Table S1: Clinical variables

Number	Variable	Description
1	Age	-
2	Gender	-
3	Systolic BP (mmHg)	Maximum arterial pressure during contraction of the left ventricle of the heart.
4	Diastolic BP (mmHg)	Minimum arterial pressure when the ventricles of the heart fill with blood.
5	BMI (kg/m^2)	A person's weight in kilograms divided by the square of height in meters.
6	Fasting Blood Glucose (mg/dL)	Level of glucose in the blood after an overnight fast.
7	Total Cholesterol (mg/dL)	Calculated as LDL+HDL+Triglycerides/5, used to assess heart disease risk.
8	Triglycerides (mg/dL)	Lipids that are used to store energy and give energy to muscles.
9	HDL Cholesterol	Moves excess cholesterol from the cells to the liver.
10	LDL Cholesterol	Transports lipids around the body within the water outside cells.
11	Fibrinogen	A coagulation factor that is essential for blood clot formation.

Except age and gender, all clinical variables are used for predicting coronary calcium within random forest models in conjunction with SNP predictors.

Table S2: General statistics of clinical variables among controls and case subjects $(89^{th}-99^{th} CAC \text{ score percentile})$ in the ClinSeq® cohort

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Number	Variable	p-value	Cases	Cases	Controls	Controls
			mean	SD	mean	SD
1	Age	0.82	58.25	4.70	57.88	4.33
2	Gender	-	All males	-	All males	-
3	Systolic BP (mmHg)	0.51	129.91	10.45	126.97	14.18
4	Diastolic BP (mmHg)	0.70	78.06	7.04	76.91	9.33
5	BMI (kg/m^2)	0.09	28.74	5.03	26.17	2.79
6	Fasting Blood Glucose (mg/dL)	0.07	106.44	16.74	97.69	8.34
7	Total Cholesterol (mg/dL)	0.78	190.75	49.02	186.75	30.88
8	Triglycerides (mg/dL)	0.17	127.13	62.69	98.75	49.77
9	HDL Cholesterol (mg/dL)	0.11	49.38	11.59	56.00	11.44
10	LDL Cholesterol (mg/dL)	0.74	115.63	38.28	111.44	30.88
11	Fibrinogen (mg/dL)	0.37	312.38	33.28	299.63	45.61

Mean and standard deviation (SD) values of the clinical variables in the ClinSeq® cohort. Per variable, a p-value is computed using a two-sample t-test (with univariate criterion) by testing the null hypothesis that the case and control vectors are from populations with equal means without making the assumption that the two populations have equal variance values for any predictor.

Table S3: General statistics of clinical variables among controls and case subjects $(89^{th}-99^{th}$ CAC score percentile) in the FHS cohort

Number	Variable	p-value	Cases	Cases	Controls	Controls
		P	mean	SD	mean	SD
1	Age	0.58	51.28	5.57	50.53	5.98
2	Gender	-	All males	-	All males	-
3	Systolic BP (mmHg)	0.10	125.86	17.07	120.00	12.03
4	Diastolic BP (mmHg)	0.72	78.56	10.32	77.81	6.67
5	BMI (kg/m^2)	0.21	28.41	4.44	27.23	3.38
6	Fasting Blood Glucose (mg/dL)	0.07	102.25	10.78	98.06	8.39
7	Total Cholesterol (mg/dL)	0.97	194.22	36.50	193.89	31.34
8	Triglycerides (mg/dL)	0.65	130.33	72.43	122.89	64.47
9	HDL Cholesterol (mg/dL)	0.86	46.78	13.05	46.25	12.76
10	LDL Cholesterol (mg/dL)	0.81	121.38	32.00	123.06	28.43
11	Fibrinogen (mg/dL)	0.09	361.86	97.01	329.33	58.59

Mean and standard deviation (SD) values of the clinical variables in the FHS cohort. Per variable, a p-value is computed using a two-sample t-test (with univariate criterion) by testing the null hypothesis that the case and control vectors are from populations with equal means without making the assumption that the two populations have equal variance values for any predictor.

Number	SNP	Locus	p-value	GWAS	Number	SNP	Locus	p-value	GWAS
1	rs4456611	BCL2	4.1E-4	[1]	37	rs34014631	C10 orf 76	4.3E-6	[2]
2	rs3789422	ABCA4	8.5E-5	[1]	38	rs11777747	FLJ43860	7.9E-6	[2]
3	rs13386681	ATOH8	1.6e-4	[1]	39	rs9506514	IFT88 [*]	4.9E-6	[2]
4	rs10499276	OPRM1 *	6.9E-5	[1]	40	rs7070038	IPMK [*]	6.6E-6	[2]
5	rs13260	COL4A1	8.7E-5	[1]	41	rs7765175	MARCKS *	4.7E-6	[2]
6	rs6667260	ITPKB	8.0E-5	[1]	42	rs10502575	MCART2 *	1.5e-7	[2]
7	rs3768991	NPAS2	3.7e-4	[1]	43	rs10803016	PLD5	7.4E-6	[2]
8	rs17056112	ADRA1A	3.3e-4	[1]	44	rs16976171	RIT2 *	3.6E-6	[2]
9	rs4977574	CDKN2B-AS1	9.0e-5	[1]	45	rs7856675	SLC1A1	8.3E-6	[2]
10	rs2891168	CDKN2B-AS1	1.7e-4	[1]	46	rs9907236	SOX9 *	1.7E-6	[2]
11	rs10757274	CDKN2B-AS1	2.2e-4	[1]	47	rs2622633	ZFPM2	6.5E-6	[2]
12	rs10757272	CDKN2B-AS1	3.5e-4	[1]	48	rs1537370	CDKN2B-AS1	2.3E-11	[3]
13	rs2834669	RUNX1	3.9e-4	[1]	49	rs9349379	PHACTR1	2.7e-11	[4]
14	rs10483853	NUMB	6.1E-6	[5]	50	rs163189	PRDM6	7.5E-3	[4]
15	rs10519394	PCDH18 [*]	1.1E-5	[5]	51	rs599839	PSRC1	3.9E-3	[4]
16	rs9321354	TAAR5 [*]	3.4 E-5	[5]	52	rs646776	CELSR2	7.9E-12	[4]
17	rs220457	C17orf79 *	3.8e-4	[5]	53	rs2259816	HNF1A	4.8E-7	[4]
18	rs722208	ESR1	5.0e-3	[5]	54	rs3184504	SH2B3	8.6E-8	[4]
19	rs1365057	CD44 *	7.7E-3	[5]	55	rs9818870	MRAS	7.4E-13	[4]
20	rs1467558	CD44	2.0E-2	[5]	56	rs11206510	PCSK9	9.6E-9	[4]
21	rs2190305	CREB5	1.2E-6	[6]	57	rs12146493	DKFZp761E198	7.4E-3	[4]
22	rs9574536	SPRY2 *	2.4E-6	[6]					
23	rs7158225	FLRT2*	5.3e-6	[6]					
24	rs17819063	FTO	4.2e-5	[6]					
25	rs432695	CDYL *	2.3e-7	[6]					
26	rs4867326	CDH6 *	4.7e-7	[6]					
27	rs622348	MIR759 *	3.8e-6	[6]					
28	rs16872734	GPR125	7.0E-6	[6]					
29	rs2727551	PRKAG2	5.2e-5	[6]					
30	rs10096362	CDH17 [*]	2.2e-6	[6]					
31	rs9843942	TGFBR2	3.0e-6	[6]					
32	rs1679195	LPP	$3.4 \text{E}{-5}$	[6]					
33	rs2618157	THBS1 *	$5.3 \text{E}{-5}$	[6]					
34	rs6032769	<i>SLC35C2</i> *	1.3e-5	[6]					
35	rs1062087	TBC1D4	4.2e-7	[6]					
36	rs3758014	ARHGEF10	7.8E-5	[6]					

Table S4: List of SNPs associated with CAC in past GWAS and meta-analyses (SNP Set 1)

Genotypes of these SNPs (previously associated with CAC) are used for predicting the binary CAC state among the ClinSeq® subjects. Nearest genes are listed for intergenic SNPs (marked with asterisk).

Number	SNP	Locus	Number	SNP	Locus
1	rs243170	FOXN3	37	rs8107904	$EMR2^*$
2	rs243172	FOXN3	38	rs9290557	NAALADL2
3	rs328395	LOC100506172 [*]	39	rs9804449	$FGF3^*$
4	rs342393	NRG3	40	rs9967032	DOK6
5	rs480220	NRG3	41	rs10036954	C5 or f34
6	rs514237	NRG3	42	rs10054519	C5 or f28
7	rs571797	NRG3	43	rs10059993	NNT-AS1
8	rs750582	$C5 or f28^*$	44	rs10065689	NNT
9	rs1130329	RBAK-LOC389458	45	rs10079672	AFAP1L1
10	rs1288331	$SLC1A7^*$	46	rs10458221	$EEF1E1$ - $BLOC1S5^*$
11	rs1366410	NNT	47	rs11131194	RPUSD3
12	rs1389401	$ASB7^*$	48	rs11575624	HABP2
13	rs1505279	$C15 or f54^*$	49	rs11575634	HABP2
14	rs1887413	TTL^*	50	rs11674863	LOC101927701
15	rs2217855	FBX08 [*]	51	rs11767632	YAE1D1 [*]
16	rs2241097	TLR5	52	rs12521249	PAIP1 [*]
17	rs2390285	MACC1	53	rs12645809	ANTXR2
18	rs4255867	DOK6	54	rs13159307	FBXL17 [*]
19	rs4410460	KCNH8 [*]	55	rs13220973	$LOC401324^{*}$
20	rs4491835	SCN11A*	56	rs13429160	LOC101927701
21	rs4622486	$C15 or f54^*$			
22	rs4632970	AGK			
23	rs4676660	$WDR48^*$			
24	rs4793853	MSI2			
25	rs6014727	CASS4			
26	rs6024879	CASS4			
27	rs6069753	CASS4			
28	rs6451696	C5 or f28			
29	rs6565484	RPTOR			
30	rs6849832	$DDIT4L^*$			
31	rs6860493	NNT			
32	rs7176702	MEGF11			
33	rs7225157	DNAH9			
34	rs7501899	$C17 or f54^*$			
35	rs7531219	$PPP2R5A^*$			
36	rs7713479	NNT-AS1			

Table S5: List of highly predictive SNPs not previously associated with coronary calcium in past GWAS and meta-analyses (SNP Set 2)

Nearest genes are listed for intergenic SNPs (marked with a sterisk $\ensuremath{^*}\xspace).$ Table S6: The network of genes derived by GeneMANIA from a database of 244 studies in humans. The loci of the 21 predictive SNPs are used as the input gene set for network construction. Gene symbols and names are based on the information from the HUGO Gene Nomenclature Committee (HGNC).

Number	Gene symbol	Gene name
1	MACC1	Metastasis Associated In Colon Cancer 1
2	NRG3	Neuregulin 3
3	ANTXR2	Anthrax Toxin Receptor 2
4	FBXL17	F-Box And Leucine-Rich Repeat Protein 17
5	YAE1D1	Yae1 Domain Containing 1
6	PAIP1	Poly(A) Binding Protein Interacting Protein 1
7	FOXN3	Forkhead Box N3
8	C5 or f28	Chromosome 5 Open Reading Frame 28
9	EMR2 (ADGRE2)	EGF-like module-containing mucin-like hormone receptor-like 2
		(Adhesion G Protein-Coupled Receptor E2)
10	TLR5	Toll Like Receptor 5
11	NNT	Nicotinamide Nucleotide Transhydrogenase
12	WDR70	WD repeat domain 70
13	FASTKD3	FAST Kinase Domains 3
14	AIMP1	Aminoacyl TRNA Synthetase Complex-Interacting Multifunctional Protein 1
15	EGLN1	Egl-9 Family Hypoxia Inducible Factor 1
16	C5 or f22	Chromosome 5 Open Reading Frame 22
17	MICU2	Mitochondrial Calcium Uptake 2
18	NIPBL	NIPBL, Cohesin Loading Factor
19	N6AMT1	N-6 adenine-specific DNA methyltransferase 1
20	MARCH6	Membrane Associated Ring-CH-Type Finger 6
21	ZNF131	Zinc Finger Protein 131
22	SRP72	Signal Recognition Particle 72kDa
23	ARID5B	AT-Rich Interaction Domain 5B
24	CEP72	Centrosomal Protein 72
25	TIPRL	TOR Signaling Pathway Regulator
26	FAM172A	Family With Sequence Similarity 172 Member A
27	EMC2	ER Membrane Protein Complex Subunit 2
28	EDEM1	ER Degradation Enhancing Alpha-Mannosidase Like Protein 1
29	CYB5R4	Cytochrome B5 Reductase 4
30	RETN	Resistin
31	FUT3	Fucosyltransferase 3 (Lewis Blood Group)

Network of genes derived from GeneMANIA based on 244 studies in humans.

Table S7: Enriched diseases and biological functions in the gene network relevant to cardiovascular disease with p-values ranging between 1.0E-2 and 5.0E-2 (statistically less significant than the diseases and biological functions listed in Table 4) as identified by IPA based on Fisher's exact test.

Category	Disease or Function	Genes
Cardiovascular System Development and Function	Abnormal morphology of dilated vasculature	ANTXR2
Lipid Metabolism	Recognition of lipid	TLR5
Connective Tissue Development and Function	Morphology of adipocytes	ARID5B, RETN
Endocrine System Development and Function	Insulin sensitivity	CYB5R4, RETN
Cell Signaling	Handling of Ca^{2+}	MICU2
Organismal Injury and Abnormalities	Infection of kidney	TLR5
Metabolic Disease	Susceptibility to type 2 diabetes mellitus	RETN
Hematological System Development and Function	Decreased hematocrit of organism	EGLN1
Respiratory System Development and Function	Respiratory minute volume	EGLN1
Cardiovascular System Development and Function	Morphogenesis of heart	EGLN1, NIPBL
Protein Synthesis	Quantity of hemoglobin in blood	EGLN1
Tissue Morphology	Morphology of connective tissue	ARID5B, CYB5R4 RETN_TLR5
Cellular Movement	Migration of fibroblasts	AIMP1, ARID5B
Cardiovascular System Development and Function	Contractility of ventricular myocytes	TLR5
Cellular Compromise, Hepatic System Disease	Oxidative stress response of hepatocytes	CYB5R4
Cell-To-Cell Signaling and Interaction	Activation of kidney cell lines	TLR5
Cellular Assembly and Organization, Inflammatory Response	Formation of neutrophil extracellular trap	RETN
Cardiovascular System Development and Function	Functional recovery of heart	EGLN1
Free Radical Scavenging	Metabolism of superoxide	CYB5R4
Endocrine System Development and Function	Quantity of insulin in blood	CYB5R4, TLR5
Cell Morphology, Cellular Function and Maintenance	Autophagy of cytoplasm	TLR5
Carbohydrate Metabolism	Synthesis of oligosaccharide	FUT3
Cell Death and Survival	Apoptosis of peripheral blood lymphocytes	AIMP1
Metabolic Disease	Hypoinsulinemia	CYB5R4
Cell-To-Cell Signaling and Interaction	Activation of smooth muscle cells	RETN
Cardiovascular Disease, Organismal Injury and Abnormalities	Dysfunction of endothelial tissue	RETN
Metabolic Disease	Insulin-dependent diabetes mellitus	NRG3, RETN, TLR5
Endocrine System Disorders, Metabolic Disease	Insulin resistance of liver	RETN
Protein Synthesis	Quantity of protein in blood	CYB5R4, EGLN1, TLR5
Cardiovascular System Development and Function	Morphogenesis of ventricular septum	EGLN1
Cell Morphology, Cellular Assembly and Organization	Size of mitochondria	CYB5R4
Connective Tissue Development and Function	Mass of adipose tissue	CYB5R4, TLR5
Connective Tissue Development and Function	Differentiation of fibroblast cell lines	EGLN1, RETN
Molecular Transport, Nucleic Acid Metabolism	Quantity of NADPH	NNT
Cellular Assembly and Organization	Activation of mitochondria	RETN
Immune Cell Trafficking, Inflammatory Response	Cellular infiltration by monocytes	RETN
Cellular Compromise	Stress response of cells	CYB5R4, RETN
Connective Tissue Development and Function	Abnormal morphology of adipocytes	ARID5B
Cardiovascular System Development and Function	Density of capillary vessel	EGLN1
Carbohydrate Metabolism	Disposal of D-glucose	RETN
		Continued on next page

Category	Disease or Function	Genes
Hematological System Development and Function	Hematocrit of blood	EGLN1
Immune Cell Trafficking, Inflammatory Response	Cellular infiltration by macrophages	EGLN1, RETN
Cardiovascular System Development and Function	Abnormal morphology of trabeculae carne	EGLN1
Nutritional Disease	Obesity	ARID5B, RETN, TLR5
Hematological System Development and Function	Cell viability of neutrophils	ADGRE2
Cell-mediated Immune Response	Development of Th17 cells	TLR5
Hematological Disease, Immunological Disease	Growth of lymphoma	AIMP1
Cardiovascular System Development and Function	Morphogenesis of cardiac muscle	EGLN1
Connective Tissue Development and Function	Function of adipose tissue	TLR5
Protein Synthesis	Production of cytokine	TLR5
Cardiovascular System Development and Function	QT interval of heart	NRG3

Table S7 – Continued from previous page

ve n	st the source of	of the interact	ions (ne	etwork	s prev	lously publish	lea) under "Ro	er .						
#	Gene 1	Gene 2	INT	Ref	#	Gene 1	Gene 2	INT	Ref	#	Gene 1	Gene 2	INT	Ref
1	C5orf28	PAIP1	CE	[7]	48	C5orf22	C5orf28	CE	[8]	95	AIMP1	NNT	CE	[9]
2	WDR70	PAIP1	CE	[7]	49	C5orf22	NNT	CE	[8]	96	C5orf22	PAIP1	CE	[9]
3	WDR70	C5orf28	CE	[7]	50	C5orf22	WDR70	CE	[8]	97	MARCH6	NNT	CE	[9]
4	FASTKD3	PAIP1	CE	[7]	51	C5orf22	FASTKD3	CE	[8]	98	ZNF131	NNT	CE	[9]
5	FASTKD3	C5orf28	CE	[7]	52	MICU2	PAIP1	CE	[8]	99	SRP72	MICU2	CE	[9]
6	FASTKD3	WDR70	CE	[7]	53	MICU2	C5orf28	CE	[8]	100	TIPRL	TLR5	CE	[9]
7	AIMP1	C5orf28	CE	[7]	54	MICU2	AIMP1	CE	[8]	101	EMC2	AIMP1	CE	[9]
8	EGLN1	FOXN3	CE	[7]	55	NIPBL	C5orf28	CE	[8]	102	C5orf28	PAIP1	CE	[10]
9	C5orf22	NNT	CE	[7]	56	NIPBL	C5orf22	CE	[8]	103	C5orf22	NNT	CE	[10]
10	MICU2	PAIP1	CE	[7]	57	N6AMT1	C5orf28	CE	[8]	104	C5orf22	FASTKD3	CE	[10]
11	NIPBL	NNT	CE	[7]	58	N6AMT1	FASTKD3	CE	[8]	105	MICU2	FBXL17	CE	[10]
12	NIPBL	C5orf22	CE	[7]	59	MARCH6	C5orf22	CE	[8]	106	MICU2	PAIP1	CE	[10]
13	N6AMT1	C5orf28	CE	[7]	60	MARCH6	NIPBL	CE	[8]	107	ZNF131	C5orf28	CE	[10]
14	MARCH6	C5orf28	CE	[7]	61	ZNF131	WDR70	CE	[8]	108	EDEM1	ARID5B	CE	[10]
15	MARCH6	FASTKD3	CE	[7]	62	ZNF131	FASTKD3	CE	[8]	109	FBXL17	ANTXR2	GI	[11]
16	MARCH6	C5 or f 22	CE	[7]	63	ZNF131	C5 or f 22	CE	[8]	110	YAE1D1	ANTXR2	GI	[11]
17	MARCH6	NIPBL	CE	[7]	64	ARID5B	FOXN3	CE	[8]	111	PAIP1	YAE1D1	GI	[11]
18	ZNF131	PAIP1	CE	[7]	65	CEP72	FASTKD3	CE	[8]	112	FOXN3	FBXL17	GI	[11]
19	ZNF131	WDR70	CE	[7]	66	FAM172A	C5orf28	CE	[8]	113	NNT	ANTXR2	GI	[11]
20	ZNF131	FASTKD3	CE	[7]	67	FAM172A	MARCH6	CE	[8]	114	NNT	FOXN3	GI	[11]
21	ZNF131	C5orf22	CE	[7]	68	EMC2	PAIP1	CE	[8]	115	WDR70	EMR2	GI	[11]
22	ZNF131	MICU2	CE	[7]	69	EDEM1	NNT	CE	[8]	116	AIMP1	MACC1	GI	[11]
23	ZNF131	NIPBL	CE	[7]	70	C5orf28	YAE1D1	CE	[12]	117	AIMP1	YAE1D1	GI	[11]
24	ZNF131	MARCH6	CE	[7]	71	FASTKD3	YAE1D1	CE	[12]	118	AIMP1	PAIP1	GI	[11]
25	SRP72	C5orf28	CE	[7]	72	AIMP1	YAE1D1	CE	[12]	119	EGLN1	FOXN3	GI	[11]
26	SRP72	AIMP1	CE	[7]	73	AIMP1	C5orf28	CE	[12]	120	C5orf22	FOXN3	GI	[11]
27	ARID5B	FOXN3	CE	[7]	74	MICU2	WDR70	CE	[12]	121	MICU2	ANTXR2	GI	[11]
28	CEP72	PAIP1	CE	[7]	75	TIPRL	SRP72	CE	[12]	122	MICU2	FOXN3	GI	[11]
29	CEP72	C5orf28	CE	[7]	76	FAM172A	WDR70	CE	[12]	123	NIPBL	ANTXR2	GI	[11]
30	TIPRL	C5orf28	CE	[7]	77	EMC2	YAE1D1	CE	[12]	124	NIPBL	EMR2	GI	[11]
31	TIPRL	FASTKD3	CE	[7]	78	EMC2	C5orf28	CE	[12]	125	N6AMT1	FBXL17	GI	[11]
32	TIPRL	ZNF131	CE	[7]	79	EMC2	FASTKD3	CE	[12]	126	N6AMT1	FOXN3	GI	[11]
33	FAM172A	FOXN3	CE	[7]	80	CYB5R4	MICU2	CE	[12]	127	MARCH6	FBXL17	GI	[11]
34	EMC2	C5orf28	CE	[7]	81	RETN	EMR2	CE	[12]	128	MARCH6	YAE1D1	GI	[11]
35	EMC2	AIMP1	CE	[7]	82	FUT3	MACC1	CE	[12]	129	SRP72	PAIP1	GI	[11]
36	EMC2	SRP72	CE	[7]	83	NNT	PAIP1	CE	[13]	130	SRP72	FOXN3	GI	[11]
37	EDEM1	EMR2	CE	[7]	84	NIPBL	FOXN3	CE	[13]	131	SRP72	NIPBL	GI	[11]
38	CYB5R4	PAIP1	CE	[7]	85	NIPBL	NNT	CE	[13]	132	FAM172A	MICU2	GI	[11]
39	RETN	TLR5	CE	[7]	86	MARCH6	PAIP1	CE	[13]	133	EMC2	YAE1D1	GI	[11]
40	FUT3	TLR5	CE	[7]	87	MARCH6	NIPBL	CE	[13]	134	EMC2	AIMP1	GI	[11]
41	C5orf28	PAIP1	CE	[8]	88	SRP72	FOXN3	CE	[13]	135	EDEM1	FBXL17	GI	[11]
42	WDR70	C5orf28	CE	[8]	89	TIPRL	NNT	CE	[13]	136	EDEM1	C5orf28	GI	[11]
43	WDR70	NNT	CE	[8]	90	FAM172A	NNT	CE	[13]	137	EDEM1	MARCH6	GI	[11]
44	FASTKD3	PAIP1	CE	[8]	91	FAM172A	NIPBL	CE	[13]	138	CYB5B4	FBXL17	GI	[11]
45	FASTKD3	C5orf28	CE	[8]	92	FAM172A	MARCH6	CE	[13]	139	CYB5R4	FOXN3	GI	[11]
46	EGLN1	NNT	CE	[8]	93	NNT	PAIP1	CE	[9]	140	CYB5R4	NNT	GI	[11]
47	C5orf22	PAIP1	CE	[8]	94	AIMP1	PAIP1	CE	[9]	141	RETN	C5orf28	GI	[11]
-1	0001122		<u>с</u> ц	[9]	01			<u>_</u>	[9]	149	FUT3	AIMP1	GI	[11]
													<u></u>	1 * * 1

Table S8: Interactions within the advanced coronary calcium network generated by GeneMANIA (network shown in Figure 6). The nature of interactions (INT) between gene pairs are based either on co-expression (CE) or genetic interactions (GI). We list the source of the interactions (networks previously published) under "Ref".

References

- Ferguson, J.F., Matthews, G.J., Townsend, R.R., Raj, D.S., Kanetsky, P.A., Budoff, M., Fischer, M.J., Rosas, S.E., Kanthety, R., Rahman, M., *et al.*: Candidate gene association study of coronary artery calcification in chronic kidney disease: findings from the CRIC study (Chronic Renal Insufficiency Cohort). Journal of the American College of Cardiology **62**(9), 789–798 (2013)
- Wojczynski, M.K., Li, M., Bielak, L.F., Kerr, K.F., Reiner, A.P., Wong, N.D., Yanek, L.R., Qu, L., White, C.C., Lange, L.A., *et al.*: Genetics of coronary artery calcification among African Americans, a meta-analysis. BMC medical genetics 14(1), 75 (2013)
- van Setten, J., Isgum, I., Smolonska, J., Ripke, S., de Jong, P.A., Oudkerk, M., de Koning, H., Lammers, J.-W.J., Zanen, P., Groen, H.J., *et al.*: Genome-wide association study of coronary and aortic calcification implicates risk loci for coronary artery disease and myocardial infarction. Atherosclerosis 228(2), 400–405 (2013)
- 4. O'Donnell, C.J., Kavousi, M., Smith, A.V., Kardia, S.L., Feitosa, M.F., Hwang, S.-J., Sun, Y.V., Province, M.A., Aspelund, T., Dehghan, A., *et al.*: Genome-wide association study for coronary artery calcification with follow-up in myocardial infarction. Circulation **124**(25), 2855–2864 (2011)
- O'Donnell, C.J., Cupples, L.A., D'Agostino, R.B., Fox, C.S., Hoffmann, U., Hwang, S.-J., Ingellson, E., Liu, C., Murabito, J.M., Polak, J.F., *et al.*: Genome-wide association study for subclinical atherosclerosis in major arterial territories in the NHLBI's Framingham Heart Study. BMC medical genetics 8(Suppl 1), 4 (2007)
- Polfus, L.M., Smith, J.A., Shimmin, L.C., Bielak, L.F., Morrison, A.C., Kardia, S.L., Peyser, P.A., Hixson, J.E.: Genome-wide association study of gene by smoking interactions in coronary artery calcification. PloS one 8(10), 74642 (2013)
- Gysin, S., Paquette, J., McMahon, M.: Analysis of mrna profiles after mek1/2 inhibition in human pancreatic cancer cell lines reveals pathways involved in drug sensitivity. Molecular Cancer Research 10(12), 1607–1619 (2012)
- Salaverria, I., Philipp, C., Oschlies, I., Kohler, C.W., Kreuz, M., Szczepanowski, M., Burkhardt, B., Trautmann, H., Gesk, S., Andrusiewicz, M., et al.: Translocations activating irf4 identify a subtype

of germinal center-derived b-cell lymphoma affecting predominantly children and young adults. Blood **118**(1), 139–147 (2011)

- Bild, A.H., Yao, G., Chang, J.T., Wang, Q., Potti, A., Chasse, D., Joshi, M.-B., Harpole, D., Lancaster, J.M., Berchuck, A., *et al.*: Oncogenic pathway signatures in human cancers as a guide to targeted therapies. Nature **439**(7074), 353–357 (2006)
- Bahr, T.M., Hughes, G.J., Armstrong, M., Reisdorph, R., Coldren, C.D., Edwards, M.G., Schnell, C., Kedl, R., LaFlamme, D.J., Reisdorph, N., *et al.*: Peripheral blood mononuclear cell gene expression in chronic obstructive pulmonary disease. American journal of respiratory cell and molecular biology 49(2), 316–323 (2013)
- 11. Lin, A., Wang, R.T., Ahn, S., Park, C.C., Smith, D.J.: A genome-wide map of human genetic interactions inferred from radiation hybrid genotypes. Genome research **20**(8), 1122–1132 (2010)
- Innocenti, F., Cooper, G.M., Stanaway, I.B., Gamazon, E.R., Smith, J.D., Mirkov, S., Ramirez, J., Liu, W., Lin, Y.S., Moloney, C., *et al.*: Identification, replication, and functional fine-mapping of expression quantitative trait loci in primary human liver tissue. PLoS Genet 7(5), 1002078 (2011)
- Wang, Q., Diskin, S., Rappaport, E., Attiyeh, E., Mosse, Y., Shue, D., Seiser, E., Jagannathan, J., Shusterman, S., Bansal, M., *et al.*: Integrative genomics identifies distinct molecular classes of neuroblastoma and shows that multiple genes are targeted by regional alterations in dna copy number. Cancer research 66(12), 6050–6062 (2006)