5	PLK2	3	Zaina 2014 Circ Cardiovasc Genet
5	POLK	1	Rask-Andersen 2016 Hum Mol Genet, Zaina 2014 Circ Cardiovasc Genet
5	POLS	1	Zaina 2014 Circ Cardiovasc Genet
5	PRDM6	1	Zaina 2014 Circ Cardiovasc Genet
5	PRR7	1	Rask-Andersen 2016 Hum Mol Genet
5	PWWP2A	1	Zaina 2014 Circ Cardiovasc Genet
5	RXFP3	1	Zaina 2014 Circ Cardiovasc Genet
5	SEMA5A	1	Zaina 2014 Circ Cardiovasc Genet
5	SEMA6A	1	Zaina 2014 Circ Cardiovasc Genet
5	SFRS12	1	Zaina 2014 Circ Cardiovasc Genet
5	SYNPO	1	Zaina 2014 Circ Cardiovasc Genet
5	TRPC7	1	Zaina 2014 Circ Cardiovasc Genet
5	TSK1B	1	Zaina 2014 Circ Cardiovasc Genet
5	VCAN	2	Zaina 2014 Circ Cardiovasc Genet
6	AK056211	1	Zhana 2014 Gene
6	AK097143	1	Zaina 2014 Circ Cardiovasc Genet
6	AK097147	1	Castillo-Diaz 2014 J Mol Med
6	AK097147	1	Zhana 2014 Gene
6	ANKS1A	4	Zaina 2014 Circ Cardiovasc Genet
6	APOBEC2	2	Zaina 2014 Circ Cardiovasc Genet
6	APOM	1	Nazarenko 2014 PLoS One
6	ARIID1B	3	Yamada 2014 J Mol Med, Zaina 2014 Circ Cardiovasc Genet
6	ATXN1	1	Zaina 2014 Circ Cardiovasc Genet
6	BACH2	1	Zaina 2014 Circ Cardiovasc Genet
6	BEND6	2	Rask-Andersen 2016 Hum Mol Genet, Zaina 2014 Circ Cardiovasc Genet
6	BET3L	1	Zaina 2014 Circ Cardiovasc Genet
6	C6orf174	1	Zaina 2014 Circ Cardiovasc Genet
6	C6orf25	1	Zaina 2014 Circ Cardiovasc Genet
6	C6orf54	1	Nazarenko 2014 PLoS One
6	CDKAL1	1	Zaina 2014 Circ Cardiovasc Genet
6	CITED2	1	Castillo-Diaz 2014 J Mol Med
6	CNKS3	1	Zaina 2014 Circ Cardiovasc Genet
6	DAAM2	1	Zaina 2014 Circ Cardiovasc Genet
6	ENP1	1	Zaina 2014 Circ Cardiovasc Genet
6	ENP3	1	Zaina 2014 Circ Cardiovasc Genet
6	EPB41L2	1	Zaina 2014 Circ Cardiovasc Genet
6	EPM2A	1	Zaina 2014 Circ Cardiovasc Genet
6	F13A1	1	Nazarenko 2014 PLoS One
6	FAM26D	1	Zaina 2014 Circ Cardiovasc Genet
6	FBXL4	2	EK 2016 Hum Mol Genet
6	FLIP1	1	Zaina 2014 Circ Cardiovasc Genet
6	FKS656	1	Castillo-Diaz 2014 J Mol Med
6	FOXC1	1	Rask-Andersen 2016 Hum Mol Genet

6	FRK	1	Nazarenko 2014 PLoS One
6	FYN	3	Yamada 2014 J Mol Med, Zaina 2014 Circ Cardiovasc Genet
6	G6B	1	Rask-Andersen 2016 Hum Mol Genet
6	GABRR2	1	Nazarenko 2014 PLoS One
6	GCNT2	2	Nazarenko 2014 PLoS One
6	GRIK2	1	Nazarenko 2014 PLoS One
6	GSTA3	1	Nazarenko 2014 PLoS One
6	HCRTR2	1	Yamada 2014 J Mol Med
6	HECA	1	Ek 2016 Hum Mol Genet
6	HIST1H2BJ	1	Nazarenko 2014 PLoS One
6	HIST1H3E	1	Sharma 2014 Gene
6	HIST1H4F	1	Zaina 2014 Circ Cardiovasc Genet
6	HSD17B8	1 (with SLC39A7)	Rask-Andersen 2016 Hum Mol Genet
6	ID4	1	Zaina 2014 Circ Cardiovasc Genet
6	IGF2R	2	Zaina 2014 Circ Cardiovasc Genet
6	IL22RA2	1	Zaina 2014 Circ Cardiovasc Genet
6	KIAA0240	1	Zaina 2014 Circ Cardiovasc Genet
6	KIAA0408	1 (with C6orf174)	Zaina 2014 Circ Cardiovasc Genet
6	LOC65847	1	Zaina 2014 Circ Cardiovasc Genet
6	MATP	1	Rask-Andersen 2016 Hum Mol Genet
6	MARCKS	1	Rask-Andersen 2016 Hum Mol Genet
6	ME1	3	Rask-Andersen 2016 Hum Mol Genet
6	MUTED	1	Castillo-Diaz 2014 J Mol Med
6	MYLK4	1	Zaina 2014 Circ Cardiovasc Genet
6	NEDD9	1	Zaina 2014 Circ Cardiovasc Genet
6	NFKBIE	1	Nazarenko 2014 PLoS One
6	NHSL1	1	Zaina 2014 Circ Cardiovasc Genet
6	NKAPL	1	Rask-Andersen 2016 Hum Mol Genet
6	NOTCH4	1	Zaina 2014 Circ Cardiovasc Genet
6	PACRG	1	Sharma 2014 Gene
6	PARK2	2	Zaina 2014 Circ Cardiovasc Genet
6	PHACTR1	1	Zaina 2014 Circ Cardiovasc Genet
6	PHACTR2	3	Rask-Andersen 2016 Hum Mol Genet, Zaina 2014 Circ Cardiovasc Genet
6	PLAGL1	1	Zaina 2014 Circ Cardiovasc Genet
6	PLEKHG1	2	Zaina 2014 Circ Cardiovasc Genet
6	PPIL1	1	Zaina 2014 Circ Cardiovasc Genet
6	PRDM13	1	Rask-Andersen 2016 Hum Mol Genet
6	PSMB8	1	Nazarenko 2014 PLoS One
6	RFX6	1	Rask-Andersen 2016 Hum Mol Genet
6	RHAG	1	Nazarenko 2014 PLoS One
6	RNGTT	1	Rask-Andersen 2016 Hum Mol Genet
6	RRAGD	1	Zaina 2014 Circ Cardiovasc Genet
6	RREB1	1	Zaina 2014 Circ Cardiovasc Genet
6	RSPh9	1	Ek 2016 Hum Mol Genet
6	RUNX2	1	Zaina 2014 Circ Cardiovasc Genet
6	SLC17A4	2	Sharma 2014 Gene
6	SLC36B3	1	Zaina 2014 Circ Cardiovasc Genet
6	SLC39A7	1 (with HSD17B8)	Zaina 2014 Circ Cardiovasc Genet
6	SMAP1	1	Zaina 2014 Circ Cardiovasc Genet
6	SMOC2	5	Rask-Andersen 2016 Hum Mol Genet, Zaina 2014 Circ Cardiovasc Genet
6	STXBp5	1	Zaina 2014 Circ Cardiovasc Genet
6	TBL3	2	Zaina 2014 Circ Cardiovasc Genet
6	TBX18	1	Rask-Andersen 2016 Hum Mol Genet
6	TOP21	1	Nazarenko 2014 PLoS One
6	THBS2	1	Rask-Andersen 2016 Hum Mol Genet
6	TNKB	12	Nazarenko 2014 PLoS One
6	TPD52L1	2	Rask-Andersen 2016 Hum Mol Genet
6	TRNA_Val	2	Zaina 2014 Circ Cardiovasc Genet
6	TSPY02	1	Zaina 2014 Circ Cardiovasc Genet
6	UST	2	Rask-Andersen 2016 Hum Mol Genet
6	UTRN	1	Zaina 2014 Circ Cardiovasc Genet
6	ZBTB12	32	Ek 2016 Hum Mol Genet
6	ZNF311	1	Zaina 2014 Circ Cardiovasc Genet
6	ZNF389	1	Nazarenko 2014 PLoS One
7	ABCB4	2	Zaina 2014 Circ Cardiovasc Genet
7	ADAM22	1	Zaina 2014 Circ Cardiovasc Genet
7	AHR	1 (upstream, downstream: SNX13)	Nazarenko 2014 PLoS One, Zaina 2014 Circ Cardiovasc Genet
7	ANLN	1	Zaina 2014 Circ Cardiovasc Genet
7	ASB4	2	Sharma 2014 Gene
7	ASZ1	1 (upstream, downstream: CFTR)	Zaina 2014 Circ Cardiovasc Genet
7	ATP6V0d4	1	Zaina 2014 Circ Cardiovasc Genet
7	C1GALT1	1	Rask-Andersen 2016 Hum Mol Genet, Zaina 2014 Circ Cardiovasc Genet
7	C7orf16	1	Rask-Andersen 2016 Hum Mol Genet
7	C7orf25	1	Rask-Andersen 2016 Hum Mol Genet
7	C7orf60	1 (upstream, downstream: GPR85)	Rask-Andersen 2016 Hum Mol Genet
7	CALD1	2	Nazarenko 2014 PLoS One, Zaina 2014 Circ Cardiovasc Genet
7	CAMK2B	1	Zaina 2014 Circ Cardiovasc Genet
7	CD36	1	Zaina 2014 Circ Cardiovasc Genet
7	CDK6	1	Zaina 2014 Circ Cardiovasc Genet
7	CFTR	1 (downstream, upstream: ASZ1)	Zaina 2014 Circ Cardiovasc Genet
7	CHCHD3	1	Nazarenko 2014 PLoS One, Zaina 2014 Circ Cardiovasc Genet
7	CLDN15	1	Rask-Andersen 2016 Hum Mol Genet
7	CPED1	1	Zaina 2014 Circ Cardiovasc Genet
7	CRCP	1	Zaina 2014 Circ Cardiovasc Genet
7	CREB5	4	Rask-Andersen 2016 Hum Mol Genet
7	CTTNBP2	1	Zaina 2014 Circ Cardiovasc Genet
7	CUX1	3	Zaina 2014 Circ Cardiovasc Genet
7	DENND2A	1	Guerrera 2015 Clin Epigenet
7	DFNA4	2	Rask-Andersen 2016 Hum Mol Genet
7	DOCK4	1	Zaina 2014 Circ Cardiovasc Genet
7	EEDP1	1	Zaina 2014 Circ Cardiovasc Genet
7	EGFR	2	Rask-Andersen 2016 Hum Mol Genet
7	EPHB6	1	Zaina 2014 Circ Cardiovasc Genet
7	FAM180A	1	Nazarenko 2014 PLoS One, Zaina 2014 Circ Cardiovasc Genet
7	FBXL13	4 (with LRRK17)	Zaina 2014 Circ Cardiovasc Genet
7	FBXL18	3 (with MIR589)	Zaina 2014 Circ Cardiovasc Genet
7	FEZF1	1	Zaina 2014 Circ Cardiovasc Genet
7	FLNC	1	Zaina 2014 Circ Cardiovasc Genet
7	FOXP1	1	Zaina 2014 Circ Cardiovasc Genet
7	FOXP2	1	Zaina 2014 Circ Cardiovasc Genet
7	GARS	1	Zaina 2014 Circ Cardiovasc Genet
7	GPR85	1 (downstream, upstream: C7orf60)	Zaina 2014 Circ Cardiovasc Genet
7	GRMB	1	Rask-Andersen 2016 Hum Mol Genet
7	HEATR2	1	Zaina 2014 Circ Cardiovasc Genet
7	HOXA11AS	2	Zaina 2014 Circ Cardiovasc Genet
7	HOXA2	9	Nazarenko 2014 PLoS One, Zaina 2014 Circ Cardiovasc Genet
7	HOXA3	23	Zaina 2014 Circ Cardiovasc Genet
7	HOXA6	2	Zaina 2014 Circ Cardiovasc Genet
7	HOXA7	1	Zaina 2014 Circ Cardiovasc Genet
7	HOXA9	4	Zaina 2014 Circ Cardiovasc Genet
7	ICA1	1	Zaina 2014 Circ Cardiovasc Genet
7	IQCE	1	Ek 2016 Hum Mol Genet
7	KIAA0895	1	Zaina 2014 Circ Cardiovasc Genet
7	LAMB1	1	Nazarenko 2014 PLoS One
7	LAT2	1	Zaina 2014 Circ Cardiovasc Genet
7	LEP	1	Zaina 2014 Circ Cardiovasc Genet
7	LHPL3	1	Rask-Andersen 2016 Hum Mol Genet
7	LMD2	1	Zaina 2014 Circ Cardiovasc Genet
7	LRRC17	4 (with FBXL13)	Zaina 2014 Circ Cardiovasc Genet
7	MAD1L1	2	Rask-Andersen 2016 Hum Mol Genet
7	MAGI2	1	Zaina 2014 Circ Cardiovasc Genet
7	MEST	5	Rask-Andersen 2016 Hum Mol Genet
7	MIR589	3 (with FBXL13)	Zaina 2014 Circ Cardiovasc Genet
7	NDUF4	1	Zaina 2014 Circ Cardiovasc Genet
7	NUDCD3	1	Zaina 2014 Circ Cardiovasc Genet
7	PDGF4	1	Zaina 2014 Circ Cardiovasc Genet
7	PLXNA4	3	Zaina 2014 Circ Cardiovasc Genet
7	POU6F2	1	Zaina 2014 Circ Cardiovasc Genet
7	PRKAG2	1	Zaina 2014 Circ Cardiovasc Genet
7	PRKAR1B	1	Zaina 2014 Circ Cardiovasc Genet
7	PTPRN2	2	Ek 2016 Hum Mol Genet
7	RADIL	1	Zaina 2014 Circ Cardiovasc Genet
7	RAPGEF5	1	Yamada 2014 J Mol Med
7	RELN	1	Zaina 2014 Circ Cardiovasc Genet
7	RHEB	1	Zaina 2014 Circ Cardiovasc Genet
7	RNP216	4	Zaina 2014 Circ Cardiovasc Genet
7	SDK1	1	Yamada 2014 J Mol Med, Zaina 2014 Circ Cardiovasc Genet
7	SEMA3D	1	Zaina 2014 Circ Cardiovasc Genet
7	SEMA3E	1	Rask-Andersen 2016 Hum Mol Genet
7	SFRP4	2	Zaina 2014 Circ Cardiovasc Genet
7	SLC26A4	1	Rask-Andersen 2016 Hum Mol Genet, Zaina 2014 Circ Cardiovasc Genet
7	SMARDC3	1	Nazarenko 2014 PLoS One
7	SMURF1	1	Zaina 2014 Circ Cardiovasc Genet



9	TNFSF8	1		Nazarenko 2014 PLoS One
9	TRAF1	1		Nazarenko 2014 PLoS One
9	TRIM14	1		Zaina 2014 Circ Cardiovasc Genet
9	TLIL11	1		Zaina 2014 Circ Cardiovasc Genet
9	TUSC1	1 (downstream, upstream: ELAVL2)		Sharma 2014 Gene
9	UBE2R2	1		Zaina 2014 Circ Cardiovasc Genet
10	ABLM1	1		Zaina 2014 Circ Cardiovasc Genet
10	ACBD5	1 (upstream, downstream: LOC387646)		Castillo-Diaz 2014 J Mol Med
10	ADAM12	1		Zaina 2014 Circ Cardiovasc Genet
10	ADARB2	4		Zaina 2014 Circ Cardiovasc Genet
10	ANK3	2		Zaina 2014 Circ Cardiovasc Genet
10	ARHGAP12	3		Zaina 2014 Circ Cardiovasc Genet
10	ASCC1	1 (with C10orf104)		Zaina 2014 Circ Cardiovasc Genet
10	BAMBI	1		Zaina 2014 Circ Cardiovasc Genet
10	BICC1	1		Zaina 2014 Circ Cardiovasc Genet
10	BMPR1A	2		Rask-Andersen 2016 Hum Mol Genet
10	BNIP3	1		Zaina 2014 Circ Cardiovasc Genet
10	BTB16	1		Yamada 2014 J Mol Med
10	C10orf104	1 (with ASCC1)		Zaina 2014 Circ Cardiovasc Genet
10	C10orf11	2		Rask-Andersen 2016 Hum Mol Genet
10	C10orf118	1		Zaina 2014 Circ Cardiovasc Genet
10	C10orf30	1		Marcante 2014 PLoS One
10	C10orf79	1		Zaina 2014 Circ Cardiovasc Genet
10	C10orf82	1		Nazarenko 2014 PLoS One
10	CAMK1D	1		Castillo-Diaz 2014 J Mol Med
10	CDNF	1		Zaina 2014 Circ Cardiovasc Genet
10	COL13A1	1		Zaina 2014 Circ Cardiovasc Genet
10	COL17A1	1		Zaina 2014 Circ Cardiovasc Genet
10	CRTAC1	1		Zaina 2014 Circ Cardiovasc Genet
10	CTBP2	1		Rask-Andersen 2016 Hum Mol Genet
10	CTNNA3	2 (CpG and CGI)		Zaina 2014 Circ Cardiovasc Genet
10	CUGBP2	1		Nazarenko 2014 PLoS One
10	CYP2C18	1		Zaina 2014 Circ Cardiovasc Genet
10	DIP2C	4		Rask-Andersen 2016 Hum Mol Genet
10	DOCK1	1 (with FAM196A)		Zaina 2014 Circ Cardiovasc Genet
10	DPYSL4	1		Zaina 2014 Circ Cardiovasc Genet
10	EBF3	2		Rask-Andersen 2016 Hum Mol Genet
10	FAM107B	1		Zaina 2014 Circ Cardiovasc Genet
10	FAM170B	2		Zaina 2014 Circ Cardiovasc Genet
10	FAM190B	1		Zaina 2014 Circ Cardiovasc Genet
10	FAM196A	1 (with DOCK1)		Zaina 2014 Circ Cardiovasc Genet
10	FAM53B	1		Zaina 2014 Circ Cardiovasc Genet
10	FLJ49893	3 (2 CpGs and 1 CGI)		Nazarenko 2014 PLoS One, Sharma 2014 Gene
10	FRMD4A	1		EK 2016 Hum Mol Genet
10	FRMPD2	1		Nazarenko 2014 PLoS One
10	GDF10	1		Zaina 2014 Circ Cardiovasc Genet
10	GPR158	1		Rask-Andersen 2016 Hum Mol Genet
10	GRK5	3		Zaina 2014 Circ Cardiovasc Genet
10	HECTD2	1 (with LOC100188947)		Rask-Andersen 2016 Hum Mol Genet, Zaina 2014 Circ Cardiovasc Genet
10	HK1	1		Zaina 2014 Circ Cardiovasc Genet
10	IL2RA	1		Zaina 2014 Circ Cardiovasc Genet
10	KCNMA1	2		Rask-Andersen 2016 Hum Mol Genet
10	KIAA0317	2		Zaina 2014 Circ Cardiovasc Genet
10	LBX1	1		Zaina 2014 Circ Cardiovasc Genet
10	LGII	1		Rask-Andersen 2016 Hum Mol Genet
10	LHPP	1		Zaina 2014 Circ Cardiovasc Genet
10	LOC100188947	1 (with HECTD2)		Nazarenko 2014 PLoS One
10	LOC282997	1 (with PDCD4)		Zaina 2014 Circ Cardiovasc Genet
10	LOC387646	1 (downstream, upstream: ACBD5)		Rask-Andersen 2016 Hum Mol Genet
10	LZTS2	1		Zaina 2014 Circ Cardiovasc Genet
10	MGMT	1		Zaina 2014 Circ Cardiovasc Genet
10	MICU1	1		Rask-Andersen 2016 Hum Mol Genet
10	MIR604	1 (with SVIL)		Zaina 2014 Circ Cardiovasc Genet
10	MMRN2	1		Zaina 2014 Circ Cardiovasc Genet
10	MYST4	1		Zaina 2014 Circ Cardiovasc Genet
10	NTSC2	1		Zaina 2014 Circ Cardiovasc Genet
10	PCDH21	1		Zaina 2014 Circ Cardiovasc Genet
10	PDCD4	1 (with LOC282997)		Rask-Andersen 2016 Hum Mol Genet
10	PDZD8	1		Zaina 2014 Circ Cardiovasc Genet
10	PFKP	4		Zaina 2014 Circ Cardiovasc Genet
10	PHYH1P1	1		Zaina 2014 Circ Cardiovasc Genet
10	PIP4K2A	1		Zaina 2014 Circ Cardiovasc Genet
10	PLEKH41	5		Zaina 2014 Circ Cardiovasc Genet
10	PNLIP	2		Guarrera 2015 Clin Epigenet
10	PNLIPRP1	5		Zaina 2014 Circ Cardiovasc Genet, Nazarenko 2014 PLoS One
10	PTPRE	1		Zaina 2014 Circ Cardiovasc Genet, Nazarenko 2014 PLoS One
10	RBM20	1		Zaina 2014 Circ Cardiovasc Genet
10	SEC31L2	1		Nazarenko 2014 PLoS One
10	SH2D4B	2		Nazarenko 2014 PLoS One, Zaina 2014 Circ Cardiovasc Genet
10	SH3PX2DA	1		Zaina 2014 Circ Cardiovasc Genet
10	SORBS1	7		Zaina 2014 Circ Cardiovasc Genet
10	SORCS1	1		Zaina 2014 Circ Cardiovasc Genet
10	SORCS3	1		Rask-Andersen 2016 Hum Mol Genet
10	SPCCK2	1		Zaina 2014 Circ Cardiovasc Genet
10	SUO	1		Zaina 2014 Circ Cardiovasc Genet
10	SVIL	6 (1 with MIR604)		Rask-Andersen 2016 Hum Mol Genet
10	TACO2	1		Zaina 2014 Circ Cardiovasc Genet
10	TET1	1		Zaina 2014 Circ Cardiovasc Genet
10	TMEM23	1		Zaina 2014 Circ Cardiovasc Genet
10	TMEM72	1		Zaina 2014 Circ Cardiovasc Genet
10	VCL	1		Zaina 2014 Circ Cardiovasc Genet
10	VWA2	1		Zaina 2014 Circ Cardiovasc Genet
10	WDFY4	1		Rask-Andersen 2016 Hum Mol Genet
10	ZEB1	1		Zaina 2014 Circ Cardiovasc Genet
10	ZNF438	3		Zaina 2014 Circ Cardiovasc Genet
10	ZNF503-AS2	1		Rask-Andersen 2016 Hum Mol Genet
11	SS_rRNA	1		Rask-Andersen 2016 Hum Mol Genet
11	AK127457	1 (downstream, upstream: ASAM)		Zaina 2014 Circ Cardiovasc Genet
11	ALX4	4		Nazarenko 2014 PLoS One, Rask-Andersen 2016 Hum Mol Genet
11	AMBRA1	1		Zaina 2014 Circ Cardiovasc Genet
11	AN01	1		Rask-Andersen 2016 Hum Mol Genet
11	AN03	1		Zaina 2014 Circ Cardiovasc Genet
11	ASAM	1 (upstream, downstream: AK127457)		Castillo-Diaz 2014 J Mol Med
11	ASCL2	1		Zaina 2014 Circ Cardiovasc Genet
11	BC047021	1 (upstream, downstream: MGCG13125)		Zaina 2014 Circ Cardiovasc Genet
11	BCL9L	1		Zaina 2014 Circ Cardiovasc Genet
11	BRSK2	1		Zaina 2014 Circ Cardiovasc Genet
11	C11orf2	1		Zaina 2014 Circ Cardiovasc Genet
11	C11orf41	1		Zaina 2014 Circ Cardiovasc Genet
11	C11orf45	1		Zaina 2014 Circ Cardiovasc Genet
11	C11orf52	1		Zaina 2014 Circ Cardiovasc Genet
11	CARS	2		Rask-Andersen 2016 Hum Mol Genet
11	CD3D	1		Zaina 2014 Circ Cardiovasc Genet
11	CD44	1		Zaina 2014 Circ Cardiovasc Genet
11	CD59	1		Zaina 2014 Circ Cardiovasc Genet
11	CDON	1		Zaina 2014 Circ Cardiovasc Genet
11	CHC048	1		Zaina 2014 Circ Cardiovasc Genet
11	CHRNA10	1		Zaina 2014 Circ Cardiovasc Genet
11	CPT1A	2		Zaina 2014 Circ Cardiovasc Genet
11	CTTN	1		Zaina 2014 Circ Cardiovasc Genet
11	CVBSR2	1		Zaina 2014 Circ Cardiovasc Genet
11	DBX1	1 (upstream, downstream: HTATIP2)		Zaina 2014 Circ Cardiovasc Genet
11	DLG2	2		Nazarenko 2014 PLoS One, Zaina 2014 Circ Cardiovasc Genet
11	DSCAM1	2		Sharma 2014 Gene, Zaina 2014 Circ Cardiovasc Genet
11	EIF3F	2		Zaina 2014 Circ Cardiovasc Genet
11	ETS1	1		Zaina 2014 Circ Cardiovasc Genet
11	FAM111B	1		Zaina 2014 Circ Cardiovasc Genet
11	FAU	1		Zaina 2014 Circ Cardiovasc Genet
11	FEZ1	1		Zaina 2014 Circ Cardiovasc Genet
11	FGF19	2		Rask-Andersen 2016 Hum Mol Genet
11	FLI1	1		Zaina 2014 Circ Cardiovasc Genet
11	GAB2	1		Zaina 2014 Circ Cardiovasc Genet
11	GAL	1		Zaina 2014 Circ Cardiovasc Genet
11	GAS2	1		Zaina 2014 Circ Cardiovasc Genet
11	GIF	1		Zaina 2014 Circ Cardiovasc Genet
11	GRAMD1B	1		Zaina 2014 Circ Cardiovasc Genet
11	HBBP1	1		Zaina 2014 Circ Cardiovasc Genet
11	HTATIP2	1 (downstream, upstream: DBX1)		Zaina 2014 Circ Cardiovasc Genet
11	HTR3B	1		Zaina 2014 Circ Cardiovasc Genet
11	IGSF9B	1		Zaina 2014 Circ Cardiovasc Genet
11	JAM3	1		Nazarenko 2014 PLoS One
11	KCNC1	1		Nazarenko 2014 PLoS One
11	KCNO1DN	1		Nazarenko 2014 PLoS One

11	KCNO1OT1	1	
11	LGR4	2	
11	LOC220070	1	
11	LOC399959	3	
11	LRRK4C	1	
11	LSP1	2	
11	MAML2	1	
11	MGC13125	1 (downstream, upstream: BC047021)	
11	MICAL2	2	
11	MMP12	1	
11	MMP20	1	
11	MRGPRF	1	
11	MRGPRX2	2	
11	MRV11	1	
11	MS4A2	1	
11	MS4A3	1	
11	MS4A4A	1	
11	MUC6	1	
11	NAV2	4	
11	NFM	1	
11	NUMA1	3	
11	NUP160	1	
11	ODZ4	1	
11	OLFML1	1	
11	OR51S1	2	
11	P2RX3	1	
11	PANX1	2	
11	PC	1	
11	PDGF	1	
11	PKNOX2	2 (CpG and CGI)	
11	PPFA1	1	
11	PRR5L	2	
11	PTDSS2	2	
11	RAPSN	1	
11	RICS	1	
11	RNH1	1	
11	SAPS3	1 (upstream, downstream: GAL)	
11	SCUBE2	1	
11	SDHA2	1	
11	SEREF	1	
11	SHANK2	2	
11	SLC22A12	1	
11	SLC22A18	2	
11	SLC37A4	1	
11	SORL1	2	
11	SPON1	2	
11	ST5	1	
11	TEAD1	2	
11	TMEM136	1	
11	TOLLIP	1	
11	USP2	1	
11	WT1	2	
11	ZBTB16	2	
11	ZBTB44	1	
12	AACS	1	
12	ACAD10	2	
12	ANAPC7	1	
12	ANO2	1	
12	ANO4	1	
12	ANO6	3	
12	AOP5	1	
12	ARF3	1	
12	ARHGAP9	1	
12	ARHGDIB	2	
12	ART4	6	
12	AVIL	1	
12	BHLHE41	3	
12	BTBD11	4	
12	C12orf12	1 (downstream, upstream: LOC338758)	
12	C12orf56	1	
12	C10L4	3	
12	CCDC60	1	
12	CD163	1	
12	CHFR	1	
12	CHST11	3	
12	EID3	1	
12	FAM19A2	1	
12	FBXO21	1	
12	FLJ21908	1	
12	FRS2	1	
12	GALNT9	1	
12	GT2	1	
12	GNB3	1	
12	GRIP1	5	
12	H0C10	1 (downstream, upstream: HOXC11)	
12	HOXC11	3 (1 upstream, downstream: HOXC10)	
12	HOXC4	13 (4 with HOXA5 and HOXA6, 1 with HOXA5)	
12	HOXC5	6 (1 with HOXA4, 4 with HOXA5)	
12	HOXA6	4 (with HOXA4 and HOXA5)	
12	HOXC9	1	
12	IKP	1	
12	ITFG2	1	
12	ITGA5	1	
12	KCNJ8	1	
12	KCTD10	1	
12	KRT4	1	
12	KRT7	1	
12	KRTHB1	1	
12	KRTHB6	1	
12	LOC283404	1	
12	LOC338758	1 (upstream, downstream: C12orf12)	
12	LRMP	1	
12	MAPKAPK5	2	
12	METTL7A	1	
12	MYBPC1	1	
12	NFYB	1	
12	NR2C1	1	
12	NT5DC3	1	
12	NUAK1	1	
12	PAH	1	
12	PCBP2	1	
12	PITPNM2	1	
12	PLEKH45	1	
12	PPMH1	1	
12	PROKLE1	2	
12	PRPH	1	
12	PSMD9	2	
12	PTPRB	1	
12	R3HDM2	1	
12	RASAL1	1	
12	RASSF3	2	
12	RDH5	1	
12	SBNO1	1 (upstream, downstream: SETD8)	
12	SETD1B	1	
12	SETD8	1 (downstream, upstream: SBNO1)	
12	SHMT2	1	
12	SLC16A7	1 (downstream, upstream: UNQ287)	
12	SLC6A13	2	
12	SOAT2	1	
12	SSH1	1	
12	STAC3	1	
12	TAS2R9	1	
12	TMMC3	1	
12	TMEM116	1	
12	TMEM132D	1	
12	TXNRD1	1	
12	UNQ287	1 (upstream, downstream: SLC16A7)	
12	WDR66	1	
13	A2LD1	1	
13	ABCC4	1	
13	ATP11A	2	
13	COL4A1	4	

13	CRYL1	1	Zaina 2014 Circ Cardiovasc Genet
13	DACH1	1	Zaina 2014 Circ Cardiovasc Genet
13	DCT	1	Nazarenko 2014 PLoS One
13	DOCK9	4	Zaina 2014 Circ Cardiovasc Genet
13	EDNRB	1	Nazarenko 2014 PLoS One
13	EFNB2	1	Zaina 2014 Circ Cardiovasc Genet
13	ENOX1	1	Yamada 2014 J Mol Med
13	EPSTI1	1	Zaina 2014 Circ Cardiovasc Genet
13	ESD	1	Zaina 2014 Circ Cardiovasc Genet
13	F10	2	Zaina 2014 Circ Cardiovasc Genet
13	FARP1	2	Guarrera 2015 Clin Epigenet
13	FREM2	5	Zaina 2014 Circ Cardiovasc Genet
13	GUCY1B2	1	Nazarenko 2014 PLoS One
13	KIAA0853	1 (downstream, upstream: NUR70)	Castillo-Diaz 2014 J Mol Med
13	KLF12	1	Zaina 2014 Circ Cardiovasc Genet
13	LRCH1	2	Zaina 2014 Circ Cardiovasc Genet
13	MIR548F5	1	Zaina 2014 Circ Cardiovasc Genet
13	NUR70	1 (upstream, downstream: KIAA0853)	Castillo-Diaz 2014 J Mol Med
13	RASA3	1	Zaina 2014 Circ Cardiovasc Genet
13	RNASEP2B	1	Zaina 2014 Circ Cardiovasc Genet
13	SCE1	2	Nazarenko 2014 PLoS One, Zaina 2014 Circ Cardiovasc Genet
13	SLC46A3	1	Zaina 2014 Circ Cardiovasc Genet
13	SLC7A1	2	Zaina 2014 Circ Cardiovasc Genet
13	SPRY2	2	Zaina 2014 Circ Cardiovasc Genet
13	STK24	1	Zaina 2014 Circ Cardiovasc Genet
13	TMC03	2	Zaina 2014 Circ Cardiovasc Genet
13	UGGT2	1	Zaina 2014 Circ Cardiovasc Genet
13	ZIC5	1	Rask-Andersen 2016 Hum Mol Genet
14	ACOT2	2	Rask-Andersen 2016 Hum Mol Genet
14	AK056212	1 (upstream, downstream: SDCCAG1)	Nazarenko 2014 PLoS One, Zaina 2014 Circ Cardiovasc Genet
14	AKT1	1	Sharma 2014 Gene
14	ALKBH	1	Zaina 2014 Circ Cardiovasc Genet
14	ASB2	1	Nazarenko 2014 PLoS One
14	BATF	1	Zaina 2014 Circ Cardiovasc Genet
14	BDKRB1	1	Nazarenko 2014 PLoS One
14	BMP4	1 (downstream, upstream: DDHD1)	Nazarenko 2014 PLoS One, Zaina 2014 Circ Cardiovasc Genet
14	C14orf138	1 (with SCS2)	Sharma 2014 Gene
14	C14orf179	1	Zaina 2014 Circ Cardiovasc Genet
14	C14orf43	1	Nazarenko 2014 PLoS One
14	C14orf48	2	Zaina 2014 Circ Cardiovasc Genet
14	CATSPERB	1	Nazarenko 2014 PLoS One
14	CLEC14A	1	Nazarenko 2014 PLoS One
14	DAAM1	3	Zaina 2014 Circ Cardiovasc Genet
14	DDHD1	1 (upstream, downstream: BMP4)	Sharma 2014 Gene
14	EGLN3	1	Zaina 2014 Circ Cardiovasc Genet
14	EML1	1	Zaina 2014 Circ Cardiovasc Genet
14	FERMT2	1	Zaina 2014 Circ Cardiovasc Genet
14	FOXN3	1	Zaina 2014 Circ Cardiovasc Genet
14	GALNT1	1	Zaina 2014 Circ Cardiovasc Genet
14	GSC	2 (CpG and CGI)	Zaina 2014 Circ Cardiovasc Genet
14	IF27	1	Zaina 2014 Circ Cardiovasc Genet
14	IGHE	1	Oudejans 2016 PLoS One
14	J02	1	Nazarenko 2014 PLoS One
14	JPH4	1	Nazarenko 2014 PLoS One
14	KIAA0247	1	Zaina 2014 Circ Cardiovasc Genet
14	KIAA1737	1	Zaina 2014 Circ Cardiovasc Genet
14	LGMN	1	Zaina 2014 Circ Cardiovasc Genet
14	LOC145474	1	Zaina 2014 Circ Cardiovasc Genet
14	LOC161247	1	Zaina 2014 Circ Cardiovasc Genet
14	LRFN5	1	Zaina 2014 Circ Cardiovasc Genet
14	LTBP2	2	Zaina 2014 Circ Cardiovasc Genet
14	MDDA2	1	Zaina 2014 Circ Cardiovasc Genet
14	NIN	2	Zaina 2014 Circ Cardiovasc Genet
14	PAX9	2	Zaina 2014 Circ Cardiovasc Genet
14	PELJ2	1	Zaina 2014 Circ Cardiovasc Genet
14	PRKCH	1	Zaina 2014 Circ Cardiovasc Genet
14	RNASE3	1	Zaina 2014 Circ Cardiovasc Genet
14	SDCCAG1	1 (downstream, upstream: AK056212)	Nazarenko 2014 PLoS One
14	SOS2	1 (with C14orf138)	Zaina 2014 Circ Cardiovasc Genet
14	TTLL5	1	Zaina 2014 Circ Cardiovasc Genet
14	WDR20	1	Zaina 2014 Circ Cardiovasc Genet
14	XRCC3	1	Zaina 2014 Circ Cardiovasc Genet
14	ZFYVE21	2	Zaina 2014 Circ Cardiovasc Genet
15	AAGAB	1	Zaina 2014 Circ Cardiovasc Genet
15	ADAMTS17	1	Zaina 2014 Circ Cardiovasc Genet
15	ADAMTSL3	1	Zaina 2014 Circ Cardiovasc Genet
15	ALDH1A2	1	Zaina 2014 Circ Cardiovasc Genet
15	ALPK3	1	Rask-Andersen 2016 Hum Mol Genet
15	ANXA2	1	Zaina 2014 Circ Cardiovasc Genet
15	ATP10A	1	Zaina 2014 Circ Cardiovasc Genet
15	ATP10C	1 (upstream, downstream: BC038777)	Rask-Andersen 2016 Hum Mol Genet
15	BC038777	1 (downstream, upstream: ATP10C)	Zaina 2014 Circ Cardiovasc Genet
15	BNC1	1	Zaina 2014 Circ Cardiovasc Genet
15	BTBD1	1	Zaina 2014 Circ Cardiovasc Genet
15	C15orf23	1	Zaina 2014 Ccirc Cardiovasc Genet
15	C15orf41	1	Zaina 2014 Ccirc Cardiovasc Genet
15	C2CD4A	1	Rask-Andersen 2016 Hum Mol Genet
15	CA12	2	Zaina 2014 Ccirc Cardiovasc Genet
15	CCDC23	1	Zaina 2014 Ccirc Cardiovasc Genet
15	CDNDBP1	1	Zaina 2014 Ccirc Cardiovasc Genet
15	CGNL1	1	Zaina 2014 Ccirc Cardiovasc Genet
15	CHRN43	1	Zaina 2014 Ccirc Cardiovasc Genet
15	CHSY1	3	Zaina 2014 Ccirc Cardiovasc Genet
15	CSNK1A1P	1 (with C15orf41)	Zaina 2014 Ccirc Cardiovasc Genet
15	EDC3	1	Rask-Andersen 2016 Hum Mol Genet
15	FGF7	1	Zaina 2014 Ccirc Cardiovasc Genet
15	FLJ35695	1	Zaina 2014 Ccirc Cardiovasc Genet
15	FMN1	1	Zaina 2014 Ccirc Cardiovasc Genet
15	GABRA5	1	Rask-Andersen 2016 Hum Mol Genet
15	GABRG3	1	Zaina 2014 Ccirc Cardiovasc Genet
15	GALK2	1	Zaina 2014 Ccirc Cardiovasc Genet
15	GCNT3	3	Zaina 2014 Ccirc Cardiovasc Genet
15	GOLGA6A	1	Rask-Andersen 2016 Hum Mol Genet
15	HAPLN3	1	Zaina 2014 Ccirc Cardiovasc Genet
15	HERC1	1	Rask-Andersen 2016 Hum Mol Genet
15	KIAA1199	1	Zaina 2014 Ccirc Cardiovasc Genet
15	LOC145845	1	Zaina 2014 Ccirc Cardiovasc Genet
15	LOC91948	1	Zaina 2014 Ccirc Cardiovasc Genet
15	LOXL1	1	Rask-Andersen 2016 Hum Mol Genet
15	LRRK49	1	Zaina 2014 Ccirc Cardiovasc Genet
15	MEIS2	1	Zaina 2014 Ccirc Cardiovasc Genet
15	MIR1469	1	Rask-Andersen 2016 Hum Mol Genet
15	MIR629	3 (with TLE3)	Zaina 2014 Ccirc Cardiovasc Genet
15	MRPL42P5	1	Rask-Andersen 2016 Hum Mol Genet, Zaina 2014 Circ Cardiovasc Genet
15	NR2F2	2	Zaina 2014 Ccirc Cardiovasc Genet
15	NTRK3	1	Zaina 2014 Ccirc Cardiovasc Genet
15	PAQR5	1	Zaina 2014 Ccirc Cardiovasc Genet
15	PARP9	1	Zaina 2014 Ccirc Cardiovasc Genet
15	PTBG	1	Zaina 2014 Ccirc Cardiovasc Genet
15	RAB8B	1	Zaina 2014 Ccirc Cardiovasc Genet
15	RASGRF1	2	Yamada 2014 J Mol Med
15	RGM1	1	Rask-Andersen 2016 Hum Mol Genet, Zaina 2014 Ccirc Cardiovasc Genet
15	RNF36	1	Nazarenko 2014 PLoS One
15	RORA	1	Zaina 2014 Ccirc Cardiovasc Genet
15	SHF	1	Rask-Andersen 2016 Hum Mol Genet
15	SNRPN	1	Gómez-Úriz 2015 Human Mol Genet
15	SV2B	1	Zaina 2014 Ccirc Cardiovasc Genet
15	TBC1D28	2	Zaina 2014 Ccirc Cardiovasc Genet
15	THSD4	6	Nazarenko 2014 PLoS One, Zaina 2014 Ccirc Cardiovasc Genet
15	TLE3	3 (with MIR629)	Zaina 2014 Ccirc Cardiovasc Genet
15	TLN2	1	Zaina 2014 Ccirc Cardiovasc Genet
15	TMC05	1	Nazarenko 2014 PLoS One
15	TMC05A	1	Zaina 2014 Ccirc Cardiovasc Genet
15	ZNF710	1	Nazarenko 2014 PLoS One
16	A2BP1	3	Zaina 2014 Ccirc Cardiovasc Genet
16	ABCC1	2	Nazarenko 2014 PLoS One, Zaina 2014 Ccirc Cardiovasc Genet
16	ABCC6	1	Zaina 2014 Ccirc Cardiovasc Genet
16	ADCY9	3	Zaina 2014 Ccirc Cardiovasc Genet
16	BANP	1	Zaina 2014 Ccirc Cardiovasc Genet
16	C16orf145	1	Castillo-Diaz 2014 J Mol Med
16	C16orf73	1	Rask-Andersen 2016 Hum Mol Genet
16	C16orf88	1	Rask-Andersen 2016 Hum Mol Genet
16	C1QTNF8	2	Zaina 2014 Ccirc Cardiovasc Genet

16	<i>CBFA2T3</i>	4	Guerrera 2015 Clin Epigenet, Zaina 2014 Circ Cardiovasc Genet
16	<i>CBNL1</i>	1	Rask-Andersen 2016 Hum Mol Genet
16	<i>CCDC101</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>CDH5</i>	2	Zaina 2014 Circ Cardiovasc Genet
16	<i>CDH8</i>	1	Rask-Andersen 2016 Hum Mol Genet
16	<i>CHST6</i>	1	Nazarenko 2014 PLoS One
16	<i>CII7A</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>CLDN6</i>	1	Nazarenko 2014 PLoS One
16	<i>CLEC16A</i>	2	Zaina 2014 Circ Cardiovasc Genet
16	<i>CMIP</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>CNOT1</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>CPNE7</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>CTCF</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>CX3CL1</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>DHX38</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>EMP2</i>	3	Nazarenko 2014 PLoS One
16	<i>FAM18A</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>GALNS</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>GPRC5B</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>GPI2</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>GSP1T1</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>HPR</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>HSD17B2</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>HSPC065</i>	1	Nazarenko 2014 PLoS One
16	<i>IGFALS</i>	1	Nazarenko 2014 PLoS One
16	<i>ITGAX</i>	1	Nazarenko 2014 PLoS One
16	<i>KIAA0513</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>KIAA0556</i>	3	Zaina 2014 Circ Cardiovasc Genet
16	<i>LCKMT1</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>LDHD</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>LUTAF</i>	1	Castillo-Díaz 2014 J Mol Med
16	<i>LOC283932</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>LOC55565</i>	1	Castillo-Díaz 2014 J Mol Med
16	<i>MIR36571</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>MTHFSD</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>MTSS1L</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>MYH11</i>	1 (with <i>NDE1</i> )	Zaina 2014 Circ Cardiovasc Genet
16	<i>NDE1</i>	1 (with <i>MYH11</i> )	Zaina 2014 Circ Cardiovasc Genet
16	<i>NKD1</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>NOD2</i>	1	Yamada 2014 J Mol Med
16	<i>NOMO3</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>NP1PL1</i>	1	Oudejans 2016 PLoS One
16	<i>PARN</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>PKD1</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>PKMYT1</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>PLA2G10</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>PRKCB</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>PRSS8</i>	1	Nazarenko 2014 PLoS One
16	<i>PSKH1</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>SLC12A4</i>	2	Zaina 2014 Circ Cardiovasc Genet
16	<i>SLC22A31</i>	1	Rask-Andersen 2016 Hum Mol Genet
16	<i>SLC7A6</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>TGFH11</i>	1	Nazarenko 2014 PLoS One
16	<i>TKE</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>VAT1L</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>WFDC1</i>	1	Nazarenko 2014 PLoS One
16	<i>WWP2</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>ZCHC14</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>ZFHX3</i>	1	Zaina 2014 Circ Cardiovasc Genet
16	<i>ZNF423</i>	1	Ek 2016 Hum Mol Genet
17	<i>SEPT9</i>	7	Zaina 2014 Circ Cardiovasc Genet
17	<i>41343</i>	2	Yamada 2014 J Mol Med, Zaina 2014 Circ Cardiovasc Genet
17	<i>AATK</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>ABR</i>	2	Nazarenko 2014 PLoS One
17	<i>ACACA</i>	2	Yamada 2014 J Mol Med, Zaina 2014 Circ Cardiovasc Genet
17	<i>ACOX1</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>AK057317</i>	1	Rask-Andersen 2016 Hum Mol Genet
17	<i>AKAP1</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>ALOX12</i>	1	Nazarenko 2014 PLoS One
17	<i>ANKFY1</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>ARSG</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>ASPA</i>	1	Nazarenko 2014 PLoS One
17	<i>ATXN7L3</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>AXIN2</i>	4	Zaina 2014 Circ Cardiovasc Genet
17	<i>BAHCC1</i>	1	Rask-Andersen 2016 Hum Mol Genet
17	<i>BA1AP2</i>	4	Zaina 2014 Circ Cardiovasc Genet
17	<i>BLMH</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>C17orf85</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>CA10</i>	1	Ek 2016 Hum Mol Genet
17	<i>CA4</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>CASKIN2</i>	2	Zaina 2014 Circ Cardiovasc Genet
17	<i>CCDC46</i>	1	Rask-Andersen 2016 Hum Mol Genet
17	<i>CCL2</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>COL1A1</i>	2	Nazarenko 2014 PLoS One
17	<i>DHPSB</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>EVRA</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>EVBB</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>FLJ22222</i>	1 (downstream, upstream: <i>FLJ35767</i> )	EK 2016 Hum Mol Genet
17	<i>FLJ26096</i>	1 (with <i>LOC645851</i> )	Zaina 2014 Circ Cardiovasc Genet
17	<i>FLJ36220</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>FLJ35767</i>	1 (upstream, downstream: <i>FLJ22222</i> )	Zaina 2014 Circ Cardiovasc Genet
17	<i>GALR2</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>GAST</i>	1	Nazarenko 2014 PLoS One
17	<i>GFAP</i>	2	Zaina 2014 Circ Cardiovasc Genet
17	<i>GLP2R</i>	1	Oudejans 2016 PLoS One
17	<i>HOBX3</i>	1	Nazarenko 2014 PLoS One
17	<i>HOBX5</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>HOBX6</i>	1	Castillo-Díaz 2014 J Mol Med
17	<i>HRNPBP3</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>IF35</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>KIAA1554</i>	1	Rask-Andersen 2016 Hum Mol Genet
17	<i>KRT15</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>KRT23</i>	1	Nazarenko 2014 PLoS One
17	<i>KRT24</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>LHX1</i>	1 (downstream, upstream: <i>MRM1</i> )	Nazarenko 2014 PLoS One
17	<i>LLGL2</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>LOC100499467</i>	1	Nazarenko 2014 PLoS One
17	<i>LOC645851</i>	1 (with <i>FLJ25006</i> )	Zaina 2014 Circ Cardiovasc Genet
17	<i>LRRK37B</i>	1	Rask-Andersen 2016 Hum Mol Genet
17	<i>MAP3K14</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>MARCH10</i>	1	Nazarenko 2014 PLoS One
17	<i>MGC29671</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>MIR180</i>	1	Nazarenko 2014 PLoS One
17	<i>MIR21</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>MPRIP</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>MRC2</i>	1	EK 2016 Hum Mol Genet
17	<i>MSM1</i>	1 (upstream, downstream: <i>LHX1</i> )	EK 2016 Hum Mol Genet
17	<i>MS2</i>	2	Zaina 2014 Circ Cardiovasc Genet
17	<i>MYH10</i>	3	Rask-Andersen 2016 Hum Mol Genet
17	<i>MYH14</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>MYO18A</i>	1	Nazarenko 2014 PLoS One
17	<i>MYOGD</i>	4	Zaina 2014 Circ Cardiovasc Genet
17	<i>NBR1</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>NDEL1</i>	4	Zaina 2014 Circ Cardiovasc Genet
17	<i>NFE2L1</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>NUFIP2</i>	1 (upstream, downstream: <i>TAOK1</i> )	Zaina 2014 Circ Cardiovasc Genet
17	<i>NXN</i>	3	Nazarenko 2014 PLoS One
17	<i>OR1E2</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>PITPNC1</i>	1	Rask-Andersen 2016 Hum Mol Genet
17	<i>PITPNM3</i>	2	Zaina 2014 Circ Cardiovasc Genet
17	<i>PLXDC1</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>PMP22</i>	2	Zaina 2014 Circ Cardiovasc Genet
17	<i>PRKCA</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>RAP1GAP2</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>RPTOR</i>	3	Zaina 2014 Circ Cardiovasc Genet
17	<i>RTN4RL1</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>SCARF1</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>SEC14L1</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>SEZ6</i>	1	Rask-Andersen 2016 Hum Mol Genet
17	<i>SLC13A5</i>	1	Rask-Andersen 2016 Hum Mol Genet
17	<i>SLC16A3</i>	1	Zaina 2014 Circ Cardiovasc Genet
17	<i>SLC25A11</i>	1	Nazarenko 2014 PLoS One
17	<i>SLC25A19</i>	1	Zaina 2014 Circ Cardiovasc Genet

17	SLC9A3R1	1	Zaina 2014 Circ Cardiovasc Genet
17	SMG6	2	Zaina 2014 Circ Cardiovasc Genet
17	SMTNL2	1	Zaina 2014 Circ Cardiovasc Genet
17	SPACA3	1	Nazarenko 2014 PLoS One
17	SSH2	1	Zaina 2014 Circ Cardiovasc Genet
17	ST6GALNAC1	1	Nazarenko 2014 PLoS One
17	SUZ12P	1	Rask-Andersen 2016 Hum Mol Genet
17	TAOK1	1	Castillo-Diaz 2014 J Mol Med
17	TMEM88	1	Nazarenko 2014 PLoS One
17	TNFAIP1	1	Zaina 2014 Circ Cardiovasc Genet
17	TRIM37	1	Zaina 2014 Circ Cardiovasc Genet
17	TRPV2	1	EK 2016 Hum Mol Genet
17	VMP1	5	EK 2016 Hum Mol Genet
18	ALPK2	1	Zaina 2014 Circ Cardiovasc Genet
18	ATP6BP1	1	Zaina 2014 Circ Cardiovasc Genet
18	CABLES1	4	Zaina 2014 Circ Cardiovasc Genet
18	CDH20	1	Zaina 2014 Circ Cardiovasc Genet
18	CELF4	1	Rask-Andersen 2016 Hum Mol Genet
18	DOC	1 (upstream, downstream: MBD2)	Castillo-Diaz 2014 J Mol Med
18	GATA9	1	Zaina 2014 Circ Cardiovasc Genet
18	IER3IP1	1 (upstream, downstream: SMAD2)	Castillo-Diaz 2014 J Mol Med
18	KCTD1	1	Zaina 2014 Circ Cardiovasc Genet
18	KIAA0092	1	Rask-Andersen 2016 Hum Mol Genet
18	LIPG	1	Zaina 2014 Circ Cardiovasc Genet
18	MBD2	1 (downstream, upstream: DCC)	Castillo-Diaz 2014 J Mol Med
18	NEO04L	1	Zaina 2014 Circ Cardiovasc Genet
18	NETO1	1	Zaina 2014 Circ Cardiovasc Genet
18	ONECUT2	2	Zaina 2014 Circ Cardiovasc Genet
18	SERPINB4	1	Rask-Andersen 2016 Hum Mol Genet
18	SERPINB7	1	Nazarenko 2014 PLoS One
18	SMAD2	1 (downstream, upstream: IER3IP1)	Nazarenko 2014 PLoS One
19	AP2S1	1	Castillo-Diaz 2014 J Mol Med
19	C5AR1	1	Nazarenko 2014 PLoS One
19	CD37	1	Gomez-Uriz 2015 Human Mol Genet
19	DNASE2	1	Nazarenko 2014 PLoS One
19	EHD2	1	Rask-Andersen 2016 Hum Mol Genet
19	ELSPBP1	2	Nazarenko 2014 PLoS One
19	EPN1	2	Zaina 2014 Circ Cardiovasc Genet
19	ERCC1	1	EK 2016 Hum Mol Genet
19	F2RL3	2	Zaina 2014 Circ Cardiovasc Genet
19	FFAR2	1	EK 2016 Hum Mol Genet, Nazarenko 2014 PLoS One
19	FLJ36070	1	Nazarenko 2014 PLoS One
19	FSD1	1	Nazarenko 2014 PLoS One
19	GDF15	1	Rask-Andersen 2016 Hum Mol Genet
19	GMFG	1	Nazarenko 2014 PLoS One
19	GPR77	2	Nazarenko 2014 PLoS One
19	HOOK2	1 (upstream)	EK 2016 Hum Mol Genet
19	IGFL2	2	Zaina 2014 Circ Cardiovasc Genet
19	INSR	1	Rask-Andersen 2016 Hum Mol Genet
19	KANK2	1	Zaina 2014 Circ Cardiovasc Genet
19	KCNJ14	1	Nazarenko 2014 PLoS One
19	KOV1	1	Rask-Andersen 2016 Hum Mol Genet
19	KHSRP	1	Zaina 2014 Circ Cardiovasc Genet
19	KU11	1	Nazarenko 2014 PLoS One
19	KLK10	1	Rask-Andersen 2016 Hum Mol Genet
19	LOC100504495	1	Nazarenko 2014 PLoS One
19	LOC386758	1	Castillo-Diaz 2014 J Mol Med
19	M6PRBP1	1 (downstream, upstream: TICAM1)	Rask-Andersen 2016 Hum Mol Genet
19	MIR1470	1	Zaina 2014 Circ Cardiovasc Genet
19	MIRPL4	1	Nazarenko 2014 PLoS One
19	MYO9B	1	Rask-Andersen 2016 Hum Mol Genet
19	NFIX	1	Nazarenko 2014 PLoS One
19	ONECUT3	1	EK 2016 Hum Mol Genet
19	PLEKH4	1	Zaina 2014 Circ Cardiovasc Genet
19	PTPR5	1	Rask-Andersen 2016 Hum Mol Genet
19	RAB3D	1	Zaina 2014 Circ Cardiovasc Genet
19	RAB8A	1	Nazarenko 2014 PLoS One
19	RFX2	1	Rask-Andersen 2016 Hum Mol Genet
19	SBNO2	2	Nazarenko 2014 PLoS One
19	SEMA6B	1	Rask-Andersen 2016 Hum Mol Genet
19	SHANK1	1	Nazarenko 2014 PLoS One
19	SHC2	1	Rask-Andersen 2016 Hum Mol Genet
19	SLC1A5	1	Nazarenko 2014 PLoS One
19	TCF3	1	Rask-Andersen 2016 Hum Mol Genet
19	TEX101	2	Nazarenko 2014 PLoS One
19	TFPT	1	Rask-Andersen 2016 Hum Mol Genet
19	TICAM1	2 (1 upstream, downstream: M6PRBP1)	Nazarenko 2014 PLoS One
19	TPM4	2	Castillo-Diaz 2014 J Mol Med, Zaina 2014 Circ Cardiovasc Genet
19	TRIM28	1	Zaina 2014 Circ Cardiovasc Genet
19	WIZ	1	Rask-Andersen 2016 Hum Mol Genet
19	ZNF154	1	Zaina 2014 Circ Cardiovasc Genet
19	ZNF321	1	Rask-Andersen 2016 Hum Mol Genet
19	ZNF358	1	Zaina 2014 Circ Cardiovasc Genet
19	ZNF480	1	Nazarenko 2014 PLoS One
19	ZNF506	1	Rask-Andersen 2016 Hum Mol Genet
19	ZNF528	1	Nazarenko 2014 PLoS One
19	ZNF582	3	Rask-Andersen 2016 Hum Mol Genet
19	ZNF675	1 (upstream, downstream: ZNF681)	Nazarenko 2014 PLoS One
19	ZNF681	1 (downstream, upstream: ZNF675)	Castillo-Diaz 2014 J Mol Med, Zaina 2014 Circ Cardiovasc Genet
19	ZNF682	1	Zaina 2014 Circ Cardiovasc Genet
19	ZNF730	1	Rask-Andersen 2016 Hum Mol Genet
20	ABHD12	1	Zaina 2014 Circ Cardiovasc Genet
20	ADA	1	Rask-Andersen 2016 Hum Mol Genet
20	ADNP	1	Zaina 2014 Circ Cardiovasc Genet
20	APCD01L	1	Rask-Andersen 2016 Hum Mol Genet
20	BPIFB3	1	Zaina 2014 Circ Cardiovasc Genet
20	C20orf194	1	Nazarenko 2014 PLoS One
20	CASS4	1	Rask-Andersen 2016 Hum Mol Genet
20	CDH4	1	Zaina 2014 Circ Cardiovasc Genet
20	CST4	1	Rask-Andersen 2016 Hum Mol Genet
20	CST7	1	Zaina 2014 Circ Cardiovasc Genet
20	DNAJC5	1	Rask-Andersen 2016 Hum Mol Genet
20	E2F1	1	Castillo-Diaz 2014 J Mol Med
20	EFCAB8	1	Rask-Andersen 2016 Hum Mol Genet
20	FKBP1A	1	Zaina 2014 Circ Cardiovasc Genet
20	GATA5	2	Nazarenko 2014 PLoS One
20	GDF5	1	Rask-Andersen 2016 Hum Mol Genet
20	HNF4A	1	Zaina 2014 Circ Cardiovasc Genet
20	HSPC072	1	Rask-Andersen 2016 Hum Mol Genet
20	JAG1	1	Zaina 2014 Circ Cardiovasc Genet
20	LINC0261	1	Rask-Andersen 2016 Hum Mol Genet
20	LOC284749	1	Zaina 2014 Circ Cardiovasc Genet
20	OVL2	1	Rask-Andersen 2016 Hum Mol Genet
20	PLCB1	1	Sharma 2014 Gene
20	PMEPA1	1	Rask-Andersen 2016 Hum Mol Genet
20	RIN2	1	Zaina 2014 Circ Cardiovasc Genet
20	RP11-49G10.8	1	Rask-Andersen 2016 Hum Mol Genet
20	SCL4	1	Zaina 2014 Circ Cardiovasc Genet
20	SLC4	1	Nazarenko 2014 PLoS One
20	SP4T42	2	Zaina 2014 Circ Cardiovasc Genet
20	SRC	1	Rask-Andersen 2016 Hum Mol Genet
20	TCF15	1	Zaina 2014 Circ Cardiovasc Genet
20	TGM3	1	Nazarenko 2014 PLoS One
20	ZNF217	1	Zaina 2014 Circ Cardiovasc Genet
20	ZNXF1	1	Nazarenko 2014 PLoS One
21	ABCG1	1	Zaina 2014 Circ Cardiovasc Genet
21	C21orf29	1	Nazarenko 2014 PLoS One
21	CHAF1B	1	Zaina 2014 Circ Cardiovasc Genet
21	CYRR1	1	Zaina 2014 Circ Cardiovasc Genet
21	DSCR8	1	Rask-Andersen 2016 Hum Mol Genet
21	OLIG2	1	Rask-Andersen 2016 Hum Mol Genet
21	PRMT2	1	Nazarenko 2014 PLoS One
21	RUNX1	1	Castillo-Diaz 2014 J Mol Med
21	S100B	1	Zaina 2014 Circ Cardiovasc Genet
21	SH3BGR	1	Nazarenko 2014 PLoS One
21	UBASH3A	2	Oudejans 2016 PLoS One
22	ABO20652	1	Zaina 2014 Circ Cardiovasc Genet
22	APOL5	1	Nazarenko 2014 PLoS One
22	APOL6	1	Guarrera 2015 Clin Epigenet
22	C22orf23	1	Sharma 2014 Gene
22	C22orf25	1	Guarrera 2015 Clin Epigenet
22	CRELD2	3 (with MIR185)	Yamada 2014 I J Mol Med, Ek 2016 Hum Mol Genet
22	FAM109B	1 (downstream)	Castillo-Diaz 2014 I J Mol Med, Rask-Andersen 2016 Hum Mol Genet
22		2	

22	<i>FBLN1</i>	1	Zaina 2014 <i>Circ Cardiovasc Genet</i>
22	<i>GGT1</i>	6	Zaina 2014 <i>Circ Cardiovasc Genet</i>
22	<i>GNB1L</i>	1	Castillo-Diaz 2014 <i>I J Mol Med</i>
22	<i>LIF</i>	1	Castillo-Diaz 2014 <i>I J Mol Med</i>
22	<i>LOC348645</i>	1	Nazarenko 2014 <i>PLoS One</i>
22	<i>LRP5L</i>	1	Zaina 2014 <i>Circ Cardiovasc Genet</i>
22	<i>MAPK1</i>	1	Gómez-Urte 2015 <i>Human Mol Genet</i>
22	<i>MGC35206</i>	1	Nazarenko 2014 <i>PLoS One</i>
22	<i>MR185</i>	3 (with <i>C2orf25</i> )	Guarrera 2015 <i>Clin Epigenet</i>
22	<i>MLC1</i>	5	Nazarenko 2014 <i>PLoS One</i> , Rask-Andersen 2016 <i>Hum Mol Genet</i> , Zaina 2014 <i>Circ Cardiovasc Genet</i>
22	<i>MN1</i>	1	Zaina 2014 <i>Circ Cardiovasc Genet</i>
22	<i>NF2</i>	1	Zaina 2014 <i>Circ Cardiovasc Genet</i>
22	<i>P2RX6</i>	1	Zaina 2014 <i>Circ Cardiovasc Genet</i>
22	<i>PARVG</i>	2	Zaina 2014 <i>Circ Cardiovasc Genet</i>
22	<i>PISD</i>	1	Zaina 2014 <i>Circ Cardiovasc Genet</i>
22	<i>PLA2G3</i>	1	Nazarenko 2014 <i>PLoS One</i>
22	<i>PLA2G6</i>	1	Zaina 2014 <i>Circ Cardiovasc Genet</i>
22	<i>POLR3H</i>	1	Zaina 2014 <i>Circ Cardiovasc Genet</i>
22	<i>RBM9</i>	1	Zaina 2014 <i>Circ Cardiovasc Genet</i>
22	<i>SERPIND1</i>	1	Nazarenko 2014 <i>PLoS One</i>
22	<i>SMTN</i>	1	Castillo-Diaz 2014 <i>I J Mol Med</i>
22	<i>TEF</i>	1	Zaina 2014 <i>Circ Cardiovasc Genet</i>
22	<i>TTF1L0</i>	1	Zaina 2014 <i>Circ Cardiovasc Genet</i>
22	<i>UBE2L3</i>	1	Zaina 2014 <i>Circ Cardiovasc Genet</i>
22	<i>ZNF280A</i>	1	Zaina 2014 <i>Circ Cardiovasc Genet</i>
22	<i>ZNRF3</i>	1	Zaina 2014 <i>Circ Cardiovasc Genet</i>
X	<i>AR</i>	2 (1 downstream, upstream: <i>EDAR2R</i> )	Nazarenko 2014 <i>PLoS One</i> , Sharma 2014 <i>Gene</i>
X	<i>CHM</i>	1	Nazarenko 2014 <i>PLoS One</i>
X	<i>CTAG1A</i>	1 (upstream and downstream)	Sharma 2014 <i>Gene</i>
X	<i>CXorf21</i>	1	Nazarenko 2014 <i>PLoS One</i>
X	<i>CXorf36</i>	1	Nazarenko 2014 <i>PLoS One</i>
X	<i>DMD</i>	1	Nazarenko 2014 <i>PLoS One</i>
X	<i>EDAR2R</i>	1 (upstream, downstream: <i>AR</i> )	Sharma 2014 <i>Gene</i>
X	<i>GLUD2</i>	1 (upstream, downstream: <i>GRIA3</i> )	Sharma 2014 <i>Gene</i>
X	<i>GPR143</i>	2	Castillo-Diaz 2014 <i>I J Mol Med</i> , Nazarenko 2014 <i>PLoS One</i>
X	<i>GRIA3</i>	1	Sharma 2014 <i>Gene</i>
X	<i>MAGEA9</i>	1	Nazarenko 2014 <i>PLoS One</i>
X	<i>MORF4L2</i>	1 (upstream, downstream: <i>TMEM31</i> )	Nazarenko 2014 <i>PLoS One</i>
X	<i>NOX1</i>	1	Castillo-Diaz 2014 <i>I J Mol Med</i>
X	<i>OTC</i>	1	Nazarenko 2014 <i>PLoS One</i>
X	<i>P2RY10</i>	1	Nazarenko 2014 <i>PLoS One</i>
X	<i>PCDH11X</i>	1	Nazarenko 2014 <i>PLoS One</i>
X	<i>PFC</i>	1	Nazarenko 2014 <i>PLoS One</i>
X	<i>PGRCMC1</i>	1	Nazarenko 2014 <i>PLoS One</i>
X	<i>PNMA6A</i>	1	Nazarenko 2014 <i>PLoS One</i>
X	<i>RGN</i>	2	Oudejans 2016 <i>PLoS One</i>
X	<i>SRPK3</i>	1	Oudejans 2016 <i>PLoS One</i>
X	<i>STAG2</i>	1	Nazarenko 2014 <i>PLoS One</i>
X	<i>TBX22</i>	1	Castillo-Diaz 2014 <i>I J Mol Med</i>
X	<i>TMEM31</i>	1 (downstream, upstream: <i>MORF4L2</i> )	

**Table 6. Differentially methylated genes identified in more than one epigenome-wide association study and associated with coronary heart disease (CHD) or an atherosclerotic related trait in at least one genome-wide association study.**

References	dm-gene(s)	GWAS catalog traits related to CHD
Nazareno 2014 PLoS One Zanna 2014 Circ Cardiovasc Genet Genes Found in Two or More GWAS	MCL1 ESRRG	Type I diabetes mellitus (pediatric autoimmune disease); Cardiac hyper trophy; Fibrogen levels (smoking status, alcohol consumption or body mass index interaction); Mean arterial pressure; Diastolic blood pressure (alcohol consumption interaction); Systolic blood pressure (alcohol consumption interaction); Gut microbiome composition
Zanna 2014 Circ Cardiovasc Genet Casto-Díaz 2014 J Mol Med Zanna 2014 Circ Cardiovasc Genet	CAPZB CLIC4 F0XP1	Type I diabetes mellitus (pediatric autoimmune disease); Protein quantitative trait loci; Quantitative traits; Subcutaneous adipose tissue
Ex 2016 Hum Mol Genet Nazareno 2014 PLoS One Ex 2016 Hum Mol Genet Rask Andersen 2016 Hum Mol Genet	AIM2 NR0B1	Obesity-related traits; Energy intake; Eating disorders; Inflammatory biomarkers; Protein quantitative trait loci; Select biomarker traits; HIV infection (Cardio atherosclerosis, Fat distribution, HDL Cholesterol)
Ex 2016 Hum Mol Genet Zanna 2014 Circ Cardiovasc Genet Guinea 2015 Clin Epigenet Zanna 2014 Circ Cardiovasc Genet	ARHGEP10 CARS CFP273	Coronary artery calcification; Obesity-related traits; Protein quantitative trait loci; Metabolic levels
Nazareno 2014 PLoS One Sharma 2014 Gene	ALX4 WT1	Obesity-related traits; Blood pressure measurement; Diabetic blood pressure; Mean arterial pressure; Biomedical quantitative traits and quantitative traits; HIV infection (Cardio atherosclerosis, Fat distribution, HDL Cholesterol)
Nazareno 2014 PLoS One Zanna 2014 Circ Cardiovasc Genet	AR ABCCL1	Cardiovascular disease risk factors; Life threatening arrhythmia; LDL cholesterol; Lipid traits; Smoking behavior; Metabolic levels; Quantitative traits; Biomedical measures; Response to statin therapy; Response to platelet aggregation inhibitor; AR-Cl24910KX levels in individuals with coronary arteries treated with trazodone
Nazareno 2014 PLoS One Zanna 2014 Circ Cardiovasc Genet	C17orf77 CALD1	Ischemic stroke (ischemic stroke); C-reactive protein levels in ischemic stroke; Creatinine levels in ischemic stroke; UvR infection (Cardio atherosclerosis, Fat distribution, HDL Cholesterol)
Nazareno 2014 PLoS One Zanna 2014 Circ Cardiovasc Genet	DL02 GRIP1	Obesity-related traits; Overweight status; Energy intake; Electrocardiographic conduction measures; Electrocadiographic traits; Phospholipid measurement; Inflammatory biomarkers; Protein quantitative trait loci; Metabolic levels; Select biomarker traits
Nazareno 2014 PLoS One Zanna 2014 Circ Cardiovasc Genet	H0XA3 H0X05 HRV1	Obesity-related traits; Fasting glucose-related traits (interaction with BMI); Visceral adipose tissue adjusted for BMI; waist-Hp ratio; Fibrinogen levels (smoking status, alcohol consumption or body mass index interaction); Fasting insulin-related traits and Quantitative traits; Body mass index and cholesterol (psychopharmacological treatment)
Nazareno 2014 PLoS One Zanna 2014 Circ Cardiovasc Genet	I6R4 DLFRA3	Phospholipid measurement; Electrocadiographic traits; Metabolic levels; IgG glycosylation
Nazareno 2014 PLoS One Zanna 2014 Circ Cardiovasc Genet	PKD2 PNLIPRP1	Obesity-related traits; Type 1 diabetes; Homeostatic levels
Nazareno 2014 PLoS One Zanna 2014 Circ Cardiovasc Genet	SCEL SH2D4B	Cardiovascular disease risk factors; Cardiovascular event reduction in the elderly at risk for vascular disease (statin therapy interaction); Coronary heart disease event reduction in response to statin therapy (interaction); Lipoprotein-associated phospholipase A2
Nazareno 2014 PLoS One Zanna 2014 Circ Cardiovasc Genet	TEAD1 THSD4	Smoking initiation; Amyotrophic lateral sclerosis; Alcohol levels
Oudjhans 2016 PLoS One Rask Andersen 2016 Hum Mol Genet Sharma 2014 Gene	C4orf49 HAN02	Cardiovascular disease risk factors; Obesity-related traits; Lipid traits; Triglycerides (Hypertension); Triglycerides/Blood Pressure/Waist Circumference - Triglycerides); Smoking behavior; Blood pressure (smoking interaction); Cholesterol and Triglycerides; HDL
Rask Andersen 2016 Hum Mol Genet Zanna 2014 Circ Cardiovasc Genet	TNS1	Cardiovascular disease risk factors; Obesity-related traits; Lipid traits; Triglycerides (Hypertension); Triglycerides/Blood Pressure/Waist Circumference - Triglycerides); Smoking behavior; Various thromboembolism; Blood pressure (smoking interaction); Protein quantitative trait loci
Rask Andersen 2016 Hum Mol Genet Zanna 2014 Circ Cardiovasc Genet	ART4 BEN06 DIP2C DOCK1 DYSF FMN1 MECOM MR0204 P0202 PHACTR2 RASGRF1 SRP4 SYTL3	Obesity-related traits; Quantitative traits; Mitral valve prolapse
Rask Andersen 2016 Hum Mol Genet Zanna 2014 Circ Cardiovasc Genet	HMNC1 TBLM	Electrocardiographic traits conduction measures; Electrocardiographic traits; Trypanosoma cruzi seropositivity (Chagas cardiopathy, QRS duration, QT interval, PR interval)
Rask Andersen 2016 Hum Mol Genet Zanna 2014 Circ Cardiovasc Genet	MECOM TBLM	Lean body mass and age at menarche (combined)
Rask Andersen 2016 Hum Mol Genet Zanna 2014 Circ Cardiovasc Genet	DIP2C DOCK1 DYSF FMN1 MECOM TBLM	Cardiovascular disease risk factors; Hematological and biochemical traits; Alzheimer's disease; Biomedical measures; Metabolic levels
Rask Andersen 2016 Hum Mol Genet Zanna 2014 Circ Cardiovasc Genet	HMNC1 TBLM	Obesity-related traits; Diabetes related insulin traits; Glucose homeostasis traits; Metabolic levels
Rask Andersen 2016 Hum Mol Genet Zanna 2014 Circ Cardiovasc Genet	MECOM TBLM	Overweight status; Obesity-related traits; Biomedical measures; Electrocardiographic traits; PR interval; Hematological and biochemical traits; Metabolic levels; Protein quantitative trait loci; Quantitative traits
Rask Andersen 2016 Hum Mol Genet Zanna 2014 Circ Cardiovasc Genet	MR0204 P0202 PHACTR2 RASGRF1 SRP4 SYTL3	Subclinical atherosclerosis (after); Blood pressure (smoking interaction); Smoking behavior; Ankle-brachial index
Rask Andersen 2016 Hum Mol Genet Zanna 2014 Circ Cardiovasc Genet	HMNC1 TBLM	Obesity-related traits; Hematological and biochemical traits; Quantitative traits; Protein quantitative trait loci; Visceral adipose tissue adjusted for BMI; Waist-to-hip ratio adjusted for body mass index
Rask Andersen 2016 Hum Mol Genet Zanna 2014 Circ Cardiovasc Genet	MECOM TBLM	Obesity-related traits; Insulin-like growth factors; Electroneurographologic traits in alcoholics; Alzheimer's disease
Sharma 2014 Gene Zanna 2014 Circ Cardiovasc Genet	CTNNB1 DSGAML1 PNK002 TGFRB3	Cardiovascular disease risk factors; Select biomarker traits; Hematological and biochemical traits; Protein quantitative trait loci; Metabolic levels
Yamada 2014 J Mol Med Zanna 2014 Circ Cardiovasc Genet	ARD12 CAMTA1 SEPT9	Alzheimer's disease; (Protein (a) - cholesterol) levels; Lipoprotein (a) levels; Ven graft stenosis in coronary artery bypass grafting; Calcium levels; Postoperative atrial fibrillation in coronary artery bypass surgery; Acute kidney injury in coronary artery bypass surgery (creatinine rise); Perioperative myocardial infarction in coronary artery bypass surgery
Yamada 2014 J Mol Med Zanna 2014 Circ Cardiovasc Genet	ARD12 CAMTA1 SEPT9	Obesity-related traits; Biomedical quantitative traits and Quantitative traits; Fibrinogen levels (smoking status, alcohol consumption or body mass index interaction); Body mass index and cholesterol (psychopharmacological treatment); Waist-to-hip ratio adjusted for body mass index and cholesterol (psychopharmacological treatment); Fibrinogen levels (smoking status, alcohol consumption or body mass index interaction); Body mass index

**Reported traits and the different mapped experimental factor ontology traits they encompass**

Mapped ontology traits of general reported traits
Cardiovascular disease risk factors
Biochemical measures
Hematological and biochemical traits
Protein quantification
Select biomarker traits
Obesity-related traits
Biomedical quantitative traits and quantitative traits