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**Novel blood pressure locus and gene discovery using GWAS and expression
datasets from blood and the kidney**

The list of authors can be found at the end of the manuscript.

1 ABSTRACT

2 Elevated blood pressure is a major risk factor for cardiovascular disease and has a substantial genetic
3 contribution. Genetic variation influencing blood pressure has the potential to identify new
4 pharmacological targets for the treatment of hypertension. To discover additional novel blood
5 pressure loci, we used 1000 Genomes Project-based imputation in 150,134 European ancestry
6 individuals and sought significant evidence for independent replication in a further 228,245
7 individuals. We report 6 new signals of association in or near *HSPB7*, *TNXB*, *LRP12*, *LOC283335*, *SEPT9*
8 and *AKT2*, and provide new replication evidence for a further 2 signals in *EBF2* and *NFKBIA*. Combining
9 large whole-blood gene expression resources totaling 12,607 individuals, we investigated all novel
10 and previously reported signals and identified 48 genes with evidence for involvement in BP
11 regulation that are significant in multiple resources. Three novel kidney-specific signals were also
12 detected. These robustly implicated genes may provide new leads for therapeutic innovation.
13

1 INTRODUCTION

2 Genetic support for a drug target increases the likelihood of success in drug development (1) and
 3 there is clear unmet need for novel therapeutic strategies to treat individuals with hypertension (2).
 4 A number of large studies have described blood pressure (BP) variant identification by genome-wide
 5 and targeted association approaches (3-19). Clinically the most predictive BP traits for cardiovascular
 6 risk are systolic blood pressure (SBP) and diastolic blood pressure (DBP), reflecting roughly the peak
 7 and trough of the BP curve, and pulse pressure (PP), the difference between SBP and DBP (20)
 8 reflecting arterial stiffness. Using these three traits, we undertook a meta-analysis of 150,134
 9 individuals from 54 genome-wide association studies of European ancestry with imputation based
 10 on the 1000 Genomes Project Phase 1. To minimize reporting of false positive associations, we
 11 sought stringent evidence for significant independent replication in a further 228,245 individuals.
 12 We further followed up novel and previously reported association signals in multiple large gene
 13 expression databases and the largest kidney tissue gene expression resource currently available.
 14 Finally, we searched for enrichment of associated genes in biological pathways and gene sets and
 15 identified whether any of the genes were known drug targets.

16 RESULTS

17 The stage 1 discovery meta-analysis included 150,134 individuals (**Online Methods; Supplementary**
 18 **Tables 1-4, Supplementary Figures 1 and 2**) and 7,994,604 variants with minor allele frequency
 19 (MAF) >1% and an effective sample size of at least 60% of the total (**Online Methods**). We identified
 20 61 signals in the discovery analysis that were candidates for novel BP signals ($P < 10^{-6}$ for any trait;
 21 **Supplementary Table 5**). To ensure robustness of signals, we examined BP associations in an
 22 additional 228,245 individuals from 15 independent studies for replication, including 140,886
 23 individuals from UK Biobank (19) (**Supplementary Table 6 and Online Methods**). We used the most
 24 significant ("sentinel") SNP and trait for each locus in replication (61 tests). Twenty-two putatively
 25 novel association signals were initially confirmed showing significant evidence of replication in the
 26 independent stage-2 studies ($P < 8.2 \times 10^{-4}$, Bonferroni correction for 61 tests) and genome-wide
 27 significance ($P < 5 \times 10^{-8}$) in a meta-analysis across all 378,376 individuals (**Online methods, Table 1,**
 28 **Supplementary Table 7**). Of these, 14 were subsequently published in two other studies (18, 19)
 29 which presented genome-wide significant associations with evidence of replication. A further two
 30 were highlighted as putative novel signals in one of those studies (18) but had not been confirmed by
 31 replication. In our study, we report the 6 remaining novel signals, and the 2 previously unconfirmed
 32 signals (in *EBF2* and in *NFKBIA*), as novel signals. The 8 novel signals included 7 signals at 7
 33 independent loci (**Supplementary Figure 3**) and one novel independent signal near a previously

1 reported hit near *TNXB* (**Online Methods, Supplementary Table 8, Supplementary Figure 4**). The
 2 novel signals show both significant evidence of replication in the independent stage-2 studies ($P <$
 3 8.2×10^{-4} , Bonferroni correction for 61 tests) and genome-wide significance ($P < 5 \times 10^{-8}$) in a meta-
 4 analysis across all 378,376 individuals. The sentinel variants at all 8 signals were common (MAF>5%)
 5 and the novel secondary signal at *TNXB* was in high linkage-disequilibrium ($r^2 > 0.8$) with a non-
 6 synonymous SNP. With the exception of rs9710247, which was only significant for association with
 7 DBP, all signals were significantly associated ($P < 0.006$, Bonferroni corrected for 8 tests) with all 3
 8 traits (**Table 1 and Supplementary Table 9**).

9 We next sought to identify which genes might have expression levels that were associated with
 10 genotypes of the BP-associated variants reported in this study and others. Strong evidence of an
 11 association with expression of a specific gene may provide clues as to which gene(s) might be
 12 functionally relevant to that signal. We took the 139 BP association signals reported prior to these
 13 studies (18, 19), and 22 novel signals of association identified and confirmed in this study and two
 14 contemporaneous studies (3-19, 21) (**Supplementary Table 10**), and searched for evidence of
 15 association with gene expression in whole-blood (four studies, total $n=12,607$; **Online Methods**) and
 16 in kidney tissue ($n=134$, the largest kidney eQTL resource currently available). Although of unclear
 17 direct relevance to BP, whole-blood was studied due to the availability of large data sets enabling a
 18 powerful assessment of expression patterns that are likely present across multiple cell and tissue
 19 types. Kidney was chosen because of the many renal pathways that regulate BP and outstanding
 20 questions about the relevance of kidney pathways to the genetic component of BP regulation in the
 21 general population (3, 15). Expression quantitative trait loci (eQTL) signals were filtered by false
 22 discovery rate (FDR<5%) and we examined *cis* (within 1Mb) associations only (**Online methods and**
 23 **Supplementary Material**).

24 The four blood eQTL data sets were NESDA-NTR (22, 23), SABRe (15), the BIOS resource (24) and
 25 GTEx(25) (**Online Methods and Supplementary Material**). The BIOS resource ($n=2,116$) has not
 26 previously been utilized in the analysis of BP associations, findings from NESDA-NTR and SABRe have
 27 been reported for a subset of the previously published signals (16, 17). For a total of 369 genes,
 28 gene-expression was associated with the BP SNP in one or more of the 4 blood datasets at
 29 experiment-wide significance (**Supplementary Table 11**). This included 14 genes for 6 of the 8 novel
 30 signals. For 110 genes, we found eQTL evidence in 2 out of 4 datasets (**Figure 1**), including 4 genes
 31 for 2 of the novel signals; *EIF4B* and *TNS2* for rs73099903 and *MAP3K10* and *PLD3* for rs9710247.
 32 SNP rs73099903 was in strong linkage disequilibrium (LD $r^2 > 0.9$) with the SNP most strongly

1 associated with *TNS2* expression in the BIOS resource. *TNS2* encodes a tensin focal adhesion
2 molecule and may have a role in renal function (26).

3 For 48 genes, we found evidence in 3 out of the 4 resources (**Table 2**), suggesting robustness of the
4 SNP-gene expression correlation signal and highlighting those genes as potential candidates in
5 genetic BP regulation. Of the 48 genes, 28 have not previously been described in eQTL analyses using
6 BP associated SNPs and all were correlated with previously reported BP association signals.

7 In the kidney dataset (TransplantLines) (27), there was association of gene expression and genotype
8 for nine SNPs and 13 genes (**Table 2, Figure 1 and Supplementary Table 12**). Nine of the SNP-gene
9 expression associations were also observed in the whole-blood eQTL datasets, suggesting that those
10 signals may not be unique to the kidney. We report three signals that were unique to the kidney and
11 not previously reported (*C4orf34*, *HIP2* and *ASIC1*) and confirm a previously reported kidney eQTL
12 signal for an anti-sense RNA for *PSMD5* (15). The same SNP was also an eQTL for *PSMD5* itself in
13 both blood and kidney. *ASIC1* encodes the Acid Sensing Ion Channel Subunit 1 which may interact
14 (and be co-expressed) with ENaC subunits which mediate trans-epithelial Na transport in the kidney
15 (28). The comparatively small number of signals using kidney tissue (**Table 2 and Figure 1**) compared
16 to whole-blood could be due to the small sample size.

17 For genes implicated by eQTL information from whole-blood, we tested for enrichment of biological
18 pathways and gene ontologies (**Online Methods**). We noted enrichment of the 48 genes implicated
19 by 3 or 4 blood eQTL resources, **Table 2**, and a further 53 genes containing a non-synonymous
20 variant with $r^2 > 0.5$ with the top SNP (**Supplementary Table 13**), in pathways and ontology terms
21 related to actin and striated muscle (**Supplementary Tables 14 and 15, Online Methods**). Network
22 analysis using the same genes highlighted further GO terms relating to muscle function, particularly
23 cardiac muscle (**Online Methods, Supplementary Table 16**). We tested the overlap of 161 non-HLA
24 BP associated variants with DNase Hypersensitivity sites identified in the Roadmap and ENCODE cell
25 lines (**Online Methods**) and identified an overall enrichment in multiple cell and tissue types
26 including heart, kidney and smooth muscle (**Supplementary Figure 5**).

27 We next investigated these genes for potential suitable drug targets using the drug gene interaction
28 database (DGIdb) (29) and found 19 genes with known drug-gene interactions and 17 additional
29 genes with predicted druggability (**Supplementary Table 17**). These findings highlight potential
30 opportunities for novel therapeutic development and possible drug re-purposing, given that a large
31 number of the genes is already now targetable.

1

2 DISCUSSION

3 Enhanced discovery of BP loci increases the potential targets for therapeutic advances. After major
4 advances in the number of BP loci known over the last years and months, we report 8 novel signals
5 that implicate 5 regions of the genome not previously connected to blood pressure regulation.

6 Six of the 8 novel signals we report had not previously been reported. Two signals (in *EBF2* and
7 *NFKBIA*) have been suggested previously but without evidence for replication (18). For these two
8 signals we present, for the first time, stringent evidence of replication, confirming their relevance to
9 blood pressure genetics.

10 The path from signal to genes is the essential next step towards realizing the therapeutic potential of
11 a genetic locus and understanding the mechanisms of BP regulation. We have used several large
12 eQTL resources as a first step to realize this objective. As expected, we observed that even across
13 eQTL studies of the same tissue, there is limited overlap in experiment-wide significant signals
14 suggesting either biologic variability, technology-specific differences in coverage of genes, or the
15 possibility of false positive results despite stringent within-experiment significance thresholds. By
16 selecting genes only significant in at least three resources, we identified 48 genes as candidates for
17 further study. These results are limited by the availability of large eQTL resources for whole-blood
18 only, which precludes well-powered comparisons across tissue types, particularly as the origin of
19 blood pressure control is unlikely to be located in the blood. Enrichment and pathway analyses using
20 these genes, and genes containing a correlated functional variant, highlight the potential relevance
21 of muscular tissue and pathways, compatible with a vascular and cardiac origin of BP genetics,
22 extending previous evidence (15). We identify a number of potential drug targets in the pathways
23 identified, providing, together with previous results, a possible avenue for development of
24 pharmacological interventions modulating blood pressure.

25 In summary, our study reports novel BP association signals and reports new candidate BP genes,
26 contributing to the transition from variants to genes to explain BP variation.

1

2 MATERIALS AND METHODS

3 Studies Stage 1

4 Results from 54 independent European-ancestry studies, totaling 150,134 individuals, were included
 5 in the Stage 1 meta-analysis: AGES (n=3215), ARIC (n=9402), ASPS (n=828), B58C (n=6458), BHS
 6 (n=4492), CHS (n=3254), Cilento study (n=999), COLAUS (n=5404), COROGENE-CTRL (n=1878),
 7 CROATIA-Vis (n=945), CROATIA-Split (n=494), CROATIA-Korcula (n=867), EGCUT (n=6395), EGCUT2
 8 (n=1844), EPIC (n=2100), ERF (n=2617), Fenland (n=1357), FHS (n=8096), FINRISK-ctrl (n=861),
 9 FINRISK CASE (n=839), FUSION (n=1045), GRAPHIC (n=1010), H2000-CTRL (n=1078), HealthABC
 10 (n=1661), HTO (n=1000), INGI-CARL (n=456), INGI-FVG (n=746), INGI-VB (n=1775), IPM (n=300),
 11 KORAS3 (n=1590), KORAS4 (n=3748), LBC1921 (n=376), LBC1936 (n=800), LOLIPOP-EW610 (n=927),
 12 MESA (n=2678), MICROS (n=1148), MIGEN (n=1214), NESDA (n=2336), NSPHS (n=1005), NTR
 13 (n=1490), PHASE (n=4535), PIVUS (n=945), PROCARDIS (n=1652), SHIP (n=4068), ULSAM (n=1114),
 14 WGHS (n=23049), YFS (n=1987), ORCADES (n=1908), RS1 (n=5645), RS2 (n=2152), RS3 (n=3018),
 15 TRAILS (n=1262), TRAILS-CC (n=282) and TWINGENE (n=9789). Full study names and general study
 16 information is given in **Supplementary Table 1**.

17

18 Study-level genotyping and association testing

19 Three quantitative BP traits were analyzed: SBP, DBP, and PP (difference between SBP and DBP).
 20 Within each study, individuals known to be taking anti-hypertensive medication had 15 mmHg
 21 added to their raw SBP value and 10 mmHg added to their raw DBP values (30). A summary of BP
 22 phenotypes in each study is given in **Supplementary Table 2**. Association testing was undertaken
 23 according to a central analysis plan that specified the use of sex, age, age², and body mass index
 24 (BMI) as covariates and optional inclusion of additional covariates to account for population
 25 stratification (**Supplementary Table 3**). Trait residuals were calculated for each trait using a normal
 26 linear regression of the medication-adjusted trait values (mmHg) onto all covariates. The genotyping
 27 array, pre-imputation quality control filters, imputation software and association testing software
 28 used by each study are listed in **Supplementary Table 4**. All studies imputed to the 1000 Genomes
 29 Project Phase 1 integrated release version 3 [March 2012] all ancestry reference panel (31). Imputed
 30 genotype dosages were used to take into account uncertainty in the imputation. Association testing
 31 was carried out using linear regression of the trait residuals onto genotype dosages under an
 32 additive genetic model. Methods to account for relatedness within a study were used where
 33 appropriate (**Supplementary Table 3**). Results for all variants (SNPs and INDELs) were then returned
 34 to the central analysis group for further quality control checks and meta-analysis.

1 Stage 1 meta-analysis

2 Central quality control checks were undertaken across all results sets. This included checks to ensure
3 allele frequency consistency (across studies and with reference populations), checks of effect size
4 and standard error distributions (i.e. to highlight phenotype issues) and generation of quantile-
5 quantile (QQ) plots and genomic inflation factor lambdas to check for over- or under-inflation of test
6 statistics. Genomic control was applied (if $\lambda > 1$) at study-level. Variants with imputation quality
7 < 0.3 were excluded prior to meta-analysis. Inverse variance weighted meta-analysis was undertaken.
8 After meta-analysis, variants with a weighted minor allele frequency of less than 1 % or N effective
9 (product of study sample size and imputation quality summed across contributing studies) $< 60\%$
10 were then excluded and meta-analysis genomic control lambda calculated and used to adjust the
11 meta-analysis results.

12 Selection of regions for follow-up

13 For each trait, regions of association were selected by ranking variants by P value, recording the
14 variant with the lowest P value as a sentinel variant and then excluding all variants $\pm 500\text{kb}$ from
15 the sentinel and re-ranking the remaining variants. This was undertaken iteratively until all sentinel
16 variants representing 1Mb regions containing associations with $P < 10^{-6}$ had been identified. To
17 identify additional signals represented by secondary sentinel variants within 500kb of each of the
18 sentinel variants, GCTA (32) was used to run conditional analyses (conditioned on the first sentinel
19 variant) on each of the 1Mb regions using GWAS summary statistics and LD information from ARIC.
20 This was done both for putatively novel regions and for regions that had previously been reported. A
21 chi-squared test of heterogeneity of effect sizes across the 54 studies was run for each sentinel
22 variant and those with $P < 0.05$ for heterogeneity were excluded from further follow-up. Variants
23 with $P < 10^{-6}$ after conditioning on the sentinel SNP (novel or known) in the region and for which any
24 attenuation of the $-\log_{10} P$ value was less than 1.5 fold, were also taken forward for replication.

25 Studies stage 2

26 Data from 14 independent studies, totaling 87,360 individuals, and the first release of UK Biobank,
27 totaling 140,886 individuals, were combined to replicate the findings from stage 1 (i.e. totaling
28 228,245 individuals). Stage 2 study details, including full study names, are given in **Supplementary**
29 **Table 6** and included 3C-Dijon ($n=4061$), Airwave ($n=14023$), ASCOT-SC ($n=2462$), ASCOT-UK
30 ($n=3803$), BRIGHT ($n=1791$), GAPP ($n=1685$), GoDARTs ($n=7413$), GS:SFHS ($n=9749$), HCS ($n=2112$),
31 JUPITER ($n=8718$), LifeLines ($n=13376$), NEO ($n=5731$), TwinsUK ($n=4973$), UK Biobank-CMC
32 ($n=140,886$) and UKHLS ($n=7462$). Analysis was undertaken using the same methods as described for
33 Stage 1 studies. UK Biobank-CMC utilized a newer imputation reference panel than the other studies

1 and where a requested variant was not available, a proxy was used (next most significant P value
2 with linkage disequilibrium $r^2 > 0.6$ with original top variant). Results from all stage 2 studies were
3 meta-analyzed using inverse-variance weighted meta-analysis. Two of the variants, rs1048238 and
4 chr1:243458005:1, were not available in the largest study in Stage 2 (UK Biobank-CMC) and so proxy
5 variants were selected (based on P value and LD).

6 **Stage 1 + Stage 2 meta-analysis**

7 Following meta-analysis of stage 1 and stage 2 results, signals with a $P > 5 \times 10^{-8}$ were excluded. Of
8 the signals with a final $P < 5 \times 10^{-8}$, support for independent replication within the stage 2 studies only
9 was sought. Any signals which had $P < 5 \times 10^{-8}$ and evidence for independent replication in stage 2
10 alone, indicated by $P < 8.2 \times 10^{-4}$ (Bonferroni correction for 61 tests) were reported as novel signals of
11 association with BP. Any signals which were subsequently reported by other BP GWAS that were
12 accepted for publication during the time this analysis was ongoing, or signals for which
13 independence from another known signal could not be established, were removed from our list of
14 novel signals at this stage (**Supplementary Table 5**).

15 **Genotype and gene expression**

16 We searched for signals of association of genotype with gene expression for the 22 signals (including
17 8 novel) signals described in this study (**Supplementary Table 7**) and all signals reported prior to our
18 study (**Supplementary Table 10**) (3-17, 21) in 3 whole-blood data sets, 1 kidney data set and the
19 GTEx multiple tissue data resource, which included whole-blood (25). We selected cis signals of
20 association which were significant after controlling for 5% False Discovery Rate (FDR). The 3 whole-
21 blood eQTL data sets were the NHLBI Systems Approach to Biomarker Research in Cardiovascular
22 Disease initiative whole-blood eQTL resource (SABRe) (microarray, $n=5257$), NESDA-NTR
23 (microarray, $n=4896$), BIOS (RNAseq, $n=2116$). The whole-blood data from GTEx was based on data
24 from 338 samples. The kidney data set comprised 236 donor-kidney samples from 134 donors (27).
25 Full details of each data set can be found in the **Supplementary Material**.

26 **LD lookup**

27 The 1000 Genomes Project phase 3 release of variant calls was used (Feb. 20th, 2015), using 503
28 subjects of European ancestry(31). r^2 between the sentinel SNPs and all other bi-allelic SNPs within
29 the corresponding 2 Mb area was calculated using the Tabix and PLINK software package (v1.07) (33,
30 34). Annotation was performed using the ANNOVAR software package(35).

31 **Gene-based pathway analysis**

1 All genes identified in 3 or 4 of the whole-blood eQTL resources above (**Table 2**), and genes
2 containing a non-synonymous variant with $r^2 > 0.5$ with the sentinel variant (**Supplementary Table**
3 **13**), were tested for enrichment of biological pathways and gene ontology terms using
4 ConsensusPathDB (36) using a FDR < 5% cut-off. Enriched pathways and GO terms containing genes
5 only implicated by a single BP-associated variant were not reported.

6 **Network analysis**

7 To construct a functional association network, we combined two prioritized candidate gene sets into
8 a single query gene set as (i) genes mapping to the non-synonymous SNPs (nsSNPs) in high LD
9 ($r^2 > 0.5$) with the corresponding sentinel BP associated SNP, and (ii) genes with eQTL evidence from 3
10 or 4 of the blood eQTL resources. Three sentinel SNPs (rs185819, rs926552 and rs805303) mapping
11 to the HLA region on chromosome 6 were excluded from downstream analyses. The single query
12 gene set was then used as input for the functional network analysis(37). We used the Cytoscape (38)
13 software platform extended by the GeneMANIA(39) plugin (Data Version: 8/12/2014)(40). All the
14 genes in the composite network, either from the query or the resulting gene sets, were then used
15 for functional enrichment analysis against Gene Ontology terms (GO terms) (41) to identify the most
16 relevant GO terms using the same plugin (40).

17 **DNase1 Hypersensitivity overlap enrichment across tissue and cell-types**

18 The Functional element Overlap analysis of the Results of Genome Wide Association Study (GWAS)
19 Experiments (Forge tool v1.1)(42) was used to test for enrichment of overlap of BP SNPs in tissues
20 and cell lines from the Roadmap and ENCODE projects. All 164 SNPs were entered and 143 were
21 included in the analysis. SNPs from 9 commonly used GWAS arrays were used to select background
22 sets of SNPs for comparison and 10,000 background repetitions were run. A Z-score threshold of
23 ≥ 3.39 (estimated false positive rate of 0.5%) was used to declare significance.

24 **Drug-gene interactions**

25 Genes used for pathway and gene ontology enrichment analyses were further investigated for
26 potential druggable targets using the drug gene interaction database (DGIdb). The known drug-gene
27 interactions search parameters were set investigate all 15 databases in DGIdb and include all types
28 of interactions. The analysis performed for druggability prediction included all 9 databases
29 exclusively inspecting expert curated data only.

30

1 **NOTE:** Supplementary Information and Source Data files are available in the online version of the
2 paper.

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5 funding sources is provided in the **Supplementary Material**.

6 **CONFLICTS OF INTERESTS**

7 The authors declare competing financial interests (see corresponding section in the Supplementary
8 Material).
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1 **FIGURE LEGENDS**

2 **Figure 1: Overlap of eQTL evidence from four whole-blood and one kidney resource**

3 The figure indicates overlap of evidence for eQTLs from four whole-blood studies (SABRe, NESDA-
4 NTR, BIOS, and GTEx) and from one kidney resource (TransplantLines). Every colored line indicates
5 that this gene was analysis-wide significant in a given resource (see **Online Methods**). Only genes
6 identified by at least two resources are shown. The genes are sorted by genomic position on the y-
7 axis.

8

1 **FIGURES**

2 **Figure 1**

3

4

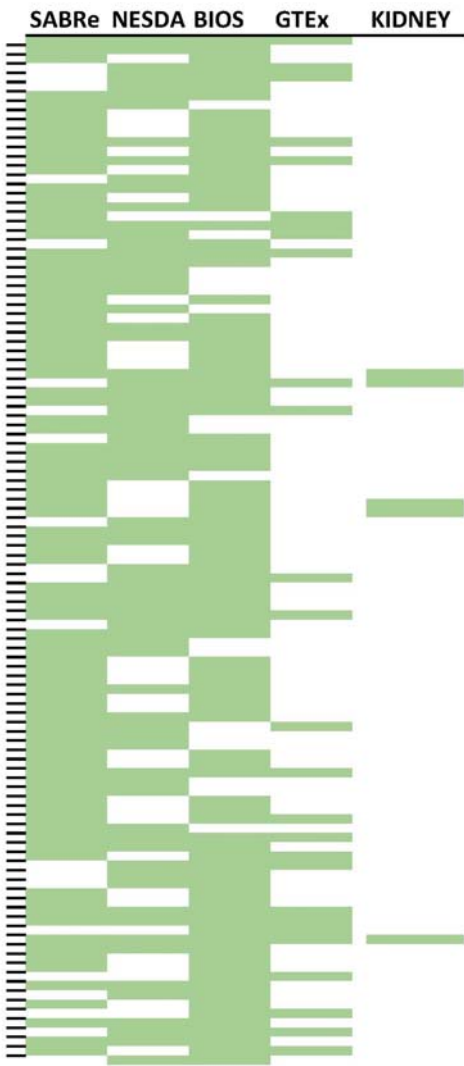


Table 1. Novel genome-wide significant signals of association

Results from stage 1 and stage 2, and the meta-analysis of stage 1 and stage 2, for all novel genome-wide significant signals of association. *P* values of association for all 3 traits from a meta-analysis of stages 1 and 2 are also presented. Genome-wide significant *P* values ($P < 5 \times 10^{-8}$) are in bold. Abbreviations: CAF: coded allele frequency se: standard error, Neff: effective sample size. [#]Novel signal at previously reported locus. ¹For intragenic variants the nearest genes are listed, all other variants are intronic unless indicated otherwise; ns= non-synonymous, s=synonymous, UTR= Untranslated Region. Results from proxy SNPs are indicated by (**proxy**); rs848309 was a proxy SNP for rs1048238 and rs10926988 was a proxy SNP for chr1:243458005:l.

		Results for most significant trait									Stage 1 + stage 2 meta-analysis P values for all traits		
		Stage 1		Stage 2			Stage 1+ stage 2						
Variant ID (noncoded/coded allele) chr:position, Nearest gene(s)(type ¹)	CAF	Beta (se)	P value	Neff	Beta (se)	P value	Neff	Beta (se)	P value	Neff	SBP	DBP	PP
SBP													
rs1048238 (C/T) 1:16341649, <i>HSPB7</i> (3'UTR)	0.571	0.366 (0.074)	8.09E-07	140299	NA	NA	NA	NA	NA	NA	NA	NA	NA
rs848309(proxy) (T/C) 1:16308447	0.567	0.347 (0.072)	1.70E-06	146755	0.347 (0.071)	9.10E-07	140462	0.347 (0.051)	7.07E-12	287217	7.07E-12	1.07E-10	5.48E-06
[#] rs185819 (T/C) 6:32,050,067, <i>TNXB</i> (ns)	0.513	0.534 (0.073)	1.93E-13	142397	0.277 (0.053)	1.49E-07	221748	0.365 (0.043)	1.04E-17	364144	1.04E-17	2.24E-11	8.50E-11
rs6557876 (C/T) 8:25,900,675, <i>EBF2</i>	0.252	-0.411 (0.084)	8.50E-07	143653	-0.350 (0.060)	5.66E-09	225803	-0.371 (0.049)	2.85E-14	369457	2.85E-14	2.50E-10	1.51E-09
rs35783704 (G/A) 8:105,966,258, <i>LRP12/ZFPM2</i>	0.109	-0.609 (0.121)	4.96E-07	133924	-0.310 (0.089)	4.78E-04	215528	-0.414 (0.072)	7.08E-09	349452	7.08E-09	1.60E-06	2.92E-06
rs73099903 (C/T) 12:53,440,779, <i>LOC283335</i>	0.074	0.768 (0.143)	8.05E-08	136064	0.396 (0.098)	5.32E-05	207253	0.515 (0.081)	1.95E-10	343318	1.95E-10	4.53E-06	5.46E-06
rs8904 (G/A) 14:35,871,217, <i>NFKB1A</i> (3' UTR)	0.375	0.377 (0.076)	6.76E-07	140424	0.278 (0.054)	2.31E-07	224771	0.311 (0.044)	1.31E-12	365195	1.31E-12	1.13E-04	3.44E-12
rs57927100 (C/G) 17:75,317,300, <i>SEPT9</i>	0.258	-0.489 (0.086)	1.10E-08	136624	-0.220 (0.061)	3.12E-04	210563	-0.310 (0.050)	4.04E-10	347188	4.04E-10	1.16E-10	1.81E-05
DBP													
rs9710247 (A/G) 19:40,760,449, <i>AKT2</i>	0.447	0.252 (0.051)	8.11E-07	109695	0.129 (0.032)	5.76E-05	198332	0.164 (0.027)	1.61E-09	308028	3.82E-02	1.61E-09	5.03E-01

Table 2: BP associated SNPs associated with expression of the same gene across 4 or 3 independent whole-blood eQTL resources and the kidney resource. Signals of association of SNP genotype and gene expression in other non-blood tissues in GTEx and in kidney are also indicated. Blood dataset order: (i) SABRe, (ii) NESDA-NTR, (iii) BIOS, (iv) GTEx (whole-blood). Top eQTL: Top GWAS SNP is top eQTL SNP (or in high LD, $r^2 > 0.9$, with top eQTL SNP) in at least one data set. eQTL signal previously reported: Genes for which eQTL signals have been previously reported for that sentinel SNP(15-17). For full list, see **Supplementary Table 12**.

Sentinel SNP	Chr	Position	Gene	Blood data sets	Top eQTL	Signal in other tissue(s) in GTEx	Signal in kidney	eQTL signal previously reported
Signal in 4 whole-blood eQTL resources								
rs17367504	1	11862778	<i>CLCN6</i>	YYYY		Y		Y
rs2169137	1	204497913	<i>MDM4</i>	YYYY	Y	Y		Y
rs10926988	1	243483279	<i>SDCCAG8</i>	YYYY		Y		
rs319690	3	47927484	<i>MAP4</i>	YYYY	Y	Y		Y
rs12521868	5	131784393	<i>SLC22A5</i>	YYYY		Y		
rs900145	11	13293905	<i>ARNTL</i>	YYYY		Y		Y
rs1060105	12	123806219	<i>CDK2AP1</i>	YYYY	Y	Y	Y	
rs1378942	15	75077367	<i>SCAMP2</i>	YYYY				
rs1126464	16	89704365	<i>CHMP1A</i>	YYYY		Y		Y
rs1126464	16	89704365	<i>FANCA</i>	YYYY				Y
rs12946454	17	43208121	<i>DCAKD</i>	YYYY		Y	Y	Y
Signal in 3 (out of 4) whole-blood eQTL resources								
rs17367504	1	11862778	<i>MTHFR</i>	YYYN		Y		Y
rs871524	1	38411445	<i>FHL3</i>	NYYY		Y		
rs871524	1	38411445	<i>SF3A3</i>	NYYY		Y		
rs4660293	1	40028180	<i>PABPC4</i>	YYYN	Y	Y		Y
rs6749447	2	169041386	<i>STK39</i>	YYYN	Y			
rs347591	3	11290122	<i>ATG7</i>	YYYN		Y		
rs319690	3	47927484	<i>ZNF589</i>	YYNY		Y		
rs12521868	5	131784393	<i>SLC22A4</i>	YYYN		Y		
rs1563788	6	43308363	<i>CRIP3</i>	YYYN	Y			Y
rs10943605	6	79655477	<i>PHIP</i>	YYYN	Y	Y		Y
rs4728142	7	128573967	<i>IRF5</i>	NYYY		Y	Y	Y
rs4728142	7	128573967	<i>TNPO3</i>	YYYN			Y	
rs2898290	8	11433909	<i>BLK</i>	YYYN		Y		
rs2898290	8	11433909	<i>FAM167A</i>	NYYY		Y		
rs2898290	8	11433909	<i>FDFT1</i>	YYYN		Y		
rs2071518	8	120435812	<i>NOV</i>	YYYN		Y		
rs76452347	9	35906471	<i>TPM2</i>	YYYN				

rs10760117	9	123586737	<i>MEGF9</i>	YYYN		Y		Y
rs4494250	10	96563757	<i>HELLS</i>	YYYN				Y
rs11191548	10	104846178	<i>NT5C2</i>	YYYN	Y			
rs661348	11	1905292	<i>TNNT3</i>	NYYY		Y		
rs2649044	11	9763969	<i>SBF2</i>	YYYN				
rs2649044	11	9763969	<i>SWAP70</i>	YYYN	Y	Y		?
rs7129220	11	10350538	<i>ADM</i>	YYYN				Y
rs7103648	11	47461783	<i>MYBPC3</i>	YYYN				
rs3741378	11	65408937	<i>CTSW</i>	YYYN				
rs7302981	12	50537815	<i>LIMA1</i>	YYYN				Y
rs7302981	12	50537815	<i>ATF1</i>	YNYN		Y		
rs1036477	15	48914926	<i>FBN1</i>	YNYN				
rs1378942	15	75077367	<i>CSK</i>	YYYN	Y	Y		Y
rs1378942	15	75077367	<i>MPI</i>	NYYY		Y		
rs1378942	15	75077367	<i>ULK3</i>	YNYN		Y		Y
rs12946454	17	43208121	<i>NMT1</i>	YYYN				Y
rs2304130	19	19789528	<i>GATAD2A</i>	YYYN				
rs867186	20	33764554	<i>EIF6</i>	NYYY		Y		
rs6095241	20	47308798	<i>PREX1</i>	YYYN				
rs9306160	21	45107562	<i>RRP1B</i>	YNYN	Y	Y		

AUTHORS / AFFILIATIONS / CONTRIBUTIONS / ACKNOWLEDGMENTS

Louise V. Wain¹, Ahmad Vaez^{2,3}, Rick Jansen⁴, Roby Joehanes^{5,6}, Peter J. van der Most², A. Mesut Erzurumluoglu¹, Paul O'Reilly⁷, Claudia P. Cabrera^{8,9}, Helen R. Warren^{8,9}, Lynda M. Rose¹⁰, Germaine C. Verwoert¹¹, Jouke-Jan Hottenga¹², Rona J. Strawbridge^{13,14}, Tonu Esko^{15,16,17}, Dan E. Arking¹⁸, Shih-Jen Hwang^{19,20}, Xiuqing Guo²¹, Zoltan Kutalik^{22,23}, Stella Trompet^{24,25}, Nick Shrine¹, Alexander Teumer^{26,27}, Janina S. Ried²⁸, Joshua C. Bis²⁹, Albert V. Smith^{30,31}, Najaf Amin³², Ilja M. Nolte², Leo-Pekka Lyytikäinen^{33,34}, Anubha Mahajan³⁵, Nicholas J. Wareham³⁶, Edith Hofer^{37,38}, Peter K. Joshi³⁹, Kati Kristiansson⁴⁰, Michela Traglia⁴¹, Aki S. Havulinna⁴⁰, Anuj Goel^{42,35}, Mike A. Nalls^{43,44}, Siim Sõber⁴⁵, Dragana Vuckovic^{46,47}, Jian'an Luan³⁶, Fabiola Del Greco M.⁴⁸, Kristin L. Ayers⁴⁹, Jaume Marrugat⁵⁰, Daniela Ruggiero⁵¹, Lorna M. Lopez^{52,53,54}, Teemu Niiranen⁴⁰, Stefan Enroth⁵⁵, Anne U. Jackson⁵⁶, Christopher P. Nelson^{57,58}, Jennifer E. Huffman⁵⁹, Weihua Zhang^{60,61}, Jonathan Marten⁶², Ilaria Gandin⁴⁷, Sarah E Harris^{52,63}, Tatijana Zemonik⁶⁴, Yingchang Lu⁶⁵, Evangelos Evangelou^{60,66}, Nabi Shah^{67,68}, Martin H. de Borst⁶⁹, Massimo Mangino^{70,71}, Bram P. Prins⁷², Archie Campbell^{73,74}, Ruifang Li-Gao⁷⁵, Ganesh Chauhan^{76,77}, Christopher Oldmeadow⁷⁸, Gonçalo Abecasis⁷⁹, Maryam Abedi⁸⁰, Caterina M. Barbieri⁴¹, Michael R. Barnes^{8,9}, Chiara Batini¹, John Beilby^{81,82,83}, BIOS Consortium⁸⁴, Tineka Blake¹, Michael Boehnke⁵⁶, Erwin P. Bottinger⁶⁵, Peter S. Braund^{57,58}, Morris Brown^{8,9}, Marco Brumat⁴⁷, Harry Campbell³⁹, John C. Chambers^{60,61,85}, Massimiliano Cocca⁴⁷, Francis Collins⁸⁶, John Connell⁸⁷, Heather J. Cordell⁸⁸, Jeffrey J. Damman⁸⁹, Gail Davies^{52,90}, Eco J. de Geus¹², Renée de Mutsert⁷⁵, Joris Deelen⁹¹, Yusuf Demirkale⁹², Alex S.F. Doney⁶⁷, Marcus Dörr^{93,27}, Martin Farrall^{42,35}, Teresa Ferreira³⁵, Mattias Fränberg^{13,14,94}, He Gao⁶⁰, Vilmantas Giedraitis⁹⁵, Christian Gieger⁹⁶, Franco Giulianini¹⁰, Alan J. Gow^{52,97}, Anders Hamsten^{13,14}, Tamara B. Harris⁹⁸, Albert Hofman^{11,99}, Elizabeth G. Holliday⁷⁸, Jennie Hui^{81,82,100,83}, Marjo-Riitta Jarvelin^{101,102,103,104}, Åsa Johansson⁵⁵, Andrew D. Johnson^{6,105}, Pekka Jousilahti⁴⁰, Antti Jula⁴⁰, Mika Kähönen^{106,107}, Sekar Kathiresan^{108,109,110}, Kay-Tee Khaw¹¹¹, Ivana Kolcic¹¹², Seppo Koskinen⁴⁰, Claudia Langenberg³⁶, Marty Larson⁶, Lenore J. Launer⁹⁸, Benjamin Lehne⁶⁰, David C.M. Liewald^{52,90}, Lifelines Cohort Study¹¹³, Li Lin¹¹⁴, Lars Lind¹¹⁵, François Mach¹¹⁴, Chrysovalanto Mamasoula¹¹⁶, Cristina Menni⁷⁰, Borbala Mifsud⁸, Yuri Milaneschi¹¹⁷, Anna Morgan⁴⁷, Andrew D. Morris¹¹⁸, Alanna C. Morrison¹¹⁹, Peter J. Munson⁹², Priyanka Nandakumar¹⁸, Quang Tri Nguyen⁹², Teresa Nutile⁵¹, Albertine J. Oldehinkel¹²⁰, Ben A. Oostra³², Elin Org¹⁵, Sandosh Padmanabhan^{121,74}, Aarno Palotie¹²², Guillaume Paré¹²³, Alison Pattie⁹⁰, Brenda W.J.H. Penninx¹¹⁷, Neil Poulter¹²⁴, Peter P. Pramstaller^{48,125,126}, Olli T. Raitakari^{127,128}, Meixia Ren^{8,129}, Kenneth Rice¹³⁰, Paul M. Ridker^{10,131}, Harriette Riese¹²⁰, Samuli Ripatti¹²², Antonietta Robino¹³², Jerome I. Rotter¹³³, Igor Rudan³⁹, Yasaman Saba¹³⁴, Aude Saint Pierre^{48,135}, Cinzia F. Sala⁴¹, Antti-Pekka Sarin¹²², Reinhold Schmidt³⁷, Rodney Scott^{78,136,137}, Marc A. Seelen⁶⁹, Denis C. Shields¹³⁸, David Siscovick¹³⁹, Rossella Sorice^{51,140}, Alice Stanton¹⁴¹, David J. Stott¹⁴², Johan Sundström¹¹⁵, Morris Swertz¹⁴³, Kent D.

Taylor^{144,145}, Simon Thom¹⁴⁶, Ioanna Tzoulaki⁶⁰, Christophe Tzourio^{76,77,147}, André G. Uitterlinden^{11,148}, Understanding Society Scientific group⁸⁴, Uwe Vöcker^{149,27}, Peter Vollenweider¹⁵⁰, Sarah Wild³⁹, Gonneke Willemssen¹², Alan F. Wright⁶², Jie Yao²¹, Sébastien Thériault¹²³, David Conen¹⁵¹, Attia John^{78,136,137}, Peter Sever¹⁵², Stéphanie Debette^{76,77,153}, Dennis O. Mook-Kanamori^{75,154}, Eleftheria Zeggini⁷², Tim D. Spector⁷⁰, Pim van der Harst¹⁵⁵, Colin N.A. Palmer⁶⁷, Anne-Claire Vergnaud⁶⁰, Ruth J.F. Loos^{36,156,157}, Ozren Polasek¹¹², John M. Starr^{52,158}, Giorgia Grotto^{47,46}, Caroline Hayward^{159,74}, Jaspal S. Kooner^{160,61,85}, Cecilia M. Lindgren^{17,35}, Veronique Vitart⁵⁹, Nilesh J. Samani^{57,58}, Jaakko Tuomilehto^{161,162,163,164}, Ulf Gyllenstein⁵⁵, Paul Knekt⁴⁰, Ian J. Deary^{52,90}, Marina Ciullo^{51,140}, Roberto Elosua⁵⁰, Bernard D. Keavney¹⁶⁵, Andrew A. Hicks⁴⁸, Robert A. Scott³⁶, Paolo Gasparini^{46,47}, Maris Laan^{45,166}, YongMei Liu¹⁶⁷, Hugh Watkins^{42,35}, Catharina A. Hartman¹²⁰, Veikko Salomaa⁴⁰, Daniela Toniolo⁴¹, Markus Perola^{40,122,168}, James F. Wilson^{39,62}, Helena Schmidt^{134,169}, Jing Hua Zhao³⁶, Terho Lehtimäki^{33,34}, Cornelia M. van Duijn³², Vilmundur Gudnason^{30,31}, Bruce M. Psaty^{29,170,171,172}, Annette Peters²⁸, Rainer Rettig¹⁷³, Alan James^{174,175}, J Wouter Jukema²⁴, David P. Strachan¹⁷⁶, Walter Palmas¹⁷⁷, Andres Metspalu¹⁵, Erik Ingelsson^{178,179}, Dorret I. Boomsma¹², Oscar H. Franco¹¹, Murielle Bochud²², Christopher Newton-Cheh^{180,108,110,17}, Patricia B. Munroe^{8,9}, Paul Elliott¹⁰⁴, Daniel I. Chasman^{10,131}, Aravinda Chakravarti¹⁸, Joanne Knight¹⁸¹, Andrew P. Morris^{182,35}, Daniel Levy^{183,20}, Martin D. Tobin¹, Harold Snieder^{2*}, Mark J. Caulfield^{8,9*}, Georg B. Ehret^{18,114*}

*: contributing equally

Corresponding authors: Louise V. Wain (louisewain@le.ac.uk) and Georg B. Ehret (georg@rhon.ch)

AFFILIATIONS

1. Department of Health Sciences, University of Leicester, Leicester LE1 7RH, UK
2. Department of Epidemiology, University of Groningen, University Medical Center Groningen, Hanzeplein 1, 9713 GZ Groningen, The Netherlands
3. Research Institute for Primordial Prevention of Non-communicable Disease, Isfahan University of Medical Sciences, Isfahan, Iran
4. Department of Psychiatry, VU University Medical Center, Neuroscience Campus Amsterdam, Amsterdam, The Netherlands
5. Hebrew SeniorLife, Harvard Medical School, 1200 Centre Street Room #609, Boston, MA 02131, USA
6. National Heart, Lung and Blood Institute's Framingham Heart Study, Framingham, MA 01702, USA
7. Institute of Psychiatry, Psychology and Neuroscience, King's College London, London SE5 8AF, UK
8. Clinical Pharmacology, William Harvey Research Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, EC1M 6BQ, UK
9. NIHR Barts Cardiovascular Biomedical Research Unit, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, EC1M 6BQ, UK
10. Division of Preventive Medicine, Brigham and Women's Hospital, Boston MA 02215, USA

11. Department of Epidemiology, Erasmus MC, Rotterdam, 3000CA, The Netherlands
12. Department of Biological Psychology, Vrije Universiteit, Amsterdam, EMGO+ institute, VU University medical center, Amsterdam, The Netherlands
13. Cardiovascular Medicine Unit, Department of Medicine Solna, Karolinska Institutet, Stockholm, 17176, Sweden
14. Centre for Molecular Medicine, Karolinska Universitetsjukhuset, Solna, 171 76, Sweden
15. Estonian Genome Center, University of Tartu, Tartu, 51010, Estonia
16. Divisions of Endocrinology/Children's Hospital, Boston, MA 02115, USA
17. Broad Institute of Harvard and MIT, Cambridge, MA 02139 USA
18. Center for Complex Disease Genomics, McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University School of Medicine, Baltimore, MD 21205, USA
19. The Population Science Branch, Division of Intramural Research, National Heart Lung and Blood Institute national Institute of Health, Bethesda, MD 20892, USA
20. The Framingham Heart Study, Framingham MA 01702, USA
21. The Institute for Translational Genomics and Population Sciences, Department of Pediatrics, LABioMed at Harbor-UCLA Medical Center, 1124 W. Carson Street, Torrance, CA 90502, USA
22. Institute of Social and Preventive Medicine, Lausanne University Hospital, Route de la Corniche 10, 1010 Lausanne, Switzerland
23. Swiss Institute of Bioinformatics, Lausanne, Switzerland
24. Department of Cardiology, Leiden University Medical Center, Leiden, 2300RC, The Netherlands
25. Department of Gerontology and Geriatrics, Leiden University Medical Center, Leiden, 2300RC, The Netherlands
26. Institute for Community Medicine, University Medicine Greifswald, Greifswald, 17475, Germany
27. DZHK (German Centre for Cardiovascular Research), partner site Greifswald, Greifswald, 17475, Germany
28. Institute of Epidemiology II, Helmholtz Zentrum München, Neuherberg 85764, Germany
29. Cardiovascular Health Research Unit, Department of Medicine, University of Washington, Seattle, WA 98101, USA
30. Icelandic Heart Association, Kopavogur, Iceland
31. Faculty of Medicine, University of Iceland, Reykjavik, Iceland
32. Genetic Epidemiology Unit, Department of Epidemiology, Erasmus MC, Rotterdam, 3000CA, The Netherlands
33. Department of Clinical Chemistry, Fimlab Laboratories, Tampere 33520, Finland
34. Department of Clinical Chemistry, Faculty of Medicine and Life Sciences, University of Tampere, Tampere 33014, Finland
35. Wellcome Trust Centre for Human Genetics, University of Oxford, Roosevelt Drive, Oxford OX3 7BN, UK
36. MRC Epidemiology Unit, University of Cambridge School of Clinical Medicine, Institute of Metabolic Science, Cambridge Biomedical Campus, Cambridge, CB2 0QQ, UK
37. Clinical Division of Neurogeriatrics, Department of Neurology, Medical University Graz, Auenbruggerplatz 22, 8036 Graz, Austria
38. Institute of Medical Informatics, Statistics and Documentation, Medical University Graz, Auenbruggerplatz 2, 8036 Graz, Austria
39. Centre for Global Health Research, Usher Institute of Population Health Sciences and Informatics, University of Edinburgh EH89AG, Scotland, UK

40. Department of Health, National Institute for Health and Welfare (THL), Helsinki, Finland
41. Division of Genetics and Cell Biology, San Raffaele Scientific Institute, 20132 Milano, Italy
42. Division of Cardiovascular Medicine, Radcliffe Department of Medicine, University of Oxford, Oxford, OX3 9DU, UK
43. Laboratory of Neurogenetics, National Institute on Aging, NIH, Bethesda, 20892, USA
44. Kelly Services, Rockville, MD, USA
45. Human Molecular Genetics Research Group, Institute of Molecular and Cell Biology, University of Tartu, Riia St.23, 51010 Tartu, Estonia
46. Experimental Genetics Division, Sidra Medical and Research Center, PO Box 26999, Doha, Qatar
47. Department of Medical, Surgical and Health Sciences, University of Trieste, Strada di Fiume 447, Trieste, 34100, Italy
48. Center for Biomedicine, European Academy Bozen/Bolzano (EURAC), Bolzano, Italy - Affiliated Institute of the University of Lübeck, Germany
49. Department of Genetics and Genomic Sciences, Icahn School of Medicine at Mount Sinai, New York, NY, USA
50. Cardiovascular Epidemiology and Genetics, IMIM. Dr Aiguader 88, Barcelona, 08003, Spain
51. Institute of Genetics and Biophysics A. Buzzati-Traverso, CNR, via P. Castellino 111, 80131 Napoli, Italy
52. Centre for Cognitive Ageing and Cognitive Epidemiology, University of Edinburgh, 7 George Square, Edinburgh EH8 9JZ, UK
53. Department of Psychiatry, Royal College of Surgeons in Ireland, Education and Research Centre, Beaumont Hospital, Dublin, Ireland
54. University College Dublin, UCD Conway Institute, Centre for Proteome Research, UCD, Belfield, Dublin, Ireland
55. Department of Immunology, Genetics and Pathology, Uppsala Universitet, Science for Life Laboratory, Husargatan 3, Uppsala, SE-75108, Sweden
56. Department of Biostatistics and Center for Statistical Genetics, University of Michigan, Ann Arbor, MI 48109, USA
57. Department of Cardiovascular Sciences, University of Leicester, Leicester LE3 9QP, UK
58. NIHR Leicester Cardiovascular Biomedical Research Unit, Glenfield Hospital, Leicester LE3 9QP, UK
59. MRC Human Genetics Unit, IGMM, University of Edinburgh, Western General Hospital, Edinburgh, EH4 2XU Scotland, UK
60. Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, London W2 1PG, United Kingdom
61. Department of Cardiology, Ealing Hospital NHS Trust, Uxbridge Road, Southall, Middlesex UB1 3EU, UK
62. MRC Human Genetics Unit, Institute of Genetics and Molecular Medicine, University of Edinburgh, Western General Hospital, Crewe Road, Edinburgh, EH4 2XU, UK
63. Medical Genetics Section, University of Edinburgh Centre for Genomic and Experimental Medicine and MRC Institute of Genetics and Molecular Medicine, Western General Hospital, Crewe Road, Edinburgh EH4 2XU, UK
64. Department of Biology, Faculty of Medicine, University of Split, Croatia
65. The Charles Bronfman Institute for Personalized Medicine, Icahn School of Medicine at Mount Sinai, New York, NY 10029, USA

66. Department of Hygiene and Epidemiology, University of Ioannina Medical School, Ioannina, 45110, Greece
67. Medical Research Institute, University of Dundee, Ninewells Hospital and Medical School, Dundee, DD1 9SY, Scotland, UK
68. Department of Pharmacy, COMSATS Institute of Information Technology, Abbottabad, 22060, Pakistan
69. Department of Internal Medicine, Division of Nephrology, University of Groningen, University Medical Center Groningen, PO Box 30001, 9700 RB Groningen, The Netherlands
70. Department of Twin Research and Genetic Epidemiology, King's College London, Lambeth Palace Rd, London, SE1 7EH, UK
71. National Institute for Health Research Biomedical Research Centre, London SE1 9RT, UK
72. Department of Human Genetics, Wellcome Trust Sanger Institute, CB10 1HH, United Kingdom
73. Medical Genetics Section, Centre for Genomic and Experimental Medicine, Institute of Genetics and Molecular Medicine, University of Edinburgh, Edinburgh EH4 2XU, UK
74. Generation Scotland, Centre for Genomic and Experimental Medicine, University of Edinburgh, Edinburgh, EH4 2XU, UK
75. Department of Clinical Epidemiology, Leiden University Medical Center, Leiden, The Netherlands
76. INSERM U 1219, Bordeaux Population Health center, Bordeaux, France
77. Bordeaux University, Bordeaux, France
78. Hunter Medical Research Institute, New Lambton, NSW 2305, Australia
79. Center for Statistical Genetics, Dept. of Biostatistics, SPH II, 1420 Washington Heights, Ann Arbor, MI 48109-2029, USA
80. Department of Genetics and Molecular Biology, Isfahan University of Medical Sciences, Isfahan, Iran
81. Busselton Population Medical Research Institute, Western Australia
82. PathWest Laboratory Medicine of Western Australia, NEDLANDS, Western Australia
83. School of Pathology and Laboratory Medicine, The University of Western Australia, NEDLANDS, Western Australia
84. For a complete list of contributing authors, please see supplementary material.
85. Imperial College Healthcare NHS Trust, London, UK
86. Medical Genomics and Metabolic Genetics Branch, National Human Genome Research Institute, NIH, Bethesda, MD 20892, USA
87. University of Dundee, Ninewells Hospital & Medical School, Dundee, DD1 9SY, UK
88. Institute of Genetic Medicine, Newcastle University, Newcastle upon Tyne, UK
89. Department of Pathology, Amsterdam Medical Center, Meibergdreef 9, 1105 AZ, Amsterdam, The Netherlands
90. Department of Psychology, University of Edinburgh, 7 George Square, Edinburgh, EH8 9JZ, UK
91. Department of Molecular Epidemiology, Leiden University Medical Center, Leiden, 2300RC, The Netherlands
92. Center for Information Technology, NIH, USA
93. Department of Internal Medicine B, University Medicine Greifswald, Greifswald, 17475, Germany
94. Department of Numerical Analysis and Computer Science, Stockholm University, Lindstedtsvägen 3, Stockholm, 100 44, Sweden

95. Department of Public Health and Caring Sciences, Geriatrics, Uppsala 752 37, Sweden
96. Helmholtz Zentrum Muenchen, Deutsches Forschungszentrum fuer Gesundheit und Umwelt (GmbH), Ingolstaedter Landstr. 1, 85764 Neuherberg, München, Germany
97. Department of Psychology, School of Life Sciences, Heriot-Watt University, Edinburgh, EH14 4AS, UK
98. Intramural Research Program, Laboratory of Epidemiology, Demography, and Biometry, National Institute on Aging, USA
99. Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, MA 02115, USA
100. School of Population and Global Health, The University of Western Australia, NEDLANDS, Western Australia
101. Center For Life-course Health Research, P.O. Box 5000, FI-90014 University of Oulu, Finland
102. Biocenter Oulu, P.O. Box 5000, Aapistie 5A, FI-90014 University of Oulu, Finland
103. Unit of Primary Care, Oulu University Hospital, Kajaanintie 50, P.O. Box 20, FI-90220 Oulu, 90029 OYS, Finland
104. MRC-PHE Centre for Environment and Health, Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, Norfolk Place, W2 1PG London, UK
105. National Heart, Lung and Blood Institute, Cardiovascular Epidemiology and Human Genomics Branch, Bethesda, MD 20814, USA
106. Department of Clinical Physiology, Tampere University Hospital, Tampere 33521, Finland
107. Department of Clinical Physiology, Faculty of Medicine and Life Sciences, University of Tampere, Tampere 33014, Finland
108. Cardiovascular Research Center, Massachusetts General Hospital, Boston, MA 02114, USA
109. Center for Human Genetics, Massachusetts General Hospital, 185 Cambridge Street, Boston, MA 02114, USA
110. Program in Medical and Population Genetics, Broad Institute, 7 Cambridge Center, Cambridge, MA 02142, USA
111. Department of Public Health and Primary Care, Institute of Public Health, University of Cambridge, Cambridge CB2 2SR, UK
112. Department of Public Health, Faculty of Medicine, University of Split, Croatia
113. See complete listing of contributors in the Supplementary Material.
114. Cardiology, Department of Medicine, Geneva University Hospital, Rue Gabrielle-Perret-Gentil 4, 1211 Geneva 14, Switzerland
115. Department of Medical Sciences, Cardiovascular Epidemiology, Uppsala University, Uppsala 751 85, Sweden
116. Institute of Health and Society, Newcastle University, Newcastle upon Tyne, UK
117. Department of Psychiatry, EMGO Institute for Health and Care Research, VU University Medical Center, A.J. Ernststraat 1187, 1081 HL Amsterdam, The Netherlands
118. School of Molecular, Genetic and Population Health Sciences, University of Edinburgh, Medical School, Teviot Place, Edinburgh, EH8 9AG, Scotland, UK
119. Department of Epidemiology, Human Genetics and Environmental Sciences, School of Public Health, University of Texas Health Science Center at Houston, 1200 Pressler St., Suite 453E, Houston, TX 77030, USA
120. Interdisciplinary Center Psychopathology and Emotion Regulation (IPCE), University of Groningen, University Medical Center Groningen, Hanzeplein 1, PO Box 30001, 9700 RB Groningen, The Netherlands

121. British Heart Foundation Glasgow Cardiovascular Research Centre, Institute of Cardiovascular and Medical Sciences, College of Medical, Veterinary and Life Sciences, University of Glasgow, Glasgow G12 8TA, UK
122. Institute for Molecular Medicine Finland (FIMM), University of Helsinki, Helsinki, Finland
123. Department of Pathology and Molecular Medicine, McMaster University, 1280 Main St W, Hamilton, L8S 4L8, Canada
124. School of Public Health, Imperial College London, W2 1PG, UK
125. Department of Neurology, General Central Hospital, Bolzano, Italy
126. Department of Neurology, University of Lübeck, Lübeck, Germany
127. Department of Clinical Physiology and Nuclear Medicine, Turku University Hospital, Turku 20521, Finland
128. Research Centre of Applied and Preventive Cardiovascular Medicine, University of Turku, Turku 20014, Finland
129. Department of Cardiology, Fujian Provincial Hospital, Fujian Medical University, Fuzhou 350001, China
130. Department of Biostatistics University of Washington, Seattle, WA 98101, USA
131. Harvard Medical School, Boston MA, USA
132. Institute for Maternal and Child Health IRCCS Burlo Garofolo, Via dell'Istria 65, Trieste, 34200, Italy
133. The Institute for Translational Genomics and Population Sciences, Departments of Pediatrics and Medicine, LABioMed at Harbor-UCLA Medical Center, 1124 W. Carson Street, Torrance, CA 90502, USA
134. Institute of Molecular Biology and Biochemistry, Centre for Molecular Medicine, Medical University of Graz, Harrachgasse 21, 8010 Graz, Austria
135. INSERM U1078, Etablissement Français du Sang, 46 rue Félix Le Dantec, CS 51819, Brest Cedex 2 29218, France
136. Faculty of Health, University of Newcastle, Callaghan NSW 2308, Australia
137. John Hunter Hospital, New Lambton NSW 2305, Australia
138. School of Medicine, Conway Institute, University College Dublin, Ireland
139. The New York Academy of Medicine. 1216 5th Ave, New York, NY 10029, USA
140. IRCCS Neuromed, Pozzilli, Isernia, Italy
141. Molecular and Cellular Therapeutics, Royal College of Surgeons in Ireland, Dublin 2, Ireland
142. Institute of Cardiovascular and Medical Sciences, Faculty of Medicine, University of Glasgow, United Kingdom
143. Department of Genetics, University of Groningen, University Medical Center Groningen, PO Box 30001, 9700 RB Groningen, The Netherlands
144. Institute for Translational Genomics and Population Sciences. Los Angeles BioMedical Research Institute at Harbor-UCLA Medical Center, Torrance, CA, 90502, USA
145. Division of Genetic Outcomes, Department of Pediatrics, Harbor-UCLA Medical Center, Torrance, CA, 90502, USA
146. International Centre for Circulatory Health, Imperial College London, W2 1PG, UK
147. Department of Public Health, Bordeaux University Hospital, Bordeaux, France
148. Department of Internal Medicine, Erasmus MC, Rotterdam, 3000CA, The Netherlands
149. Interfaculty Institute for Genetics and Functional Genomics, University Medicine Greifswald, Greifswald, 17475, Germany

150. Department of Internal Medicine, Lausanne Universiyt Hospital, CHUV, 1011 Lausanne, Switzerland
151. Population Health Research Institute, McMaster University, Hamilton Ontario, Canada
152. National Heart and Lung Institute, Imperial College London, W2 1PG, UK
153. Department of Neurology, Bordeaux University Hospital, Bordeaux, France
154. Department of Public Health and Primary Care, Leiden University Medical Center, Leiden, The Netherlands
155. Department of Cardiology, University of Groningen, University Medical Center Groningen, PO Box 30001, 9700 RB Groningen, The Netherlands
156. The Charles Bronfman Institute for Personalized Medicine, The Icahn School of Medicine at Mount Sinai, New York, NY 10029, USA
157. Mindich Child health Development Institute, The Icahn School of Medicine at Mount Sinai, New York, NY 10029, USA
158. Alzheimer Scotland Dementia Research Centre, University of Edinburgh, 7 George Square, Edinburgh, EH8 9JZ, UK
159. Medical Research Council Human Genetics Unit, Institute of Genetics and Molecular Medicine, University of Edinburgh, Edinburgh EH4 2XU, UK
160. National Heart and Lung Institute, Imperial College London, Hammersmith Hospital Campus, Du Cane Road, London W12 0NN, UK
161. Diabetes Prevention Unit, National Institute for Health and Welfare, 00271 Helsinki, Finland
162. South Ostrobothnia Central Hospital, 60220 Seinäjoki, Finland
163. Red RECAVA Grupo RD06/0014/0015, Hospital Universitario La Paz, 28046 Madrid, Spain
164. Centre for Vascular Prevention, Danube-University Krems, 3500 Krems, Austria
165. Institute of Cardiovascular Sciences, The University of Manchester, Manchester, UK
166. Institute of Biomedicine and Translational Medicine, University of Tartu, Ravila Str. 19, 50412 Tartu, Estonia
167. Division of Public Health Sciences, Wake Forest School of Medicine, Winston-Salem, 27106, USA
168. University of Tartu, Tartu, Estonia
169. Department of Neurology, Medical University Graz, Auenbruggerplatz 22, 8036 Graz, Austria
170. Department of Epidemiology University of Washington, Seattle, WA 98101, USA
171. Department of Health Services, University of Washington, Seattle, WA 98101, USA
172. Group Health Research Institute, Group Health, Seattle, WA, 98101, USA
173. Institute of Physiology, University Medicine Greifswald, Karlsburg, 17495, Germany
174. Department of Pulmonary Physiology and Sleep, Sir Charles Gairdner Hospital, Hospital Avenue, Nedlands 6009,H57, Western Australia
175. School of Medicine and Pharmacology, University of Western Australia, Australia
176. Population Health Research Institute, St George's, University of London, London SW17 0RE, UK
177. Department of Medicine, Columbia University Medical Center, 622 West 168th Street, PH 9, East, 107, New York, NY 10032, USA
178. Department of Medical Sciences, Molecular Epidemiology and Science for Life Laboratory, Uppsala University, Uppsala 752 37, Sweden
179. Department of Medicine, Division of Cardiovascular Medicine, Stanford University School of Medicine, Stanford, CA 94305, USA
180. Center for Human Genetic Research, Massachusetts General Hospital, Boston, MA 02114, USA

181. Data Science Institute and Lancaster Medical School, Lancaster University, LA1 4YG, UK
182. Department of Biostatistics, University of Liverpool, Block F, Waterhouse Building, 1-5 Brownlow Street, Liverpool L69 3GL, UK
183. The population Science Branch, Division of Intramural Research, National Heart Lung and Blood Institute national Institute of Health, Bethesda MD 20892, USA

AUTHOR CONTRIBUTIONS

Secondary analyses

Design of secondary analyses: L.V.W., G.B.E, M.J.C., H.Snieder, M.D.T , R.Joehanes, A.V., R.Jansen, A.V., J.K., P.O.R., A.P.M., C.P.C. Computation of secondary analysis: L.V.W., G.B.E., A.P.M., M.E., T.B., L.Lin, R.Joehanes, A.V., P.J.v.d.M., R.Jansen, C.P.C.

Discovery

WGHS : Study phenotyping: P.M.R. Genotyping or analysis: D.I.C., L.M.R. Study PI: D.I.C., P.M.R.
 RS : Study phenotyping: G.C.V. Genotyping or analysis: G.C.V., A.G.U. Study PI: O.H.F., A.Hofman, A.G.U.
 NTR : Study phenotyping: E.J.d.G., G.W. Genotyping or analysis: J.J.H., E.J.d.G., G.W. Study PI: D.I.B., E.J.d.G.
 STR : Study phenotyping: E.I. Genotyping or analysis: R.J.S., M.Frånberg Study PI: E.I., A.Hamsten
 EGCUT : Genotyping or analysis: T.E. Study PI: A.Metspalu
 ARIC : Genotyping or analysis: D.E.A., A.C.M., P.N. Study PI: A.Chakravarti
 FHS : Study phenotyping: D.L. Genotyping or analysis: S.J.H. Study PI: D.L.
 MESA : Study phenotyping: J.I.R. Genotyping or analysis: W.P., X.G., J.I.R., J.Y. Study PI: W.P.
 B58C : Study phenotyping: D.P.S. Genotyping or analysis: D.P.S. Study PI: D.P.S.
 COLAUS : Study phenotyping: P.V. Genotyping or analysis: M.Bochud, Z.K. Study PI: P.V.
 PROSPER : Study phenotyping: J.W.J., D.J.S. Genotyping or analysis: S.Trompet, J.D. Study PI: J.W.J.
 BHS : Study phenotyping: A.James Genotyping or analysis: N.Shrine, J.H., J.B.
 SHIP : Study phenotyping: M.D. Genotyping or analysis: A.T., M.D., U.V. Study PI: R.R.
 KORA S4 : Genotyping or analysis: J.S.R. Study PI: A.Peters
 CHS : Study phenotyping: B.M.P. Genotyping or analysis: J.C.B., K.R., K.D.T. Study PI: B.M.P.
 AGES-Reykjavik : Genotyping or analysis: A.V.S. Study PI: V.Gudnason, T.B.H., L.J.L.
 ERF : Study phenotyping: C.M.v.D., B.A.O. Genotyping or analysis: N.A. Study PI: C.M.v.D., B.A.O.
 NESDA : Study phenotyping: B.W.J.H.P. Genotyping or analysis: I.M.N., Y.M. Study PI: H.Snieder, B.W.J.H.P.
 YFS : Study phenotyping: T.L., M.K., O.T.R. Genotyping or analysis: T.L., L.P.L., M.K., O.T.R. Study PI: T.L., M.K., O.T.R.

EPIC : Genotyping or analysis: N.J.W. Study PI: J.H.Z.

ASPS : Study phenotyping: R.Schmidt Genotyping or analysis: H.Schmidt, E.H., Y.S., R.Schmidt Study PI: H.Schmidt, R.Schmidt

ORCADES : Study phenotyping: J.F.W., H.C., S.W. Genotyping or analysis: J.F.W., P.K.J., S.W. Study PI: J.F.W.

FINRISK (COROGENE_CTRL) : Study phenotyping: P.J. Genotyping or analysis: K.K., A.P.S. Study PI: M.P., P.J.

INGI-VB : Study phenotyping: C.F.S. Genotyping or analysis: M.T., C.M.B., C.F.S. Study PI: D.T.

FINRISK_PREDICT_CVD : Study phenotyping: V.S., A.S.H. Study PI: V.S., A.Palotie, S.R.

TRAILS : Study phenotyping: H.R. Genotyping or analysis: P.J.v.d.M. Study PI: C.A.H., A.J.O.

PROCARDIS : Study phenotyping: A.G. Genotyping or analysis: A.G. Study PI: H.W., M.Farrall

HABC : Study phenotyping: Y.Liu, T.B.H. Genotyping or analysis: M.A.N. Study PI: Y.Liu, T.B.H.

KORA S3 : Study phenotyping: C.G. Genotyping or analysis: S.S., C.G., E.O. Study PI: M.Laan

INGI-FVG : Genotyping or analysis: D.V., M.Brumat, M.Cocca Study PI: P.G.

Fenland : Study phenotyping: R.A.S., J.a.L., C.L., N.J.W. Genotyping or analysis: R.A.S., J.a.L., C.L., N.J.W. Study PI: R.A.S., C.L., N.J.W.

MICROS : Genotyping or analysis: A.A.H., F.D.G.M., A.S.P. Study PI: F.D.G.M., P.P.P.

HTO : Study phenotyping: B.D.K. Genotyping or analysis: B.D.K., K.L.A., C.Mamasoula Study PI: B.D.K., H.J.C.

MIGEN : Study phenotyping: R.E., J.Marrugat, S.Kathiresan, D.S. Genotyping or analysis: R.E., S.Kathiresan, D.S. Study PI: S.Kathiresan

ULSAM : Study phenotyping: V.Giedraitis, E.I. Genotyping or analysis: A.P.M., A.Mahajan Study PI: A.P.M., V.Giedraitis, E.I.

Cilento study : Study phenotyping: R.Sorice Genotyping or analysis: D.R., T.Nutile Study PI: M.Ciullo

LBC1936 : Study phenotyping: I.J.D., A.J.G. Genotyping or analysis: L.M.L., G.D., A.J.G. Study PI: I.J.D.

H2000_CTRL : Study phenotyping: T.Niiranen Study PI: P.K., A.Jula, S.Koskinen

NSPHS : Genotyping or analysis: S.E., Å.J. Study PI: U.G.

FUSION : Genotyping or analysis: A.U.J. Study PI: J.T., M.Boehnke, F.C.

GRAPHIC : Study phenotyping: N.J.S., P.S.B., M.D.T. Genotyping or analysis: C.P.N., P.S.B., M.D.T. Study PI: N.J.S.

CROATIA_Vis : Study phenotyping: I.R. Genotyping or analysis: V.V., J.E.H. Study PI: V.V., I.R.

PIVUS : Study phenotyping: L.Lind, J.S. Genotyping or analysis: C.M.L., A.Mahajan Study PI: C.M.L., L.Lind, J.S.

LOLIPOP : Study phenotyping: J.S.K., J.C.C. Genotyping or analysis: J.S.K., W.Z., J.C.C., B.L. Study PI: J.S.K., J.C.C.

CROATIA_Korcula : Genotyping or analysis: C.H., J.Marten Study PI: C.H., A.F.W.

INGI-CARL : Study phenotyping: G.G. Genotyping or analysis: I.G., A.Morgan, A.R.

LBC1921 : Study phenotyping: J.M.S., A.Pattie Genotyping or analysis: J.M.S., S.E.H., D.C.M.L., A.Pattie Study PI: J.M.S.

CROATIA_SPLIT : Study phenotyping: O.P., I.K. Genotyping or analysis: O.P., T.Z. Study PI: O.P.

BioMe (formerly IPM) : Genotyping or analysis: Y.Lu Study PI: R.J.F.L., E.P.B.

Replication

UKB-BP : Genotyping or analysis: H.R.W., M.R.B., C.P.C., E.E., H.G., B.M., M.R., I.T. Study PI: P.E., M.J.C.

GoDARTS : Study phenotyping: C.N.A.P., A.S.F.D. Genotyping or analysis: C.N.A.P., N.Shah Study PI: C.N.A.P., A.D.M.

Lifelines : Study phenotyping: M.H.d.B. Genotyping or analysis: M.S. Study PI: P.v.d.H.

TwinsUK : Study phenotyping: C.Menni Genotyping or analysis: M.M., C.Menni Study PI: T.D.S.

Airwave Health Monitoring Study : Genotyping or analysis: A.C.V., E.E., H.G., I.T. Study PI: E.E.

The UK Household Longitudinal Study (UKHLS) : Genotyping or analysis: B.P.P. Study PI: E.Z.

Generation Scotland (GS:SFHS) : Study phenotyping: S.P. Genotyping or analysis: C.H., A.Campbell

JUPITER : Study phenotyping: P.M.R. Genotyping or analysis: D.I.C., L.M.R., F.G., P.M.R. Study PI: D.I.C., P.M.R.

NEO : Study phenotyping: R.d.M. Genotyping or analysis: D.O.M.K., R.L.G. Study PI: R.d.M.

Three City-Dijon : Study phenotyping: S.D., C.T. Genotyping or analysis: G.C. Study PI: S.D., C.T.

ASCOT-UK : Study phenotyping: P.S., N.P. Genotyping or analysis: P.B.M., H.R.W. Study PI: P.B.M., P.S., N.P., M.J.C.

ASCOT-SC : Study phenotyping: S.Thom, M.J.C. Genotyping or analysis: D.C.S., A.S., H.R.W., P.B.M. Study PI: S.Thom, M.J.C., P.B.M.

Hunter Community Study : Study phenotyping: R.Scott Genotyping or analysis: C.O., E.G.H. Study PI: A.John

GAPP : Study phenotyping: D.C. Genotyping or analysis: D.C., S.Thériault, G.P. Study PI: D.C.

BRIGHT : Study phenotyping: M.Brown, J.C. Genotyping or analysis: M.Farrall, P.B.M., H.R.W. Study PI: M.Brown, J.C., M.Farrall, P.B.M., M.J.C.

Resources for secondary analyses

eQTL NESDA NTR : Design of secondary analysis: R.Jansen Computation of secondary analysis: D.I.B., R.Jansen, B.W.J.H.P. Study PI: D.I.B., B.W.J.H.P.

eQTL kidney : Study phenotyping: J.J.D., M.A.S. Genotyping or analysis: P.J.v.d.M. Study PI: H.Snieder

eQTL BIOS : Design of secondary analysis: R.Jansen Computation of secondary analysis: R.Jansen Study PI: R.Jansen

SABRe : Study phenotyping: Y.D., P.J.M., Q.T.N. Genotyping or analysis: R.Joehanes Design of secondary analysis: D.L. Study PI: D.L.

ICBP-Steering Committee

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