Supplementary Information

Genome wide association study identifies sequence variant within the DAB2IP gene conferring susceptibility to abdominal aortic aneurysm

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Supplementary Note

Study Populations

All studies were approved by relevant institutional review boards or ethics committees, and all participants provided written informed consent.

AAA discovery samples

Iceland: Icelandic individuals with AAA (defined as diameter of infarenal aorta of ≥ 30 mm) were recruited from a registry of individuals who were admitted at Landspitali University Hospital, in Reykjavik, Iceland, 1980 – 2006. AAA patients were either followed up or treated by intervention for emergency repair of symptomatic or ruptured AAA or for an elective repair by surgery or endovascular intervention. Subjects with AAA were enrolled as part of the CVD genetics program at deCODE. The 27,712 Icelandic controls used in the AAA GWAS were selected from among individuals who have participated in various GWA studies and who were recruited as part of genetic programs at deCODE. Individuals with known cardiovascular disease were excluded as controls.

Utrecht, The Netherlands: The AAA sample set from Utrecht was recruited in 2007-2009 from eight centres in The Netherland, mainly when individuals visited their vascular surgeon in the polyclinic or, in rare cases, during hospital admission for elective or emergency AAA surgery. An AAA was defined as an infrarenal aorta ≥ 30 mm. The sample set comprised 89.9% males, with a mean AAA diameter of 58.4 mm, 61.7% had received surgery, of which 8.1 % was after rupture. The Dutch controls used in the AAA GWAS were recruited as part of the Nijmegen Biomedical Study and the Nijmegen Bladder Cancer Study (see http://dceg.cancer.gov/icbc/membership.html). The details of these studies were reported previously [1,2].

AAA follow up samples

New Zealand: Individuals from New Zealand with AAA were recruited from the Otago-Southland region of the country, the vast majority (>97%) being of Anglo-European ancestry as reported previously [3]. Approximately 80% of these individuals had undergone surgical AAA repair (typically AAA's > 50 mm in diameter). The control group consisted of elderly individuals with no previous history of vascular disease from the same geographical region. An abdominal ultrasound scan excluded concurrent abdominal aortic aneurysm from the control group and Anglo-European ancestry was required for inclusion. Controls were also asymptomatic for PAD and had ankle brachial indexes >1.

United Kingdom: UK individuals with AAA referred to vascular surgeons at 93 UK hospitals were entered into the UK Small Aneurysm Trial. For the purpose of the current study, those individuals randomized to surveillance in the UK Small Aneurysm Trial with AAA diameter 40–55 mm were selected as a case group, although some cases had been monitored before their aneurysm reached the 40-mm threshold for the trial. Mean AAA

diameter at baseline was 45 mm (32-55 mm) [4]. Controls were of European descent, recruited from England [5].

Belgium and Canada: These sample-sets include individuals with AAA who were admitted either for emergency repair of ruptured AAA or for an elective surgery to the University Hospital of Liege (Liege, Belgium) and to Dalhousie University Hospital (Halifax, Canada). AAA was defined as an infrarenal aortic diameter of 30 mm or greater. Details of these case-control sets have been previously reported [6]. All individuals were of European descent. Approximately 40% of individuals with AAA had a family history of AAA. Control samples (51% males) of European descent were obtained from spouses of individuals with AAA or from individuals admitted to the same hospitals for reasons other than AAA.

Nijmegen, The Netherlands: Individuals with AAA were recruited through a primary screening program of men aged 60-80 years. Three neighbouring districts in the east of Netherlands were selected for the AAA screening study. A diagnosis of AAA was established when an aortic diameter of 30 mm was measured. Individuals with an aortic diameter of 50 mm (app. 20% of all cases) were referred to a regional hospital for elective aneurysm repair. The control group was derived from the same screening program. For each case at least one age-match control was selected.

Pittsburgh, Pennsylvania, US: Patients admitted to the University Hospital of Pittsburgh for either elective or emergency surgery for AAA were selected for the study [7]. The cases consisted of individuals of European origin entering Presbyterian University Hospital (PUH) in Pittsburgh for aneurysm resection from 1986 to 1991. Mean aneurysm diameter was 58.6 ±15.7 mm. Controls were selected from participants of the cardiac catheterization study program at the University of Pennsylvania Medical Center in Philadelphia (PENN CATH). The control group represents individuals who did not have significant luminal stenosis on coronary angiography (luminal stenosis >50%) or a history of myocardial infarction.

Danville, Pennsylvania, US: AAA patients were enrolled through the Geisinger Clinic Department of Vascular Surgery at Geisinger Medical Center, Danville, PA[8]. AAA cases were defined as infrarenal aortic diameter ≥ 30 mm as revealed by abdominal imaging. An unselected control group was obtained through the Geisinger MyCode Project, a cohort of Geisinger Clinic primary care patients recruited for genomic studies. The MyCode controls were matched for age distribution and gender to the Geisinger Vascular Clinic AAA cases.

Denmark: The Danish AAA-samples were recruited from two population-based screening programmes for 65-74 year old men in 1994-1998 [9] and 2008-2009 (Clinical trials: NCT00662480). In both cohorts, an AAA was defined as an infrarenal aorta ≥ 30 mm - in average 40.5 mm, and 12% were above 50 mm at diagnosis. None were ruptured, and the mean age was 68.2 years. The Danish controls come from the randomised population-based intervention study (Inter99) which has been described in details elsewhere [10].

Peripheral arterial disease samples

Iceland: Patients were recruited through a registry of individuals diagnosed with PAD during the year 1998-2006, at the Landspitali University Hospital (Reykjavik, Iceland). The PAD diagnosis was confirmed by vascular imaging or segmental pressure measurements. Subjects with PAD were enrolled over a nine year period as part of the CVD genetics program at deCODE. A new set of 5,863 Icelandic population controls without history of vascular diseases and not overlapping with the set of 27,712 controls used in the GWA study, were genotyped for the risk variant and used in the association tests of PAD. These individuals were selected among individuals that had participated in various genetic programs at deCode genetics and that have not been genotyped with any of the SNP chips used.

New Zealand: Patients were recruited from the Otago-Southland region of the country, and PAD was confirmed by an ankle brachial index<0.7, pulse volume recordings and angiography/ultrasound imaging. An abdominal ultrasound scan excluded concurrent AAA from the PAD group. Controls were the same vascular disease–free individuals as described above for the New Zealand AAA sample set.

Austria: Patients and controls were recruited through the Linz Peripheral Arterial Disease (LIPAD) study during 2000 to 2002, at the St. John of God Hospital, Department of Surgery (Linz, Austria). Of the recruited patient, all with chronic atherosclerotic occlusive disease of the lower extremities associated with typical symptoms, such as claudication or leg pain on exertion, rest pain, or minor or major tissue loss, were included in this study on the basis of the final clinical diagnosis established by the attending vascular surgeons. The diagnosis was verified by interview, physical examination, non-invasive techniques, and angiography [11]. Control subjects were patients at the same hospital that fulfilled the following criteria: no clinical indication of PAD by history and physical examination; systolic brachial blood pressure equal to or less than the blood pressure in each of the right and left anterior tibial and posterior tibial arteries (ie, ABI ≥1.0) [11].

Italy: Patients and controls were recruited among subjects consecutively admitted to the Department of Medicine of the A. Gemelli University Hospital of Rome, from 2000 to 2001. Diagnosis of PAD was performed in accordance with established criteria [12]. All patients had an ankle/arm pressure index lower than 0.8 and were at Fontaine's stage II, with intermittent claudication and no rest pain or trophic lesions [13].

Denmark: Patients with PAD were consecutively included during November 1999 to January 2004. The diagnosis was established from typical findings in clinical investigation (intermittent claudication, rest pain, ulcer or gangrene, and ankle-brachial-index<0.9). All patients were enrolled at Vascular Surgery Department, Viborg Hospital, Denmark [14]. The Danish controls come from the Inter99 previously described [10].

Sweden: Patients and controls were recruited at the Department of Vascular Diseases at Malmö University Hospital (Malmö, Sweden). The diagnosis of critical limb ischemia was made in accordance with TransAtlantic Inter-Society Consensus scientific criteria[15] of ulceration, gangrene, or rest pain caused by PAD proven by ankle pressure (<50

to 70 mm Hg), reduced toe pressure (<30 to 50 mm Hg), or reduced transcutaneous oxygen tension. Diagnosis was confirmed by an experienced vascular surgery consultant and toe pressure measurements in patients with arteries in the affected leg that were non-compressible and the ankle pressure was >50 to 70 mm Hg. The control group consisted of healthy individuals included in a health screening programme for a preventive medicine project. None of those had symptomatic PAD [16].

Danville, Pennsylvania, US: Individuals with PAD were enrolled through the Geisinger Clinic Department of Vascular Surgery[8]. PAD subjects had an ankle brachial index (ABI) ≤ 0.85 in at least one leg and were confirmed to be AAA-free (infrarenal aortic diameter ≤ 2 cm) based on abdominal imaging carried out within the preceding 5 years. Controls were the same individuals as previously described above for the Danville AAA group

Myocardial infarction samples

Iceland: The GWAS of MI in Icelanders by deCODE has been previously described[17]. Briefly, cases were initially identified from a registry of over 10,000 individuals who suffered an MI before the age of 75 in Iceland between 1981 and 2002 and satisfied the MONICA criteria [18], or had an MI discharge diagnosis from the Landspitali University Hospital (LUH) (Reykjavik, Iceland) between 2003 and 2005. These patients were recruited through the cardiovascular disease genetics program at deCODE. In 2009 the sample set was expanded to include additional subjects that were given the discharge diagnosis of MI at LUH between 1987 and 2007 and had donated blood through various genetic programs at deCODE genetics. Controls were the same individuals as described above for the Icelandic PAD sample set.

Atlanta, Georgia, US: The study participants were enrolled at the Emory University Hospital, Crawford Long Hospital, the Emory Clinic and Grady Memorial Hospital, all in Atlanta, Georgia, through the Emory Genebank Study. The Emory Genebank Study was designed to investigate the association of biochemical and genetic factors to CAD in subjects undergoing cardiac catheterization. For the purpose of the current study, subjects with current or prior history of MI were defined as cases. Subjects with no or minimal CAD on cardiac catheterization and no prior history of MI or CAD were defined as controls. Information on ethnicity was self-reported.

Durham, North Carolina, US: The study participants were enrolled at Duke University Medical Center (Durham, North Carolina) through the CATHGEN biorepository, consisting of subjects above 18 years of age, recruited sequentially through the cardiac catheterization laboratories from 2001-2005. For purposes of this study, cases of MI were defined as those having a history of MI (by self-report and corroborated by review of medical records), or having suffered an MI during the study follow-up period. Subjects with no prior history of MI or CAD and no or minimal CAD on cardiac catheterization were defined as controls.

Baltimore, Maryland, US: Subjects were recruited from the ongoing prospective family study (the Johns Hopkins GeneSTAR Study) which was designed to determine the environmental and genetic causes of chronic and cardiovascular diseases. Probands with documented MI and angiographically demonstrated coronary artery stenosis ≥50% of the vessel internal diameter in at least 1 vessel before the age of 60 were identified at the time of hospitalization in any of 10 Baltimore area hospitals between 1984 and 2006 and their healthy siblings without CAD or any vascular diseases ages 30-59 were enrolled and followed for incident MI. For purposes of this study, cases were defined as those new onset-MI during 5-25 years of follow-up. Standard criteria for MI (elevations of cardiac enzymes and electrocardiographic changes) were adjudicated from medical record reviews of all siblings. Subjects who remained healthy with no CAD during follow-up were defined as controls. Ethnicity was self-reported.

Philadelphia, Pennsylvania, US: The study participants from Philadelphia were enrolled at the University of Pennsylvania Medical Center through the PENN CATH study which recruited a consecutive sample of patients undergoing cardiac catheterization at the University of Pennsylvania Medical Center (Philadelphia, Pennsylvania) between July 1998 and March 2003. For the purpose of the current study we selected from the PENN CATH study individuals diagnosed with MI based on criteria for acute MI in terms of elevations of cardiac enzymes and electrocardiographic changes, or a self-reported history of MI. Ethnicity information was self-reported. Controls were the same individuals as described above for the Pittsburgh AAA sample set.

New Zealand: Individuals who suffered an MI were identified from a registry of CAD patients with angiographically proven coronary artery stenosis ≥50% of the vessel internal diameter in at least 1 vessel. The age matched controls had no history of ischemic heart disease, including angina pectoris. All subjects were recruited from the Otago-Southland region of the country and ethnicity information was self-reported. Controls were the same individuals as described above for the New Zealand AAA sample set.

Italy. The subjects from Verona were enrolled into the Verona Heart Study (Verona, Italy) an ongoing study aimed at identifying new risk factors for CAD and MI in a population of subjects with angiographic documentation of their coronary vessels [19]. Information on MI diagnoses was gathered through medical records showing diagnostic electrocardiogram and enzyme changes, and/or the typical sequelae of MI on ventricular angiography. Control subjects had normal coronary arteries, being submitted to coronary angiography for reasons other than CAD. Controls with history or clinical evidence of atherosclerosis in vascular districts beyond the coronary bed were excluded.

Venous thromboembolism samples

Iceland: All patients with VTE diagnosed objectively by imaging techniques at the three Reykjavik acute care hospitals during 1987 to 2002 were included. These hospitals serve as acute care hospitals for about 2/3 of the Icelandic population and referral hospitals

for the whole nation. The accepted imaging techniques were: compression ultrasound, venogram, ventilation perfusion (VQ-) scan, pulmonary angiograms, computerized pulmonary angiograms or autopsy confirmed VTE. The cases were identified by a computer search of the following ICD diagnostic codes: ICD-9: 415, 415.1, 451, 451.1, 451.2, 451.8, 451.9, 453.1, 453.8, 459.1. ICD-10: I26, I26.9, I80, I80.1, I80.2, I80.3, I80.9, I82.1, I82.8, 187.0. The hospital charts of all identified patients were then reviewed by experienced physicians in order to exclude erroneous diagnoses (eg superfical thrombophlebitis, arterial emboli). Cases were also eliminated if a confirmatory imaging report could not be found. Information on the presence of other cardiovascular diseases (i.e. CAD, AAA and PAD) at the time of diagnosis is not available. However, the Icelandic CAD and AAA lists include the majority of all cases diagnosed in Iceland over a specific time period (CAD over 27,000 cases diagnoses 1981-2009, and AAA over 1,100 cases diagnosed 1980-2006). Comparison of these lists with the VTE case list shows that 2.1% have also been diagnosed with AAA and 27.4% with CAD. We have less complete information on individuals diagnosed with PAD in Iceland but based on the information we have 5.8% of the VTE cases have diagnosed with PAD. These numbers probably represent an overestimate as many VTE cases presented with their symptoms of CAD, AAA and PAD long after their diagnosis of VTE. Controls were the same individuals as described above for the Icelandic PAD sample set.

Canada: Canada 1: Cases were recruited from the Thrombosis Clinic at the Ottawa Hospital which serves as a referral basis for a community of approximately 700,000 people. Consecutive patients with at least one objectively confirmed idiopathic deep vein thrombosis (DVT) or pulmonary embolism, who had been treated for at least 3 months, were eligible for inclusion [20]..Patients were excluded if they had a malignant disorder. History of CAD and PAD was documented for the majority of cases at the time of recruitment. Of the VTE cases 6.9% had CAD and 4.9% PAD. Canada 2: Consecutive patients presenting with symptoms or signs suspected by a physician of being caused by acute pulmonary embolism (acute onset of new or worsening shortness of breath, chest pain, hemoptysis, presyncope or syncope) were eligible for the study, Of those fulfilling the inclusion criterion the following were excluded: 1) deep vein thrombosis or pulmonary embolism diagnosed within the previous 3 months; 2) no change in severity of pulmonary symptoms within the previous two weeks; 3) use of therapeutic doses of parenteral anticoagulants for greater than 48 hours; 4) Co-morbid condition making life expectancy less than three months 5) contraindication to contrast media; 6) a need for long-term use of anticoagulants; 7) pregnancy; 8) age less than 18 years; 9) refusal to give informed consent; and 10) geographic inaccessibility to follow-up 11) unable to give informed consent; 12) Spiral CT or VQ scan in the previous 7 days; and 13) previous enrollment in Canada 2 trial (PEDS). Information on other cardiovascular diseases at the time of case recruitment was not available. Controls: Friends of cases were recruited as control individuals and they were matched to cases by sex, ethnicity, and age. Controls were excluded if they had prior VTE or recent malignant disease.

Spain: The patients were enrolled from the files of the anticoagulation clinics in 4 hospitals in Spain: Hospital General Universitario (Murcia), Hospital de la Santa Creu i Sant Pau (Barcelona), Hospital Clínico Universitario (Salamanca), and Clínica Universitaria de Navarra (Pamplona). The study includes unrelated individuals of European descent with a first, objectively confirmed episode of venous thromboembolism before the age of 75 years. All cases were diagnosed appropriately by clinical probability, D-dimer levels, compression ultrasonography, ventilation perfusion lung scan, and, when necessary, phlebography or pulmonary angiography. Patients with known malignant disorders were excluded. Of the VTE cases 3.3 % had a history of CAD and 0.8% history of PAD. The control group of our study includes unrelated individuals without a history of vascular or thromboembolic disease. These controls were randomly selected among 2 sources: blood donors and traumatology and ophthalmology patients matched by age, sex, race, and geographic distribution with the cases [21].

Intracranial aneurysm samples

Iceland: Icelandic individuals with intracranial aneurysm were identified through an inpatient database from 1994 to 2006 at the Landspitali University Hospital. All individuals seen in the years 1996–2006 with the ICD10 diagnosis I60.0-7 (aneurysmal subarachnoid hemorrhage), I67.1 (ruptured cerebral aneurysm) and I69.0 (sequelae of subarachnoid hemorrhage) were enrolled, as well as individuals in the years 1994–1996 with the ICD9 diagnosis 430 (subarachnoid hemorrhage from ruptured cerebral aneurysm). Controls were the same individuals as described above for the Icelandic PAD sample set.

The Netherlands: Dutch individuals with ruptured (91.5%) or unruptured (8.5%) intracranial aneurysm admitted to the University Medical Center Utrecht. Ruptured intracranial aneurysms were defined by symptoms suggestive of subarachnoid hemorrhage (SAH) combined with subarachnoid blood on computed tomography and a proven aneurysm at angiography (conventional, computed tomography or magnetic resonance angiogram), and unruptured intracranial aneurysms were identified by computed tomography or magnetic resonance angiography or conventional angiography. Multiple intracranial aneurysms were found in 20.5% of cases. The mean age at time of SAH was 49.5 years (range 10–84), and 66.1% of the cases were females. The controls were healthy Dutch blood bank donors of European origin.

Finland: The subjects were Finnish individuals admitted for treatment of intracranial aneurysm at either the University Hospital of Kuopio or the University Hospital of Helsinki in Finland. This study group and the Finnish controls used have been described [22].

Ischemic stroke samples

Iceland: Icelandic stroke cases were recruited from a registry of individuals diagnosed with ischemic stroke or transient ischemic attack (TIA) at the major hospital in Reykjavik, the Landspitali University Hospital, during 1993–2002. Cases were classified into

ischemic subtypes according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification by a physician reviewing original imaging and data [23]. Stroke cases were enrolled through the CVD genetics program at deCODE. Controls were the same individuals as described above for the Icelandic PAD sample set.

Characteristics of study populations.

	Controls			Cases			
Sample Set	n_c	**Women (%)**	**Age (SD)**	n_a	**Women (%)**	**Age (SD)**	**Ref.**
Abdominal aortic aneurysm (AAA)							
Iceland	27,712	62	50.8 (21.4)	452	26	75.5 (8.3)	**1**
Netherlands (Utrecht)	2,791	40	58.4 (10.2)	840	10	68.1 (8.3)	**2,3**
Belgium	267	32	na	176	11	na	**1,4**
Canada	155	80	na	206	26	na	**1,4**
New Zealand	848	35	69.3 (6.6)	1,144	20	73.9 (8.9)	**1,5**
UK	667	na	na	476	17	69.1 (4.4)	**6,7**
Denmark	4,380	54	45.2 (7.9)	323	0	68.2	**8,9**
Netherlands (Nijmegen)	324	0	69.0	149	0	68.8	
US (Danville)	442	22	72 (9)	793	20	74 (8)	**10**
US (Pittsburg)	499	na	na	100	25	na	**11**
Myocardial infarction (MI)							
Iceland	27,712	62	50.8 (21.4)	2,489	29	68.6 (10.5)	**12**
Italy	390	33	59.1 (12.3)	637	22	60.0 (11.7)	**13,14**
New Zealand	848	35	69.3 (6.6)	529	29	64.1 (10.3)	**13,15**
US (Atlanta)	1,249	na	na	386	22	63.6 (10.0)	**12**
US (Baltimore)	1,565	59	45.3 (12.2)	183	15	55.3 (8.9)	**12**
US (Durham)	736	50	57.1 (11.9)	1,191	24	61.1 (11.0)	**12**
US (Philadelphia)	498	46	58.3 (11.9)	540	28	61.8 (10.8)	**12**
Peripheral artery disease (PAD)							
Iceland	27,712	62	50.8 (21.4)	1,477	39	72.5 (10.9)	**1**
Austria	433	29	67.3 (10.7	487	30	68.5 (11.0)	**16**
Denmark	4,380	54	45.2 (7.9)	464	43	65.9 (9.6)	**17**
Italy	242	31	72.7 (6.3)	181	31	72.9 (9.3)	**1, 18**
New Zealand	848	35	69.3 (6.6)	450	43	70.5 (9.7)	**1**
Sweden	143	na	na	206	na	na	**1, 19**
US (Danville)	442	22	72 (9)	438	40	69 (10)	
Venous thromboembolism (VTE)							
Iceland	27,712	62	50.8 (21.4)	946	56	70.2 (15.3)	
Canada	226	40	57.2 (15.5)	214	53	56.5 (15.3)	**20**
Spain	1,018	50	49 (36-62)	1,018	50	47 (35-63)	**21**
Intracranial Aneurysm (IA)							
Iceland	27,712	62	50.8 (21.4)	174	64	61.4 (14.4)	**1**
Finland	312	49	58.9 (12.1)	321	52	48.2 (12.4)	**22**
Netherlands	915	38	48 (12.7)	646	66	49.5 (12.9)	**1**
Ischemic stroke (IS)							
Iceland	27,712	62	50.8 (21.4)	2,225	45	74.7 (12.1)	**23**

1) Helgadottir et al. Nat Gen 40, 217-224 (2008), **2)** Kiemeney, L.A. et al. Nat Gen 40, 1307-12 (2008), **3)** Wetzels, J.F. et al. Kidney Int 72, 632-7 (2007), **4)** Ogata et al. J Vasc Surg 41, 1036-1042 (2007), **5)** Jones et al. Clin Chem 53, 679-685 (2007), **6)** Brady et al. Circulation 110, 16-21 (2004), **7)** Stefansson, H. et al. Nature 460, 744-7 (2009), **8)** Lindholt JS et al. BMJ Apr 2;330(7494):750 (2005), **9)** Jörgensen et al. Eur J Cardiovasc Prev Rehabil. Oct;10(5):377-86. (2003), **10)** Elmore et al. J Vasc Surg. Jun;49(6):1525-31 (2009), **11)** St Jean, P.L. et al. Ann Hum Genet 59, 17-24 (1995), **12)** Helgadottir et al. Science 316, 1491-1493 (2007), **13)** Gudbjartsson et al. Nat Gen 40, 609-615 (2008), **14)** Girelli et al. N Engl J Med 343, 774-780 (2000), **15)** Jones et al. Arterioscler Thromb Vasc Biol 28, 764-770 (2008), **16)** Mueller et al. J Vasc Surg 41, 808-815 (2005), **17)** Joensen et al. Atherosclerosis 196, 937-942 (2008), **18)** Flex et al. Eur J Vasc Endovasc Surg 24, 264-268 (2002), **19)** Barani et al. J Vasc Surg 42, 75-80 (2005), **20)** Wells, P.S. et al. Thromb Haemost 90, 829-34 (2003), **21)** Corral J et al. Blood. 2006;108:177-183, **22)** Weinsheimer et al. Stroke 38, 2670-2676 (2007), **23)** Gretarsdottir et al. Ann Neurol 64, 402-409 (2008).

Genotyping

Illumina genome-wide genotyping: The Icelandic and Dutch case and control samples used in the GWA AAA study were assayed with the Illumina HumanHap300, HumanHapCNV370 or HumanHap610 bead chips (Illumina, SanDiego, CA, USA). Only SNPs present on all chips were included in the analysis and SNPs were excluded if they had (a) yield lower than 95% in cases or controls, (b) minor allele frequency less than 1% in the controls, or (c) showed significant deviation from Hardy-Weinberg equilibrium in the controls ($P < 0.0001$). These criteria were applied separately to genotype data from each of the chip type used and SNPs that showed significant deviation ($P < 0.0001$ in an ANOVA test) in frequency between the chips were excluded from the analysis. Any samples with a call rate below 98% were excluded from the analysis. The final analysis included 293,677 SNPs present on all three chips. The UK control samples were genotyped as part of the S-Gene Plus cohort using the Illumina HumanHap300 and HumanHap550 BeadChips [5]. New Zealand AAA and control samples were genotyped using Affymetrix SNP 6.0 arrays and the imputation of ungenotyped SNPs was done using the IMPUTE [24] software and the HapMap (NCBI Build 36 (db126b)) CEU data as reference [25].

Single SNP genotyping: Most single SNP genotyping for all samples was carried out at deCODE genetics (Reykjavik, Iceland) applying the same platform to all populations studied. All single SNP genotyping was carried out using the Centaurus (Nanogen) platform [26]. The quality of each Centaurus SNP assay was evaluated by genotyping each assay on the CEU samples and comparing the results with the HapMap data. All assays had mismatch rate <0.5%. Additionally, all markers were re-genotyped on more than 10% of samples typed with the Illumina platform resulting in an observed mismatch in less than 0.5% of samples. Single SNP genotyping of the additional 302 AAA cases from New Zealand only genotyped for rs7025486 and not included in stage 1 replication, was done using a TaqMan assay (Applied Bio-sciences probe # C_ 29006014 _ 10) at the New Zealand site.

Expression of *DAB2IP* and rs7025486

Whole blood and adipose: The correlation between rs7025486[A] and the mRNA expression of *DAB2IP* was tested in adipose tissue and in whole blood from 674 and 1,002 Icelandic individuals, respectively. The collection of the tissue samples and the measurement of the expression was described previously[27]. Of those individuals, 609 with adipose tissue sample and 672 with blood sample had been genotyped for rs7025486 and were used for the analysis. For each variant and each expression trait at the corresponding loci, the correlation was tested by regressing the mean logarithm ($\log_{10}$) expression ratio (MLR) on the number of copies of the risk variant A a person carries. The effect of age and sex was taken into account by including age, sex and age×sex terms as an explanatory variables in the regression analysis. When analyzing expression in blood, adjustment for differential cell count was also included. The *P* values were adjusted for relatedness of the individuals by simulating genotypes through the Icelandic genealogy as previously described[28]. The corresponding

adjustment factors for the χ^2-statistic were 1.063 and 1.078 for adipose tissue and blood, respectively. The gene expression data is available from the GEO database under the accession numbers GSE7965 and GPL3991. The study from which the expression data was derived was approved by the National Bioethics Committee (NBC01-033) and the Icelandic Data Protection Authority (DPA).

Aorta and mammary artery: The aorta and mammary artery tissue samples were from the ASAP study that includes patients undergoing heart-valve surgery at Karolinska University Hospital, Stockholm, Sweden. Biopsies were obtained at surgery from dilated and non-dilated ascending aorta (117 samples; 25.6% females, mean age = 61.6+/-11.3SD) and from mammary artery (88 samples; 37.5% females, mean age = 65.0+/-11.3SD). The intima/media layer was isolated by adventicectomy, incubated with RNAlater (Ambion) and homogenized with a FastPrep (Qbiogene, Irvine, CA) using Lysing Matrix D tubes (Invitro cat.no. 6913-100). Total RNA was isolated using Trizol (BRL-Life Technologies) and RNeasy Mini kit (Qiagen) as a cleanup including treatment with RNase-free DNase set (Qiagen) according the manufacturer's instructions. The quality of RNA was analyzed with an Agilent 2100 bioanalyzer (Agilent Technologies Inc., Paolo Alto, CA, USA) and quantity was measured by a NanoDrop (Thermo Scientific). RNA from each labelled vessel sample, altogether 205 samples, was hybridized to Affymetrix ST 1.0 exon array. Array images were processed using the RMA algorithm as described previously [29] to obtain single-colour $\log_2$ expression values. The hybridizations went through standard QC process according to Affymetrix standards. Meta probe sets were analyzed from the extended set of Affymetrix defined probe groups. The expression of *DAB2IP* (probe 3187834) was tested for correlation with rs7025486 by regressing the age and sex adjusted expression values on the number of copies of the risk allele A an individual carries. This study was approved by the Ethics Committee at the Karolinska Institutet and patients were included after informed, written and signed consent.

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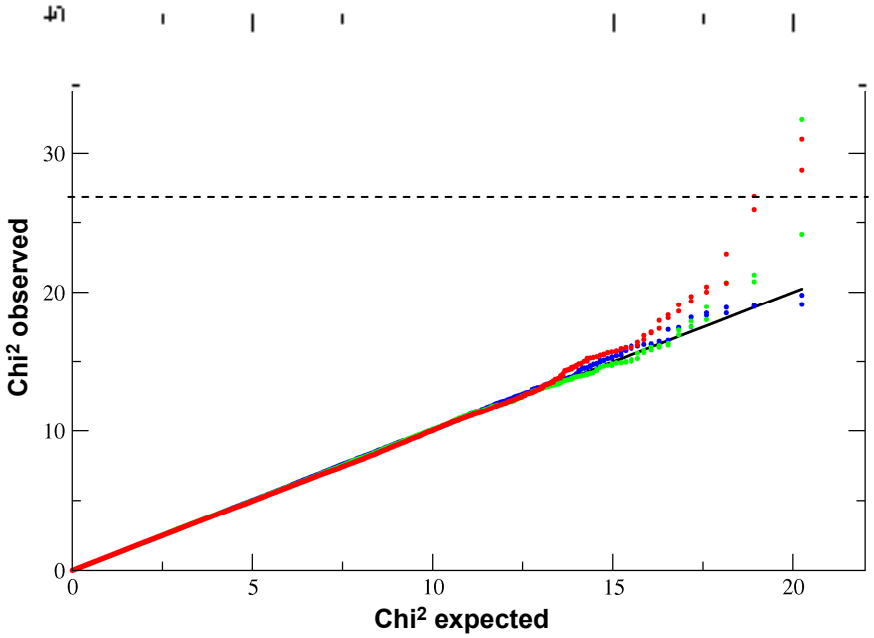
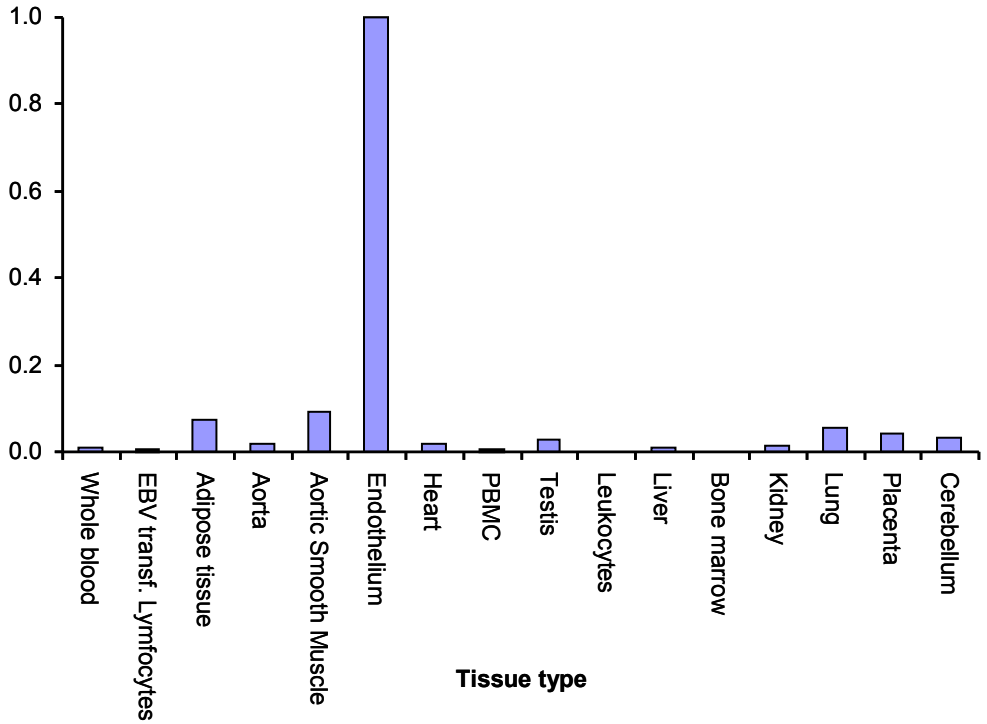
Supplementary Figure 1: A Q-Q plot of the GWA results.

A Q-Q plot of the 293,677 χ^2-statistics for GWA analysis of the two discovery samples sets from Iceland (blue dots) and The Netherlands (green dots) and for the two sets combined (red dots). The Icelandic results have been adjusted by dividing the χ^2-values by the genomic control factor λ_g = 1.143. The equiangular line (black line) is included in the plot for reference purpose and the dashed horizontal line indicates the threshold for genome-wide significance assuming a Bonferroni correction for the 293,677 SNPs tested.



Supplementary Figure 2: Expression of *DAB2IP* in various human tissues.

RNA was isolated from human whole blood, EBV transformed human lymphoblastoid cell lines, peripheral blood monocyte cells, human aortic smooth muscle cells (Sciencell, Cat.no. 6110) and human primary umbilical vein endothelial cells (HUVEC) using Qiagen RNA kits. Concentration and quality of the RNA was determined with Agilent 2100 Bioanalyzer (Agilent Technologies). cDNA were generated with High capacity cDNA reverse transcriptase kit (Applied Biosystems Inc.) and cDNA libraries for each tissue constructed by pooling the cDNA from several samples from each tissue. In addition to the libraries above, eleven commercial cDNA libraries (Clontech) were used. Real-time PCR assay was designed over the exon6-exon7 junction of the *DAB2IP* gene (RefSeq: NM_032552.2). Left primer was GCCAAGACCAAGGAGGAGAT and right primer was GACATCATCAGGTCTGTCAGGA and Roche Universal Library probe was #37. The real-time PCR was run in duplicates for each cDNA tissue library according to recommendations on an ABI Prism 7900HT Sequence Detection System. Expression levels were normalized to the expression of *DAB2IP* in heart (User Bulletin no. 2, Applied Biosystems 2001). Shown is the average expression of the duplicate experiments with the highest expression set to one for presentation purposes.



Supplementary Table 1: SNPs with P < 5.5×10^{-5} in the combined GWA analysis of the Icelandic and Dutch AAA samples.

Listed are the twenty-five SNPs with $P < 5.5\times10^{-5}$ in the combined GWAS on AAA cases and controls from Iceland and The Netherlands. For each SNP the table shows the chromosome and position in NCBI Build 36, the allele tested for association (EA), the frequency in controls (f_c)and cases (f_a), the OR and *P* value for Iceland and The Netherlands separately and combined. The three SNPs at 9p21 that reach genome-wide significance are indicated in bold. *P* values for the Icelandic sample set have been adjusted using the method of genomic control.

				Iceland				Netherland				Combined	
Chr	**SNP**	**Pos**	**EA**	f_c	f_a	**OR**	***P***	f_c	f_a	**OR**	***P***	**OR**	***P***
1	rs487174	45422830	T	0.101	0.134	1.38	0.00059	0.094	0.116	1.26	0.016	1.32	3.3×10^{-5}
"	rs1998064	227322133	A	0.746	0.798	1.35	4.8×10^{-5}	0.743	0.771	1.17	0.022	1.25	8.9×10^{-6}
2	rs355823	165905357	T	0.096	0.137	1.50	1.9×10^{-5}	0.081	0.094	1.17	0.14	1.34	3.0×10^{-5}
5	rs1372319	77994012	T	0.652	0.693	1.21	0.0041	0.698	0.736	1.20	0.0044	1.21	5.3×10^{-5}
"	rs959461	169860675	G	0.204	0.250	1.31	0.00023	0.204	0.237	1.21	0.0065	1.26	6.2×10^{-6}
6	rs9268832	32498969	T	0.511	0.561	1.22	0.0011	0.424	0.460	1.16	0.013	1.19	5.3×10^{-5}
"	rs7761436	110548401	G	0.708	0.752	1.25	0.0015	0.658	0.694	1.18	0.0083	1.21	4.3×10^{-5}
"	rs783166	161086525	T	0.084	0.111	1.37	0.0020	0.107	0.138	1.34	0.0011	1.35	7.4×10^{-6}
"	rs1652500	161101477	C	0.154	0.193	1.32	0.00056	0.199	0.233	1.22	0.0056	1.26	1.3×10^{-5}
7	rs7798936	95025282	A	0.550	0.588	1.17	0.014	0.499	0.552	1.24	0.00034	1.20	1.7×10^{-5}
"	rs6979784	127470170	G	0.745	0.769	1.14	0.063	0.810	0.860	1.44	5.4×10^{-6}	1.27	1.0×10^{-5}
"	rs2290225	127511564	C	0.506	0.523	1.07	0.26	0.505	0.571	1.31	5.5×10^{-6}	1.19	4.8×10^{-5}
9	**rs10116277**	22071397	T	0.418	0.470	1.23	0.00066	0.454	0.516	1.28	2.2×10^{-5}	1.26	6.0×10^{-8}
"	**rs1333040**	22073404	T	0.491	0.543	1.23	0.00067	0.550	0.608	1.27	6.3×10^{-5}	1.25	1.6×10^{-7}
"	**rs2383207**	22105959	G	0.457	0.524	1.31	1.3×10^{-5}	0.487	0.540	1.24	0.0003	1.27	1.9×10^{-8}
"	rs7025486	119798448	A	0.298	0.347	1.25	0.00063	0.286	0.320	1.17	0.012	1.21	2.9×10^{-5}
12	rs1671518	16280892	G	0.726	0.769	1.26	0.0014	0.719	0.757	1.21	0.0041	1.23	1.9×10^{-5}
"	rs10860944	102039897	C	0.190	0.220	1.20	0.015	0.198	0.240	1.28	0.00049	1.24	2.5×10^{-5}
14	rs4900514	99961084	T	0.645	0.667	1.10	0.14	0.608	0.689	1.43	1.3×10^{-8}	1.26	2.7×10^{-7}
15	rs1471151	93274625	T	0.600	0.644	1.21	0.0032	0.580	0.625	1.21	0.0016	1.21	1.5×10^{-5}
"	rs8025525	93303007	A	0.541	0.594	1.24	0.00065	0.526	0.571	1.20	0.0020	1.22	4.4×10^{-6}
17	rs205043	11524523	G	0.297	0.345	1.24	0.00096	0.260	0.302	1.23	0.0016	1.24	5.1×10^{-6}
19	rs17207173	58769682	T	0.310	0.368	1.30	6.0×10^{-5}	0.355	0.380	1.11	0.075	1.20	5.2×10^{-5}
21	rs2836470	38818203	C	0.851	0.880	1.28	0.0064	0.844	0.876	1.30	0.0021	1.29	3.9×10^{-5}
X	rs7052934	141294834	C	0.065	0.086	1.35	0.027	0.035	0.077	2.27	9.0×10^{-7}	1.66	1.5×10^{-6}

Supplementary Table 2: Association results for the 19 lead SNPs from the AAA GWA in the AAA follow-up set 1.

Shown are the association results for the 19 follow up SNPs in AAA case-control samples from Belgium (172 cases and 266 controls), Canada (196 cases and 150 controls), New-Zealand (842 cases and 848 controls) and UK (455 cases and 677 controls). For each SNP the table shows the chromosome and position in NCBI Build 36, the allele tested for association (EA), the frequency in controls (f_c) and cases ($f_a f_a$), the OR and *P* value.

				Belgium				Canada				New Zealand				UK			
Chr	**SNP**	**Pos**	**EA**	f_c	f_a	**OR**	***P***	f_c	f_a	**OR**	***P***	f_c	f_a	**OR**	***P***	f_c	f_a	**OR**	***P***
1	rs487174	45782123	T	0.073	0.089	1.24	0.41	0.113	0.116	1.02	0.93	0.095	0.095	1.00	0.99	0.088	0.098	1.13	0.40
"	rs1998064	228353751	A	0.786	0.777	0.95	0.76	0.742	0.753	1.06	0.74	0.783	0.757	0.86	0.17	0.758	0.766	1.04	0.67
5	rs1372319	77945695	T	0.717	0.687	0.87	0.35	0.750	0.775	1.15	0.45	0.709	0.708	0.99	0.92	0.696	0.732	1.19	0.063
"	rs959461	169812358	G	0.175	0.222	1.34	0.10	0.242	0.140	0.51	0.019	0.196	0.179	0.90	0.24	0.183	0.196	1.09	0.43
6	rs9268832	32535767	T	0.321	0.339	1.09	0.57	0.346	0.358	1.06	0.73	0.393	0.412	1.08	0.28	0.432	0.385	0.82	0.025
"	rs783166	161097227	T	0.101	0.108	1.08	0.75	0.139	0.109	0.76	0.23	0.116	0.109	0.93	0.51	0.112	0.115	1.04	0.77
"	rs1652500	161112179	C	0.180	0.186	1.04	0.84	0.212	0.179	0.81	0.29	0.194	0.190	0.97	0.76	0.199	0.215	1.10	0.36
7	rs7798936	95251189	A	0.490	0.526	1.16	0.30	0.534	0.516	0.93	0.64	0.522	0.520	0.99	0.92	0.527	0.493	0.87	0.11
"	rs6979784	127703444	G	0.844	0.794	0.71	0.061	0.845	0.823	0.85	0.43	0.815	0.828	1.09	0.34	0.810	0.816	1.04	0.71
"	rs2290225	127744838	C	0.565	0.465	0.67	0.0045	0.565	0.455	0.64	0.0048	0.530	0.529	1.00	0.95	0.508	0.498	0.96	0.63
9	rs7025486	123462224	A	0.227	0.253	1.15	0.39	0.280	0.306	1.13	0.45	0.226	0.270	1.27	0.0036	0.216	0.278	1.40	0.0008
12	rs1671518	16280892	G	0.687	0.731	1.24	0.16	0.695	0.715	1.10	0.56	0.706	0.726	1.10	0.23	0.736	0.728	0.96	0.69
"	rs10860944	102061560	C	0.164	0.167	1.02	0.92	0.214	0.193	0.87	0.48	0.194	0.198	1.02	0.80	0.217	0.202	0.91	0.36
14	rs4900514	101040796	T	0.565	0.632	1.32	0.055	0.603	0.646	1.20	0.25	0.653	0.601	0.80	0.0077	0.604	0.631	1.12	0.19
15	rs1471151	93345861	T	0.589	0.568	0.91	0.53	0.580	0.630	1.23	0.19	0.565	0.550	0.94	0.39	0.585	0.591	1.02	0.78
"	rs8025525	93374243	A	0.508	0.527	1.08	0.58	0.507	0.583	1.36	0.049	0.512	0.491	0.92	0.24	0.534	0.534	1.00	0.99
17	rs205043	11264682	G	0.212	0.246	1.21	0.26	0.260	0.302	1.23	0.23	0.266	0.276	1.06	0.53	0.265	0.249	0.92	0.39
19	rs17207173	58769682	T	0.343	0.324	0.92	0.56	0.322	0.354	1.15	0.38	0.344	0.344	1.00	0.99	0.356	0.366	1.05	0.62
21	rs2836470	38819677	C	0.859	0.856	0.98	0.91	0.813	0.877	1.64	0.019	0.863	0.862	1.00	0.99	0.872	0.875	1.03	0.84

Supplementary Table 3: Association results for the 19 GWAS lead SNPs in the AAA discovery and follow up set 1.

Association results for the 19 follow-up SNPs in the discovery (1,292 cases and 30,503 controls) and follow-up sample set 1 (1,665 cases and 1,931 controls); both separately and combined. The table shows the chromosome and position in NCBI Build 36, the allele tested for association (EA), the OR and the *P* value.

				Discovery set		Follow-up set 1		Combined	
Chr	**SNP**	**Pos**	**EA**	**OR**	***P***	**OR**	***P***	**OR (95%CI)**	***P***
1	rs487174	45782123	T	1.32	3.3×10^{-5}	1.04	0.54	1.17 (1.07-1.28)	0.00088
"	rs1998064	228353751	A	1.25	8.9×10^{-6}	0.97	0.63	1.13 (1.05-1.22)	0.0018
5	rs1372319	77945695	T	1.21	5.3×10^{-5}	1.06	0.33	1.15 (1.07-1.23)	0.00015
"	rs959461	169812358	G	1.26	6.2×10^{-6}	0.98	0.76	1.14 (1.06-1.23)	0.00084
6	rs9268832	32535767	T	1.19	5.3×10^{-5}	0.99	0.83	1.10 (1.03-1.17)	0.0032
"	rs783166	161097227	T	1.35	7.4×10^{-6}	0.96	0.56	1.16 (1.05-1.28)	0.0029
"	rs1652500	161112179	C	1.26	1.3×10^{-5}	1.01	0.93	1.15 (1.06-1.25)	0.00064
7	rs7798936	95251189	A	1.20	1.7×10^{-5}	0.95	0.4	1.10 (1.03-1.18)	0.0039
"	rs6979784	127703444	G	1.27	1.0×10^{-5}	1.00	1	1.14 (1.06-1.24)	0.00087
"	rs2290225	127744838	C	1.19	4.8×10^{-5}	0.99	0.54	1.01 (0.98-1.04)	0.42
9	rs7025486	123462224	A	1.21	2.9×10^{-5}	1.28	1.2×10^{-5}	1.24 (1.15-1.33)	1.8×10^{-9}
12	rs1671518	16280892	G	1.23	1.9×10^{-5}	1.07	0.19	1.16 (1.08-1.25)	4.8×10^{-5}
"	rs10860944	102061560	C	1.24	2.5×10^{-5}	0.97	0.62	1.11 (1.03-1.20)	0.0054
14	rs4900514	101040796	T	1.26	2.7×10^{-7}	1.01	0.84	1.15 (1.07-1.23)	5.5×10^{-5}
15	rs1471151	93345861	T	1.21	1.5×10^{-5}	0.99	0.86	1.10 (1.03-1.17)	0.0027
"	rs8025525	93374243	A	1.22	4.4×10^{-6}	1.00	0.99	1.11 (1.05-1.19)	0.00068
17	rs205043	11264682	G	1.24	5.1×10^{-6}	1.04	0.5	1.16 (1.08-1.24)	6.2×10^{-5}
19	rs17207173	58769682	T	1.20	5.2×10^{-5}	1.02	0.72	1.12 (1.05-1.20)	0.00082
21	rs2836470	38819677	C	1.29	3.9×10^{-5}	1.05	0.45	1.16 (1.07-1.27)	6.0×10^{-4}

Supplementary Table 4. Association of rs7025486-A with DAB2IP expression.

Shown are the number of individuals with genotype and expression information (N), the observed effect on expression, and a *P* value. The *P* values for blood and adipose tissue have been adjusted for related of the individuals by dividing the corresponding χ^2-statistic by 1.063 and 1.078, respectively.

Tissue	Probe	N	Effect	*P*
Blood	NM_032552	672	0.005	0.24
Adipose	NM_032552	609	-0.013	0.018
Ascending aorta intima/media	3187834	117	0.067	0.026
Mammary artery intima/media	3187834	88	-0.057	0.016

Supplementary Table 5: Association of rs7025486[A] with intracranial aneurysm and stroke.

Association of rs7025486[A] with intracranial aneurysm and stroke in case-control samples sets of European ancestry. Shown are the number of controls n_c and cases n_a, the frequency in controls f_c and in cases f_a, the OR with 95% CI, *P* value for test of association and the *P* value for the test of heterogeneity in the effect estimates. 132 ($n_{a,eff}$ = 202), 1,552 ($n_{a,eff}$ = 2,862), 38 ($n_{a,eff}$ = 261), 53 ($n_{a,eff}$ = 288), and 106 ($n_{a,eff}$ = 448) un-genotyped Icelandic intracranial aneurysm, ischemic, large vessel disease, small vessel disease and cardiogenic stroke samples were included in the analysis, respectively. The *P* value was adjusted for relatedness of the Icelandic individuals by dividing the χ^2 statistic by the genomic-control factor λ_g = 1.049 for the intracranial aneurysm, λ_g = 1.234 for Ischemic stroke, λ_g = 1.021 for large vessel disease, λ_g = 1.056 for cardiogenic stroke and λ_g = 1.025 for small vessel disease.

Sample Set (n_c/n_a)	f_c	f_a	OR (95% CI)	*P*	P_{het}
Intracranial Aneurysm					
Iceland (5,863/174)	0.292	0.308	1.08 (0.87-1.34)	0.50	
Finland (299/311)	0.196	0.227	1.21 (0.92-1.59)	0.18	
The Netherlands (256/560)	0.312	0.28	0.86 (0.68-1.08)	0.19	
Combined (6,418/1,045)			1.02 (0.89-1.17)	0.77	0.14
Stroke (Iceland only)					
Ischemic stroke (5,863/2,360)	0.292	0.305	1.07 (0.99-1.15)	0.097	
Large vessel disease (5,863/262)	0.292	0.302	1.05 (0.86-1.27)	0.63	
Cardiogenic stroke (5,863/419)	0.292	0.310	1.09 (0.94-1.27)	0.26	
Small vessel disease (5,863/270)	0.292	0.289	0.98 (0.81-1.20)	0.89	

Supplementary Table 6: Association of rs7025486[A] with venous thromboembolism and with pulmonary embolism excluding individuals with known CVD's.

Association of rs7025486[A] with venous thromboembolism and with pulmonary embolism after excluding from the cases individuals with known incident of CAD , PAD (for all sample sets) or AAA, (for the Icelandic samples). Shown are the number of controls n_c and cases n_a, the frequency in controls f_c and in cases f_a, the OR with 95% CI, *P* value for test of association and the *P* value for the test of heterogeneity in the effect estimates. 1,140 ($n_{a,eff}$ = 1,011) and 612 ($n_{a,eff}$ = 482) un-genotyped Icelandic individuals with VTE and with PE were included in the analysis, respectively. The *P* value was adjusted for relatedness of the Icelandic individuals by dividing the χ^2 statistic by the genomic-control factor λ_g = 1.275 for the VTE and λ_g = 1.176 for the PE analysis.

Sample Set (n_c/n_a)	f_c	f_a	OR (95% CI)	*P*	P_{het}
Venous Thromboembolism					
Iceland (5,863/655)	0.292	0.319	1.14 (1.02-1.28)	0.027	
Canada (226/169)	0.257	0.254	0.99 (0.71-1.37)	0.94	
Spain (888/654)	0.177	0.200	1.15 (0.96-1.35)	0.13	
Combined (6,977/1,478)			1.13 (1.03-1.24)	0.011	0.70
Pulmonary Embolism					
Iceland (5,863/296)	0.292	0.327	1.18 (1.01-1.37)	0.034	
Canada (226/69)	0.257	0.289	1.28 (0.77-1.81)	0.44	
Spain (888/228)	0.176	0.221	1.31 (1.01-1.69)	0.041	
Combined (6,977/593)			1.21 (1.07-1.37)	0.0030	0.79

Supplementary Table 7: Association of rs7025486[A] with known risk factors for arterial or venous diseases.

The upper panel shows association of rs7025486[A] with type 2 diabetes, hypertension, smoking (comparing individuals that have ever smoked with those that have never smoked), and obesity (comparing individuals with BMI > 30 to individuals with normal BMI, ie 18 < BMI < 25) in Icelandic individuals. Shown are the number of controls n_c and cases n_a, the frequency in controls f_c and in cases f_a, the OR with 95% CI and *P* value for test of association. The *P* values were adjusted for relatedness by dividing the χ^2-statistic with the genomic-control factors 1.322, 1.345, 1.252 and 1.424 for T2D, hypertension, smoking and obesity, respectively. The lower panel shows the regression of BMI, HDL, LDL and total cholesterol, triglyceride and smoking quantity (quantified as number of packs smoked per day) on the number of copies of the AAA risk variant rs7025486[A] an individual carries tested in a sample of Icelandic individuals. The table includes the number of individuals with trait measurements tested, the frequency of the risk variant in that group, the effect estimate and the standard error (se) and the *P* value. The *P* values were adjusted for relatedness by dividing the χ^2-statistic with the genomic-control factors 1.484, 1.273, 1.360, 1.180, 1.257 and 1.205 for BMI, HDL, LDL, total cholesterol, triglyceride and smoking quantity, respectively.

Sample Set (n_c/n_a)	f_c	f_a	**OR (95% CI)**	***P***
Type 2 Diabetes[1] (32,588/2,208)	0.299	0.306	1.03 (0.96-1.11)	0.42
Hypertension[2] (24,939/6,785)	0.299	0.300	1.01 (0.95-1.06)	0.86
Smoking[3] (6,071/15,295)	0.298	0.301	1.01 (0.96-1.07)	0.57
Obesity[4](9,991/6,567)	0.300	0.304	1.02 (0.96-1.08)	0.47

Sample Set (unit)	***n***	f_a	**Effect (se)**	***P***
BMI[4] (kg/m^2)	27,044	0.299	0.026 (0.060)	0.66
HDL (mmol/L)	14,416	0.298	-0.0011 (0.0056)	0.86
LDL (mmol/L)	13,952	0.298	-0.0044 (0.0076)	0.56
Total cholesterol (mmol/L)	15,693	0.299	-0.0094 (0.0153)	0.54
Triglyceride (mmol/L)	14,378	0.299	0.016 (0.007)	0.026
Smoking[3] (cpd)	15,295	0.301	-0.003 (0.011)	0.81

[1]Steinthorsdottir, V. *et al*. Nat Genet 39, 770-5 (2007), [2]Kristjansson, K. *et al*. Hypertension 39, 1044-9 (2002), [3]Thorgeirsson, T.E. *et al*. Nature 452, 638-42 (2008), [4]Thorleifsson, G. *et al*. Nat Genet 41, 18-24 (2009)