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Chapter 1

A PRIORITIZED PANEL OF CANDIDATE GENES TO BE EXPLORED FOR ASSOCIATIONS WITH THE BLOOD PRESSURE RESPONSE TO EXERCISE

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ABSTRACT

Introduction. Identifying genetic variants associated with the blood pressure (BP) response to exercise is hindered by the lack of standard criteria for candidate gene selection, underpowered samples, and a limited number of conclusive whole genome studies. We developed a prioritized panel of candidate genetic variants that may increase the likelihood of finding genotype associations with the BP response to exercise when used alone or in conjunction with high throughput genotyping studies.

Methods. We searched for candidate genetic variants meeting preestablished criteria using PubMed and published systematic reviews. These preestablished criteria were genetic variants: 1) in major BP regulatory pathways and associated with BP, the BP response to exercise or antihypertensive medication, or the health-related fitness phenotype response to exercise; 2) from high throughput genotyping studies of BP meeting statistical significance after Bonferroni correction for multiple testing; 3) associated with energy metabolism and/or body composition as obesity is a major risk factor for hypertension; 4) associated with other established and emerging cardiovascular disease (CVD) risk factors that have been implicated in the etiology of hypertension; and 5) from high throughput genotyping studies of BP meeting arbitrary statistical significance thresholds.

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Results. Meeting the inclusion criteria were: 1) 162 variants from 60 candidate genes on 19 chromosomes associated with BP, the BP response to exercise or antihypertensive medication, or the health-related fitness phenotype response to exercise categorized within major BP regulatory pathways including: the renal and renin-angiotensin systems (92 variants, 27 genes, 14 chromosomes); sympathetic nervous system (39 variants, 20 genes, 14 chromosomes); nitric oxide synthase pathway (14 variants, 4 genes, 4 chromosomes); and other related BP regulatory pathways (17 variants, 9 genes, 7 chromosomes); 2) 55 variants on 17 chromosomes from high throughput genotyping studies of BP meeting statistical significance after Bonferroni correction for multiple testing; 3) 61 variants from 22 candidate genes on 15 chromosomes associated with energy metabolism and/or body composition; 4) 86 variants from 30 candidate genes on 16 chromosomes associated with other CVD risk factors including lipids and lipoproteins (43 variants, 14 genes, 10 chromosomes) and inflammatory or thrombotic factors (43 variants, 16 genes, 11 chromosomes); and 5) 149 variants on 20 chromosomes from high throughput genotyping studies of BP meeting arbitrary statistical significance thresholds.

Conclusion. This prioritized panel of 513 genetic variants provides genomic information that can serve as a reference for future work investigating the genetic basis of the BP response to exercise.

INTRODUCTION

Hypertension is a major global public health problem. Exercise decreases BP 5-7 mmHg among those with hypertension [1]. BP reductions of this magnitude lower cardiovascular disease (CVD) risk by 20-30%. Thus, the Joint National Committee 7 recommends exercise as initial lifestyle therapy to prevent, treat, and control high blood pressure (BP) [2]. However, the BP response to exercise training is variable[3,4]. Indeed, the standard deviation often exceeds the mean BP response[5], and exercise does not lower BP in 25% of the people with high BP [3,6,7]. Reasons for this variability are unclear but may include factors such as the law of initial values and regression to the mean[7]; differences in subject characteristics such as ethnicity [4,8], gender [4], age [4,8], and body mass index [4,8,9]; and differences in the frequency, intensity, time and type or FITT components of the exercise interventions [4,8]. In addition, genetic factors have a significant role that remains to be defined [10].

Exercise genomics is the study of genetic factors contributing to human variation in the response of *health-related fitness phenotypes* such as the BP response to exercise [11]. A list of terms and definitions related to exercise genomics used and italicized in this chapter are displayed in Table 1. Experts consider genomics and the identification of responders and nonresponders to exercise interventions as key areas of research that will drive advancements in exercise science in the 21st century[12]. Future research in exercise genomics aims to: 1) gain insight in the mechanisms of biological processes related to exercise; and 2) use genetic information to design individualized exercise prescriptions to prevent, treat, and control disease processes and optimize sports performance.

However, despite the promise of exercise genomics, our understanding of what specific genetic factors account for the BP response to exercise remains poor. To date *genetic variants* from 20 different genes have been reported to be associated with the BP response following a single bout of acute exercise (i.e., postexercise hypotension) [10,13-16] or chronic exercise (i.e., an exercise training program) [17-30].

Table 1. Key Genetic Terms and Definitions Included in this Chapter [11,63,64]

3’ untranslated region	The 3’ end of a gene is the end of the deoxyribonucleic acid at which the carbon atom attached to the next genetic sequence is the third carbon atom clockwise from the oxygen atom in the last base. The 3’ untranslated region of a gene is the sequence between the 3’ end and the protein coding region of the gene. It is transcribed into messenger ribonucleic acid but does not encode any protein sequence.
5’ untranslated region	The 5’ end of a gene is the end of the deoxyribonucleic acid at which the carbon atom attached to the next genetic sequence is the fifth carbon atom clockwise from the oxygen atom in the last base. The 5’ untranslated region of a gene is the sequence between the 5’ end and the protein coding region of the gene. It is transcribed into messenger ribonucleic acid but does not encode any protein sequence.
Allele	One of the different forms of a gene that can exist at a single genetic location or locus.
Allele, major	The allele of a given variant occurring with greatest frequency in the population.
Allele, minor	The allele of a given variant occurring with least frequency in the population.
Coding synonymous	Located within the coding region of a gene’s sequence but not causing a change in the amino acid sequence of the final protein.
Complex phenotype	A phenotype influenced by genetic as well as environmental factors.
Copy number variant	A variant in which some individuals have more or less than two copies of an entire gene sequence. This variation occurs because some chromosome copies are missing the gene, some have one copy of the gene, and some have multiple copies of the gene.
Epigenomics	The study of chemical modifications of the genome that do not alter the genetic sequence but can alter the physical and chemical behavior of the genetic material.
Epigenetic	The study of heritable changes in gene expression and other phenotypes caused by mechanisms other than changes in the underlying deoxyribonucleic acid sequence.
Exercise genomics	The study of genetic factors contributing to human variation in the response of health-related fitness phenotypes to exercise.
High throughput genotyping	The use of a collection of microscopic spots of genetic material attached to a solid surface in order to genotype a high number of genetic variants simultaneously.
Genetic variant	A genetic sequence variation present at a particular position, where different individuals can have any of two or more alleles.
Genome wide association study	A study testing the association of a phenotype with a large set of common genetic variants across the entire genome.

Table 1. (Continued)

Genome wide linkage study	A study of genetic variants across the entire genome examining the non-random co-segregation of a trait of interest and genotype. The goal of these studies is to map a trait to a specific chromosomal locus where a putative gene contributing to the trait is hypothesized to be located.
Genomics	The study of all of a person's genes (the genome) including interactions of those genes with each other and the environment.
Genotype	The two alleles of genetic sequence present at corresponding locations on the homologous chromosomes of a single individual.
Haplotype	A combination of alleles at different locations on the chromosome that tend to be inherited together.
Health-related fitness phenotype	A phenotype related to hemodynamic traits such as exercise heart rate, blood pressure, and heart morphology; anthropometry and body composition; insulin and glucose metabolism; and blood lipid, lipoprotein, or hemostatic factors among others.
Imputation	A statistical technique to indirectly infer the genotypes of unascertained variants using linkage disequilibrium information that allows geneticists to evaluate association between a phenotype and genetic variants not directly genotyped.
Insertion-deletion polymorphism	A section of genetic sequence present (insertion) in some individuals but not others (deletion).
Intron	A non-coding region of genetic sequence between coding regions within a gene.
Linkage disequilibrium	The nonrandom association between two or more alleles such that certain combinations of alleles are more likely to occur together on a chromosome than other combinations of alleles.
Locus	The chromosome location of a specific gene or genetic sequence.
Minor allele frequency	The number of times the minor allele occurs in the population divided by the total number of alleles in the population.
Missense	Causing a change in the amino acid sequence of the final protein.
Near Gene-3	Located within the 3' untranslated region but within 2,000 base pairs of the coding region.
Near Gene-5	Located within the 5' untranslated region but within 2,000 base pairs of the coding region.
Nonsense	Causing a change in the amino acid sequence that produces a stop codon and causes the premature termination of translation and protein synthesis.
Prioritized panel	A list of 100-50,000 genetic variants selected by predetermined criteria to be explored for associations with a phenotype of interest.
Phenotype	Any observable or measurable trait determined by genetic and/or environmental factors.

Post-translational modification	Chemical alterations to a protein following its synthesis that can influence its activity and function in the cell.
Proteomics	The study of the complete set of proteins expressed by a genome, cell, organism, or system.
Signaling pathway	A mechanism in a biological system by which a physical or chemical stimulus induces a specific physical or chemical cellular response. Often this mechanism involves specific interactions between cellular proteins.
Single nucleotide polymorphism	A gene sequence variant consisting of alteration to a single base in the sequence.
Transcriptional regulation	Various methods by which the cell controls the process of the copying of deoxyribonucleic acid genetic sequence into ribonucleic acid molecules. These processes govern the creation of ribonucleic acid which determines the encoded proteins that will ultimately be synthesized by the cell.
Transcriptomics	The study of all of the ribonucleic acid molecules that are assembled in the cells and tissues of organisms.
Variable number tandem repeats	A short, repetitive genetic sequence for which the number of repeats varies between individuals.

These genes were found in major BP regulatory systems including the: 1) Renin-Angiotensin System [angiotensin 1 converting enzyme (*ACE*), adducin 1 alpha (*ADD1*), angiotensinogen (*AGT*), angiotensin II receptor, type 1 (*AGTR1*), and aldosterone synthase (*CYP11B2*)];2) Sympathetic Nervous System [adenosine monophosphate deaminase 1 (*AMPD1*), adrenergic receptor, beta 1 (*ADRB1*) and beta 2 (*ADRB2*), cholinergic receptor (*CHRM2*), guanine nucleotide-binding protein system alpha subunit (*GNAS*), and guanine nucleotide binding protein, beta polypeptide 3 (*GNB3*)];3) Nitric Oxide Synthase Pathway [endothelin 1 (*EDN1*), nitric oxide synthase 3 (*NOS3*), and transforming growth factor, beta 1 (*TGFB1*)]; and 4) other related BP regulatory pathways [apolipoprotein (*APOE*), cytochrome b-245 alpha polypeptide (*CYBA*),cytochrome P450 superfamily (*CYP2D6*), fatty acid binding protein 2 (*FABP2*), leptin receptor (*LEPR*), and lipoprotein lipase (*LPL*)].

Unfortunately, no definitive conclusions can be made from these candidate gene association studies because of: 1) the small number of genetic variants examined that may be subject to selection bias; 2) sample sizes underpowered to detect the small effect of each variant on the *phenotype*(s) of interest; 3) emphasis on studying *single nucleotide polymorphisms* (*SNPs*) versus those in *linkage disequilibrium* (*LD*) or *haplotype* or structural genetic variants such as *copy number variants* (*CNVs*); 4) emphasis on studying genetic variation without considering *epigenetic* effects such as*transcriptional regulation* and *post-translationalmodification*; 5) poor quality control of genotyping; 6) exercise interventions that were unstructured and poorly controlled; and 7) heterogeneous samples failing to control for population stratification of genotype phenotype associations by race, sex, age, and other factors. Collectively, these limitations have led to a general lack of replication among studies examining the BP response to exercise [31,32]. For example, only three genetic variants, *ACE* I/D (rs4340) [13,16,22,33,34], *AGT* M235T (rs699) [21,23], and *ADD1* G460W (rs4961)

[13,35], have been shown to be associated with the BP response to exercise in more than one study.

As the young field of exercise genomics continues to grow, the technology has advanced, enabling investigators to begin addressing some of the limitations stated above. In particular, new *high throughput genotyping* allows investigators to simultaneously *genotype* individuals for an increasingly greater number of genetic variants at lower and lower costs. For example, in 2005 it was possible to genotype 70,000 genetic variants within an individual for $20,000, and now in 2011 it is possible to genotype 2.5 million genetic variants in that same individual for $1,000 [32]. This technological advancement has led to the advent and proliferation of *genome wide association studies* (*GWAS*).

GWAS test the association of a phenotype with 70,000 to 2.5 million common genetic variants, meaning they occur in 1% or more of the population. The systematic and hypothesis-free approach of GWAS is less likely than the candidate gene association approach to be confounded by selection bias of variants examined. In a short time, GWAS have enabled significant advances in the field of genomics to occur. For example, in 2005 Klein et al. [36] found common variants of complement factor H gene (*CFH*) accounted for 45-61% of the risk for developing age-related macular degeneration. Previous candidate gene association studies of age-related macular degeneration failed to uncover these associations because they did not include *CFH* on the short list of genes they had the ability to examine at the time. The advent of high throughput genotyping technology enabled scientists to gain genetic and mechanistic insight into the etiology of age-related macular degeneration that was not possible previously.

While GWAS have had success in the identification of the genetic basis of some health-related phenotypes and diseases, the application of GWAS to other *complex phenotypes* such as resting BP or hypertension has not been as successful [37]. For instance, genetic variants associated with resting BP from GWAS generally account for $\leq$0.2% of the BP variability among individuals, corresponding to only a <1 mmHg difference between genotypes [38-40]. For a GWAS to have the statistical power needed to detect the subtle effects of common *alleles* on BP, 30,000-200,000 human subjects are required to be enrolled, genotyped, and phenotyped [38-40]. To accomplish enrolling this many subjects, investigators must form research collaborations consisting of anywhere from 6 [39] to 82 [40]separate study cohorts. Fortunately, there are research methods that can be used to partially circumvent the challenges presented by GWAS that include detecting small effect sizes, meeting the high statistical significance needed to test the large the number of variants examined, enrolling large samples, and ensuring adequate data quality control.

One recent approach that has evolved in the candidate gene study of complex phenotypes is to use a *prioritized panel* of genetic variants in conjunction with a GWAS [41]. A prioritized panel is a list of 100-50,000 genetic variants selected by predetermined criteria to associate with a phenotype of interest [41-43]. Prioritized panels exploit high throughput genotyping used in GWAS but have the additional benefit of selectively examining genetic variants in a hypothesis-driven fashion. In theory, prioritized panels should: 1) identify genetic variants with larger effect sizes than GWAS due to selecting variants more likely to strongly associate with the phenotype; 2) require less stringent statistical correction for multiple comparisons due to testing a smaller number of variants; and 3) require fewer subjects to adequately power studies due to larger effect sizes and less stringent statistical correction for multiple testing.

An example of a successful prioritized panel approach used in conjunction with GWAS is the Genetic Regulation of Arterial Pressure of Humans in the Community (GRAPHIC) study [44]. GRAPHIC investigators genotyped 2,020 subjects for a panel of 45,237 genetic variants with the IBC Array hypothesized to associate with any cardiovascular phenotype including BP [41]. These investigators obtained 24 hr ambulatory BP measurements on each subject [44] and then tested variants for association with BP. They found that minor allele carriers of rs2797221, an intronic variant in Usher Syndrome 2A (*USH2A*), had mean systolic 24 hr ambulatory BP 3.9 mmHg lower than non-carriers. They also found minor allele carriers of rs13306560, a variant in the near gene-5 region of methylenetetrahydrofolate reductase (*MTHFR*), had mean diastolic 24 hr ambulatory BP 2.6 mmHg lower than non-carriers.

GRAPHIC investigators noted previous GWAS had found several other genetic variants within *MTHFR* and closely neighboring genes associated with BP that accounted for a small difference in BP between genotype groups of <1 mmHg [38,39]. GRAPHIC investigators then replicated association of rs13306560 and BP in 753 subjects from the Silesian Cardiovascular Study [44]. GRAPHIC investigators concluded rs13306560 was the most significant genetic determinant of BP revealed by their study, as they found consistent significant association with BP in GRAPHIC, previous GWAS, and a validation cohort. GRAPHIC added value to previous GWAS by: 1) finding a larger effect on BP by a *MTHFR* single variant; 2) testing a lower number of variants, thus, increasing the chance that significant findings were not Type I statistical errors; and 3) requiring just 2,020 subjects rather than the 30,000-plus typically required by GWAS [38,39].

Other, smaller prioritized panels have tested2,411 variants for association with the genetic basis of BP [42] and 181 variants for association with BP response to a dietary potassium intervention [43]. These panels, like the IBC array [41] used in the GRAPHIC study, employed specific criteria to select variants for inclusion. These criteria included variants: 1) from candidate gene studies reported to be associated with BP [41]; 2) from GWAS reported to be associated with BP [41]; and 3) in major BP regulatory pathways including the renal and renin-angiotensin systems, sympathetic nervous system, nitric oxide synthase pathway, and other related BP regulatory pathways [41-43].

We now present our prioritized panel of genetic variants to be examined for association with the BP response to exercise which to our knowledge is the first of its kind in the young field of exercise genomics. We propose that this prioritized panel can be used in conjunction with a GWAS to provide insight into the genetic basis of the BP response to exercise.

METHODS

Data Sources

Our first task was to locate genetic variants described in the existing literature warranting consideration of inclusion in our prioritized panel to be examined for association with the BP response to exercise. We searched PubMed for articles describing variants between January 1, 1995 and September 15, 2011 using the terms: exercise, aerobic, training, genotype, SNP, allele, variant, GWAS, obesity, adiposity, BP, hypertension, lipid, inflammation, and thrombosis. Next we searched for variants within systematic reviews including *The Human*

Gene Map for Performance and Health-Related Fitness Phenotypes [45]and *The Human Obesity Gene Map* [46], as well as narrative reviews from *Exercise Genomics* [11], *Current Hypertension Reports* [47],and the *Journal of Applied Physiology Highlighted Topic Series* [48]. We also reviewed tables of contents from the following relevant journals from 2001-2011: *Medicine and Science in Sport and Exercise, Journal of Applied Physiology, Physiological Genomics, Hypertension, Journal of Hypertension, American Journal of Hypertension,* and *Plos One*. We examined the reference lists of all articles we located for additional variants that may qualify for inclusion. Lastly, we considered genetic variants we previously investigated in the Functional Polymorphisms Associated with Human Muscle Size and Strength study(NIH-NINDS R01 NS40606-02) [49] and a series of investigations we conducted on candidate genes associated with the BP response to exercise (American Heart Association 0150507N) [13,14,16,50].

Gene Variant Selection and Prioritization

Using previous prioritized panels in the literature for health-related phenotypes such as BP [41,42] and the BP response to dietary potassium supplementation [43], we formed five categories for inclusion on our prioritized panel of genetic variants associated with the BP response to exercise. Our categories of classification include:

Category 1- variants previously reported to be associated with the BP response to exercise. Category 1 also includes variants previously associated with health-related phenotypes such as BP, the BP response to antihypertensive medication, or the health-related fitness phenotype response to exercise. In addition, these variants localized on a gene known to code for a protein in a major BP regulatory pathway including the renal and renin-angiotensin systems, sympathetic nervous system, nitric oxide synthase pathway, or other related BP regulatory pathways. Therefore, variants in category 1, the highest prioritized category in our panel, were supported for inclusion in the panel based upon two lines of evidence: 1) previous reported associations with relevant phenotypes; and 2) biological plausibility. Thus, in our panel we employed the principle that the strongest candidate variants are those supported by more than one line of evidence [51].

Category 2- variants previously reported to be associated with BP in GWAS or other high throughput genotyping studies meeting statistical significance after Bonferroni correction for multiple testing.

Category 3- variants previously reported to be associated with energy metabolism and/or body composition as obesity is a major risk factor for hypertension [2]. The high interest of the scientific community and funding agencies in the genetic basis of obesity has led to the publication of a disproportionately high number of studies on this phenotype. For example, at least 426 reports have identified 127 candidate genes associated with obesity [46], more genes than are included in all the other categories in our panel combined. To avoid disproportionately representing obesity associated genes in our panel, we included genes in category 3only if they were listed in a commentary by Bouchard in 2007 [52] on the *Human Obesity Gene Map* [46]. This commentary features a list of genes reported to be associated with obesity replicated in five or more studies that are localized on a gene with biological plausibility [52]. Experts in the field of exercise genomics have utilized this list as a summary of the genes most relevant to the phenotypes of energy metabolism and body composition

[53]. We also updated our panel to include genes that have been more recently reported to be associated with obesity that are not included in Bouchard's commentary [52] such as fat mass and obesity associated (*FTO*).

Category 4-variants previously reported to be associated with other established and emerging CVD risk factors that have been implicated in the etiology of hypertension such as dyslipidemia or thrombosis[2].

Category 5- variants previously reported to be associated with BP in GWAS or other high throughput genotyping studies meeting arbitrary statistical significance, but not significance after Bonferroni correction for multiple testing.

Prioritized Panel Organization

Each row of the panel (see Table 2) corresponds to one genetic variant. Each column corresponds to a specific piece of information related to the genetic variants and includes:

Column One- the standard abbreviated gene name on which the variant is located. Variants from candidate gene studies (i.e., categories 1, 3, and 4) were classified according to the name of the gene. Variants from high throughput genotyping studies (i.e., categories 2 and 5) were classified according to the name of the nearest gene, as many variants showing significance in high throughput genotyping studies are not located within established genes. For example, the variant in row 200 of category 2 of Table 2 is not located within an established gene but is located nearer to the Fibroblast Growth Factor 5 gene (*FGF5*) than any other gene, so it is listed as *FGF5* in the panel. The full gene names corresponding to each abbreviation are displayed in Appendix A.

Column Two- the reference SNP (rs number) label for the variant. Rs numbers provide a universal indexing system allowing each genetic variant to be uniquely identified. For example, the rs number of the variant in row 200 of category 2 listed as nearest to *FGF5* is 16998073.

Column Three- the type of the variant. Variants were classified as *missense, nonsense, coding synonymous, intron, 3' untranslated region, 5' untranslated region, Near Gene-3*, or *Near Gene-5*. For some variants, its type is not available in the existing literature [57], and accordingly we listed it as not available. For example, the type of the variant in row 200 of category 2 listed as nearest to *FGF5* is not available.

Column Four- the phenotype reported to be associated with the variant that supported its inclusion in the panel. For example, the phenotype reported to be associated with the variant in row 200 of category 2 listed as nearest to *FGF5*is BP [38].

Column Five- the *minor allele frequency* (*MAF*) of the variant. The *minor allele* is the allele of a particular variant least common in the population. We reported the MAF of each variant and excluded variants for which the MAF was less than 1%. For example, the minor allele of the variant in row 200 of category 2 listed as nearest to *FGF5* is a thymine nucleotide (T) with a MAF of 0.19 or 19%.

Column Six- the chromosome location of the variant. This location was classified by the number of the chromosome; where available, whether it fell on the short (p) or long (q) arm; and the numerical classification of the band and sub-band location. For example, the variant in row 200 of category 2 listed as nearest to *FGF5* is located on the q arm of chromosome 4, specifically at band 21 and sub-band 21. Therefore, its chromosome location is 4q21.21.

Column Seven- the author and publication year of the reference reporting the variant to be associated with the phenotype listed in column four. For example, for the variant in row 200 of category 2 listed as nearest to *FGF5*,the reference is 'Newton-Cheh 2009' [38]. The full citations of these references are located in Appendix B.

The information contained within the panel of each genetic variant was obtained from a variety of sources and included:

The Genecards Database- used to obtain the abbreviated name of the gene (column one on Table 2) on which the variant is located as well as the full name of this gene (Appendix A). Genecards synthesizes information pertaining to specific genes and includes a universal nomenclature for each gene [58]. More information about Genecards is available at www.genecards.org.

The National Center for Biotechnology Information (NCBI) Entrez SNP Database- used to obtain the rs number label for each variant (column two on Table 2). NCBI Entrez SNP has assigned most genetic variants an rs number, allowing users to quickly locate them in the database [57,59]. It also provides synthesized information for each indexed variant including physical location, molecular function, alternative names for the variant used in the literature, and MAF. This information about physical location and molecular function includes links to sub-databases within NCBI providing further details. Genetic variants that have not been studied extensively may not have been assigned an rs number or indexed. For example, the variant located in row 264 of category 3 of Table 2 is a *LEPR insertion-deletion polymorphism* in the 3' untranslated region associated with energy metabolism [60]. Therefore, this variant was included in our panel, but we could not list the rs number for this variant as no rs number to our knowledge has been assigned to it. More information about NCBI Entrez SNP is available at www.ncbi.nlm.nih.gov/sites/entrez?db=snp.

The International Haplotype Map (HapMap) Consortium- was used to obtain the MAF for each variant (column five on Table 2) [61]. The HapMap provides genotype information for 1.5 to 4 million genetic variants among 269 individuals from four populations that include the: Yoruba Nigerian in Ibadan; Japanese in Tokyo; Han Chinese in Beijing, and northern and western European-derived American in Utah. MAF varies among populations; thus, we report the MAF from the European-derived American population. More information about the HapMap is available at www.hapmap.ncbi.nlm.nih.gov/.

The Ensembl Database- was used to obtain the chromosome location of each genetic variant (column six on Table 2) [62]. Ensembl features genome sequence information related to comparative genomics, genomic variation, and gene regulatory information. Therefore, it was ideal for determining the physical location of gene variants. More information about Ensembl is available at www.ensembl.org.

In summary, the prioritized panel in Table 2 is organized with each row corresponding to a genetic variant. The rows are classified according to the following prioritized categories: 1) in major BP regulatory pathways and associated with BP, the BP response to exercise or antihypertensive medication, or the health-related fitness phenotype response to exercise; 2) from high throughput genotyping studies of BP meeting statistical significance after Bonferroni correction for multiple testing; 3) associated with energy metabolism and/or body composition as obesity is a risk factor for hypertension; 4) associated with other established and emerging cardiovascular disease (CVD) risk factors that have been implicated in the etiology of hypertension; and 5) from high throughput genotyping studies of BP meeting arbitrary statistical significance thresholds.

The columns of the panel in Table 2 in the order they appear from left to right are the: 1) abbreviated gene name obtained from the Genecards Database; 2) rs number obtained from the NCBI Entrez SNP Database; 3) type of the variant obtained from the NCBI Entrez SNP Database; 4) phenotype the variant was reported to be associated with; 5) MAF obtained from the HapMap; 6) chromosome location obtained from the Ensembl Database; and 7) reference supporting the variant's inclusion in the panel.

CONCLUSION

We developed a prioritized panel of candidate genetic variants that may increase the likelihood of finding genetic associations with the BP response to exercise when used alone or in conjunction with high throughput genotyping studies such as GWAS. Using systematic criteria, we selected 513 genetic variants (Table 2) grouped into five prioritized categories (Table 3): 1) 162 variants from 60 candidate genes on 19 chromosomes associated with BP, the BP response to exercise or antihypertensive medication, or the health-related fitness phenotype response to exercise categorized within major BP regulatory pathways including: the renal and renin-angiotensin systems (92 variants, 27 genes, 14 chromosomes); sympathetic nervous system (39 variants, 20 genes, 14 chromosomes); nitric oxide synthase pathway (14 variants, 4 genes, 4 chromosomes); and other related BP regulatory pathways (17 variants, 9 genes, 7 chromosomes); 2) 55 variants on 17 chromosomes from high throughput genotyping studies of BP meeting statistical significance after Bonferroni correction for multiple testing; 3) 61 variants from 22 candidate genes on 15 chromosomes associated with energy metabolism and/or body composition; 4) 86 variants from 30 candidate genes on 16 chromosomes associated with other CVD risk factors including lipids and lipoproteins (43 variants, 14 genes, 10 chromosomes) and inflammatory or thrombotic factors (43 variants, 16 genes, 11 chromosomes); and 5) 149 variants on 20 chromosomes from high throughput genotyping studies of BP meeting arbitrary statistical significance thresholds.

Overall our panel (Table 2) includes 3 insertion-deletion variants, 5 *variable number tandem repeat* (*VNTR*) variants, and 29 SNPs with a MAF <5%. The remaining 478 variants are SNPs with a MAF $\geq$5%. Lastly, the panel variants are dispersed throughout the genome with 14 different chromosomes with 20 or more panel variants, and all 23 chromosomes have at least 2 panel variants.

Table 4 summarizes the types of these panel variants. Of the 513 variants, 60% are known to be non-coding (i.e., intron, near gene-5, near gene-3, 3' untranslated region, 5' untranslated region, and coding synonymous), 28% do not have information available in the existing literature to classify them as a type of variant[57], and 12% are known to be coding (i.e., missense or nonsense). Many of these variants whose types not available are from recent high throughput genotyping studies of BP (i.e., categories 2 and 5). Therefore, they are not widely known or published in the literature and to our knowledge have been not examined in studies that would classify their type.

Table 2. Prioritized Panel of Generic Variants

Gene[a]	Rs Number	Type of Variant	Phenotype	Minor Allele Frequency[b]	Chromosome Location	Reference
1) In Major BP Regulatory Pathways and Associated with BP, the BP Response to Exercise or Antihypertensive Medication, or the Health-related Fitness Phenotype Response to Exercise						
A. Renal and Renin-Angiotensin Systems						
ACE	rs2285666	Intron	BP	A (0.45)	17q23.3	Zhou 2009
ACE	rs35580653	Coding Synonymous	BP	G (0.20)	17q23.3	Bouzekri 2004
ACE	rs4305	Intron	BP	A (0.45)	17q23.3	Johnson 2011
ACE	rs4309	Coding Synonymous	BP	T (0.18)	17q23.3	Bouzekri 2004
ACE	rs4331	Coding Synonymous	BP	G (0.41)	17q23.3	Bouzekri 2004
ACE	rs4646994[c]	Intron	Exercise Response	Insertion (0.46)	17q23.3	Pescatello 2006
ACE	rs4341	Intron	Exercise Response	C (0.46)	17q23.3	Bozkurt 2008
ADD1	rs4961	Missense	Exercise Response	T (0.23)	4p16.3	Pescatello 2007
ADD1	rs4963	Missense	BP	C (0.47)	4p16.3	Bianchi 2005
ADD2	rs1541582	Intron	BP	T (0.22)	2p13.3	Kardia 2007
ADD2	rs3755375	Intron	BP	A (0.23)	2p13.3	Kardia 2007
ADD2	rs4984	Coding Synonymous	BP	T (0.17)	2p13.3	Bianchi 2005
ADD3	rs3731566	Intron	BP	G (0.30)	10q25.10	Bianchi 2005
AGT	rs11122587	Intron	BP	G (0.21)	1q42.2	Johnson 2011
AGT	rs2004776	Intron	BP	T (0.27)	1q42.2	Johnson 2011
AGT	rs2493136	Near Gene-3	Exercise Response	A (0.42)	1q42.2	Ingelsson 2007
AGT	rs699	Missense	Medication Response	C (0.41)	1q42.2	Ying-Ying 2011
AGT	rs3789669	Intron	BP	G (0.33)	1q42.2	Watkins 2009
AGT	rs3789671	Intron	BP	A (0.26)	1q42.2	Watkins 2009
AGT	rs4762	Missense	BP	T (0.12)	1q42.2	Pereira 2008
AGT	rs5046	Near Gene-3	BP	T (0.12)	1q42.2	Watkins 2009
AGT	rs5049	5' Untranslated Region	BP	G (0.20)	1q42.2	Pereira 2008
AGT	rs5050	5' Untranslated Region	BP	C (0.17)	1q42.2	Pereira 2008
AGT	rs5051	5' Untranslated Region	BP	A (0.47)	1q42.2	Pereira 2008
AGT	rs11122580	Near Gene-3	BP	G (0.13)	1q42.2	Watkins 2009
AGTR1	rs3772608	Intron	BP	A (0.05)	3q24	He 2011

Gene[a]	Rs Number	Type of Variant	Phenotype	Minor Allele Frequency[b]	Chromosome Location	Reference
AGTR1	rs5182	Coding Synonymous	BP	T (0.48)	3q24	Yazdanpanah 2007
AGTR1	rs5186	3' Untranslated Region	Exercise Response	C (0.41)	3q24	Blanchard 2006
AGTR2	rs1403543	Intron	BP	A (0.44)	Xq23	Liljedahl 2003
AGTR2	rs5194	3' Untranslated Region	BP	G (0.42)	Xq23	Liljedahl 2003
APLNR	rs2282623	3' Untranslated Region	BP	T (0.40)	11q12.1	Montasser 2011
AVPR1A	rs1042615	Coding Synonymous	Exercise Response	T (0.42)	12q14.2	Masuki 2010
AVPR1A	rs11174811	3' Untranslated Region	BP	A (0.08)	12q14.2	Nossent 2011
BDKRB2	rs2069591	3' Untranslated Region	BP	T (0.06)	14q32.1	Nossent 2011
BDKRB2	rs5225	3' Untranslated Region	BP	C (0.06)	14q32.1	Nossent 2011
CYP11B2	rs1799998	Near Gene-3	Exercise Response	C (0.27)	8q24.3	Blanchard 2006
EMILIN1	rs17881426	Intron	BP	A (0.17)	2p22.3	Shimodaira 2010
EMILIN1	rs2011616	Intron	BP	A (0.43)	2p22.3	Shimodaira 2010
EMILIN1	rs2289360	Intron	BP	A (0.37)	2p22.3	Shimodaira 2010
EMILIN1	rs2304682	Near Gene-5	BP	C (0.40)	2p22.3	Shimodaira 2010
EMILIN1	rs2536512	Missense	BP	A (0.38)	2p22.3	Shimodaira 2010
HSD11B1	rs11808690	Intron	BP	G (0.18)	1q32.2	He 2011
HSD11B2	rs5479	Coding Synonymous	BP	A (0.09)	16q22.1	He 2011
KLK1	No rs Number	Not Available	BP	C (0.09)	19q13.33	Svetkey 2011
NEDD4L	rs4149601	Intron	BP	A (0.21)	18q21.31	Luo 2009
NPPA	rs198358	Not Available	BP	G (0.27)	1p36.21	Newton-Cheh 2009
NPPA	rs5063	Missense	Medication Response	A (0.05)	1p36.21	Lynch 2008
NPPA	rs5065	Missense	Medication Response	C (0.23)	1p36.21	Lynch 2008
NPPA	rs5068	3' Untranslated Region	BP	C (0.07)	1p36.21	Newton-Cheh 2009
NR3C2	rs11099681	Intron	BP	C (0.20)	4q31.23	Montasser 2011
NR3C2	rs2048547	Intron	BP	G (0.04)	4q31.23	He 2011
NR3C2	rs4835493	Intron	BP	T (0.20)	4q31.23	Montasser 2011
NR3C2	rs5527	Missense	BP	C (0.02)	4q31.23	He 2011

Table 2. (Continued)

Gene[a]	Rs Number	Type of Variant	Phenotype	Minor Allele Frequency[b]	Chromosome Location	Reference
NR3C2	rs6848375	Intron	BP	T (0.05)	4q31.23	He 2011
RABGAP1L	rs12078839	Intron	BP	G (0.11)	1q25.1	Oguri 2010
REN	rs12089381	Intron	BP	C (0.05)	1q32.1	Johnson 2011
REN	rs1917539	Intron	BP	G (0.11)	1q32.1	Moore 2007
REN	rs12750834	Not Available	BP	T (0.19)	1q32.1	Moore 2007
REN	rs2272237	Intron	BP	G (0.39)	1q32.1	Moore 2007
REN	rs3795574	Intron	BP	T (0.10)	1q32.1	Moore 2007
REN	rs5705	Coding Synonymous	BP	C (0.15)	1q32.1	Moore 2007
SCNN1A	rs11064160	Not Available	BP	C (0.12)	12p12.3	Johnson 2011
SCNN1A	rs4149570	Not Available	BP	A (0.40)	12p12.3	Johnson 2011
SCNN1B	rs7205273	Intron	BP	T (0.26)	16p12.2	Montasser 2011
SCNN1G	rs11074553	Intron	BP	G (0.45)	16p12.2	Busst 2007
SCNN1G	rs4299163	Intron	BP	G (0.34)	16p12.2	Busst 2007
SCNN1G	rs1331086	Not Available	BP	G (0.16)	16p12.2	Busst 2007
SCNN1G	rs4073291	Intron	BP	G (0.16)	16p12.2	Zhao 2011
SCNN1G	rs4073930	Intron	BP	C (0.16)	16p12.2	Zhao 2011
SCNN1G	rs4299163	Intron	BP	C (0.10)	16p12.2	Zhao 2011
SCNN1G	rs4499238	Intron	BP	A (0.10)	16p12.2	Zhao 2011
SCNN1G	rs5723	Coding Synonymous	Medication Response	G (0.28)	16p12.2	Ying-Ying 2011
SCNN1G	rs5735	Coding Synonymous	BP	C (0.17)	16p12.2	Zhao 2011
SCNN1G	rs7404408	Intron	BP	T (0.16)	16p12.2	Zhao 2011
SLC12A3	rs11643718	Missense	BP	Q (0.22)	16q13	Keszei 2007
SLC12A3	rs12708965	Missense	BP	C (0.04)	16q13	Keszei 2007
SLC12A3	rs2399594	Intron	BP	G (0.39)	16q13	Johnson 2011
SLC4A5	rs1017783	Not Available	Exercise Response	T (0.38)	2p13.1	Taylor 2009
SLC4A5	rs6731545	Intron	Exercise Response	A (0.44)	2p13.1	Taylor 2009
SLC4A5	rs8179526	Intron	BP	C (0.47)	2p13.1	Taylor 2009
SLC9A1	rs484677	Not Available	BP	T (0.42)	1p31.1	Johnson 2011
TBXA2R	rs13306046	3' Untranslated Region	BP	A (0.10)	19p13.3	Nossent 2011

Gene[a]	Rs Number	Type of Variant	Phenotype	Minor Allele Frequency[b]	Chromosome Location	Reference
WNK1	rs1468326	Not Available	BP	A (0.11)	12p13.33	Tobin 2005
WNK1	rs2286007	Missense	BP	T (0.08)	12p13.33	Tobin 2005
WNK1	rs2286028	Intron	BP	C (0.18)	12p13.33	Tobin 2005
WNK1	rs2301880	Intron	BP	T (0.26)	12p13.33	Tobin 2005
WNK1	rs2369402	Intron	BP	A (0.22)	12p13.33	Tobin 2005
WNK1	rs765250	Intron	BP	C (0.31)	12p13.33	Tobin 2005
WNK1	rs880054	Intron	BP	C (0.44)	12p13.33	Tobin 2005
WNK1	rs953361	Intron	BP	T (0.39)	12p13.33	Tobin 2005
WNK1	rs956868	Missense	BP	A (0.14)	12p13.33	Tobin 2005
WNK4	rs9896991	Missense	BP	A (0.11)	17q21.31	Tobin 2005
B. Sympathetic Nervous System						
i. Adrenergic System						
ADRA1A	rs483392	Intron	Exercise Response	T (0.45)	8p21.2	Ingelsson 2007
ADRA1A	rs489223	Intron	Exercise Response	G (0.10)	8p21.2	Ingelsson 2007
ADRA1A	rs7820633	Intron	Exercise Response	C (0.38)	8p21.2	Ingelsson 2007
ADRA1D	rs835873	Intron	Exercise Response	T (0.17)	20p13	Ingelsson 2007
ADRA2A	rs1800038	Intron	BP	A (0.33)	10q25.2	Rana 2007
ADRA2A	rs1800544	Near Gene-5	BP	G (0.28)	10q25.2	Rana 2007
ADRA2A	rs553668	3' Untranslated Region	BP	A (0.17)	10q25.2	Rana 2007
ADRA2B	No rs Number[d]	Intron	Exercise Response	9G (0.46)	2q11.1	Laaksonen 2007
ADRB1	rs1801252	Missense	BP	G (0.15)	10q25.3	Lee 2011
ADRB1	rs1801253	Missense	Exercise Response	G (0.22)	10q25.3	Leineweber 2006
ADRB2	No rs Number	Not Available	BP	G (0.09)	5q32	Svetkey 2011
ADRB2	No rs number	Not Available	BP	A (0.23)	5q32	Svetkey 2011
ADRB2	rs2082382	Not Available	BP	G (0.41)	5q32	Johnson 2011
ADRB2	rs6580586	Not Available	BP	C (0.11)	5q32	Johnson 2011
ADRB2	rs1042714	Missense	Exercise Response	G (0.45)	5q32	Macho-Azcarate 2003
CHRM2	rs8191992	3' Untranslated Region	Exercise Response	T (0.44)	7q33	Hautala 2006
COMT	rs4680	Missense	BP	G (0.48)	22q11.21	Chi Htun 2011
PNMT	rs3764351	Near Gene-5	BP	G (0.47)	17q12	Huang 2011

Table 2. (Continued)

Gene[a]	Rs Number	Type of Variant	Phenotype	Minor Allele Frequency[b]	Chromosome Location	Reference
PNMT	rs876493	5' Untranslated Region	BP	G (0.45)	17q12	Huang 2011
ii. Guanine Binding Proteins						
GNAS	rs7121	Coding Synonymous	Exercise Response	C (0.48)	20q13.32	Pescatello 2009
GNB3	rs2301339	Intron	BP	A (0.30)	12p13	Yazdanpanah 2007
GNB3	rs4963516	Near Gene-5	BP	C (0.33)	12p13	Montasser 2011
GNB3	rs5443	Coding Synonymous	Exercise Response	T (0.47)	12p13	Rankinen 2002
GNB3	rs5446	3' Untranslated Region	BP	T (0.19)	12p13	Gu 2006
iii. Other						
AMPD1	rs17602729	Nonsense	Exercise Response	T (0.11)	1p13.2	Rubio 2005
ATP2B1	rs2070759	Intron	BP	C (0.49)	12q21.33	Tabara 2010
CA1	rs13278559	Not Available	BP	T (0.10)	8q21.2	Johnson 2011
CACNA1A	rs1985579	Intron	BP	A (0.36)	19p13.2	Johnson 2011
CACNA1C	rs16929470	Intron	BP	T (0.07)	12p12.3	Johnson 2011
CACNA1C	rs2239101	Intron	BP	C (0.13)	12p12.3	Johnson 2011
CASR	rs1801725	Missense	Exercise Response	T (0.16)	3q21.1	Lorentzon 2001
CASR	rs4678172	Intron	BP	T (0.30)	3q21.1	Jung 2009
CASR	rs6438712	Intron	BP	G (0.29)	3q21.1	Jung 2009
CASR	rs937626	Intron	BP	G (0.35)	3q21.1	Jung 2009
CASR	rs9874845	Intron	BP	T (0.34)	3q21.1	Jung 2009
SDK1	rs645106	Intron	BP	A (0.15)	7p22.2	Oguri 2010
SLC6A2	rs2242446	Near Gene-5	Medication Response	C (0.37)	16q12.2	Nonen 2008
SLC6A2	rs5569	Coding Synonymous	Medication Response	A (0.34)	16q12.2	Nonen 2008
TH	rs10770141	Near Gene-3	BP	T (0.34)	11p15.5	Nielson 2010
C. Nitric Oxide Synthase Pathway						
EDN1	No rs Number[d]	5' Untranslated Region	Exercise Response	4 repeats (0.32)	6q24.1	Charu 2006
EDN1	rs1800541	Near Gene-5	BP	G (0.31)	6q24.1	Dong 2004
EDN1	rs2070699	Intron	Exercise Response	G (0.32)	6q24.1	Rankinen 2007
EDN1	rs5369	Coding Synonymous	Exercise Response	A (0.10)	6q24.1	Rankinen 2007

Gene[a]	Rs Number	Type of Variant	Phenotype	Minor Allele Frequency[b]	Chromosome Location	Reference
EDN1	rs5370	Missense	Exercise Response	T (0.36)	6q24.1	Rankinen 2007
MMP3	No rs Number[d]	Not Available	Medication Response	5A (0.47)	11q22.2	Sherva 2010
NOS3	rs1799983	Missense	BP	T (0.36)	7q36.1	Pereira 2007
NOS3	rs1800779	Intron	Exercise Response	G (0.39)	7q36.1	Franks 2005
NOS3	rs1800783	Intron	Exercise Response	A (0.40)	7q36.1	Franks 2005
NOS3	rs2070744	Intron	Exercise Response	C (0.09)	7q36.1	Augeri 2009
NOS3	rs3800787	Intron	Exercise Response	C (0.48)	7q36.1	Franks 2005
NOS3	rs3918212	Intron	Exercise Response	C (0.01)	7q36.1	Franks 2005
NOS3	rs3918220	Intron	Exercise Response	G (0.01)	7q36.1	Franks 2005
TGFB1	rs1982073	Missense	Exercise Response	C (0.42)	19q13.2	Rivera 2001
D. Other Related BP Regulatory Pathways						
APOE	rs2223989	Missense	Exercise Response	C (0.47)	19q13.2	Hagberg 1999
APOE	rs7412	Missense	Exercise Response	T (0.16)	19q13.2	Hagberg 1999
CYBA	rs1049255	3' Untranslated Region	Exercise Response	A (0.44)	16q24.3	Feairheller 2009
CYBA	rs4673	Missense	Exercise Response	T (0.31)	16q24.3	Feairheller 2009
CYP11B2	rs4539	Missense	BP	C (0.47)	8q24.3	Kumar 2003
CYP11B2	rs3201271	3' Untranslated Region	BP	G (0.45)	8q24.3	Kumar 2003
CYP11B2	No rs Number	Not Available	BP	T (0.32)	8q24.3	Svetkey 2011
CYP11B2	rs28930074	Missense	BP	C (0.13)	8q24.3	Kumar 2003
CYP17A1	rs1004467	Intron	BP	C (0.07)	10q24.32	Liu 2011
CYP17A1	rs11191548	3' Untranslated Region	BP	C (0.08)	10q24.32	Liu 2011
CYP2D6	rs1065852	Missense	Exercise Response	T (0.23)	22q13.1	Zateyschchikov 2007
CYP3A5	rs776746	Intron	BP	A (0.06)	7q22.1	Zhang 2010
FABP2	rs1799883	Missense	Exercise Response	A (0.37)	4q26	de Luis 2006
LEPR	rs1137100	Missense	Exercise Response	A (0.49)	7q31.3	Kilpelainen 2008b
LPL	No rs Number	Intron	Exercise Response	T (0.47)	8p21.3	Hagberg 1999
LPL	No rs Number	Intron	Exercise Response	G (0.29)	8p21.3	Hagberg 1999
LPL	rs328	Nonsense	Exercise Response	G (0.10)	8p21.3	Flavell 2006
2) From High Throughput Genotyping Studies of BP Meeting Statistical Significance After Bonferroni Correction for Multiple Testing						

Table 2. (Continued)

Gene[a]	Rs Number	Type of Variant	Phenotype	Minor Allele Frequency[b]	Chromosome Location	Reference
ADAMTS8	rs11222084	Not Available	BP	T (0.38)	11q24.3	Wain 2011
ADM	rs7129220	Not Available	BP	A (0.07)	11p15.4	International Consortium 2011
ADRB1	rs2782980	Not Available	BP	T (0.20)	10q25.3	Wain 2011
AL365265.23	rs16877320	Not Available	BP	G (0.13)	6p22.3	Adeyemo 2009
ARHGAP42	rs633185	Intron	BP	G (0.35)	11q22.1	International Consortium 2011
ATP2B1	rs2681472	Intron	BP	G (0.17)	12q21.33	Levy 2009
ATP2B1	rs2681492	Intron	BP	C (0.20)	12q21.33	Levy 2009
ATXN2	rs653178	Intron	BP	C (0.48)	12q24.1	Newton-Cheh 2009
c10orf107	rs1530440	Intron	BP	T (0.19)	10q21	Newton-Cheh 2009
c10orf107	rs4590817	Intron	BP	C (0.11)	10q21.2	International Consortium 2011
C21orf91	rs2258119	Intron	BP	C (0.28)	21q21.1	Fox 2011
CACNA1H	rs3751664	Missense	BP	T (0.11)	16p13.3	Adeyemo 2009
CACNB2	rs11014166	Intron	BP	T (0.34)	10p12.31	Levy 2009
CACNB2	rs1813353	Not Available	BP	C (0.25)	10p12.31	International Consortium 2011
CACNB2	rs4373814	Not Available	BP	G (0.49)	10p12.33	International Consortium 2011
CHIC2	rs871606	Not Available	BP	T (0.85)	4q12	Wain 2011
CSK	rs1378942	Intron	BP	T (0.33)	15q24.1	Newton-Cheh 2009
CSK-ULK3	rs6495122	Not Available	BP	A (0.42)	15q24.1	Levy 2009
EBF1	rs11953630	Not Available	BP	T (0.26)	5q33.3	International Consortium 2011
FGF5	rs1458038	Not Available	BP	T (0.24)	4q21.21	International

Gene[a]	Rs Number	Type of Variant	Phenotype	Minor Allele Frequency[b]	Chromosome Location	Reference
						Consortium 2011
FGF5	rs16998073	Not Available	BP	T (0.19)	4q21.21	Newton-Cheh 2009
FIGN	rs13002573	Not Available	BP	G (0.20)	2q24.3	Wain 2011
FIGN	rs1446468	Not Available	BP	T (0.53)	2q24.3	Wain 2011
FURIN-FES	rs2521501	Intron	BP	T (0.20)	15q26.1	International Consortium 2011
GNAS - END3	rs6015450	Not Available	BP	G (0.10)	20q13.32	International Consortium 2011
GOSR2	rs17608776	Not Available	BP	C (0.14)	11p14.1	International Consortium 2011
GPR98/ARRDC3	rs10474346	Not Available	BP	C (0.29)	5q14.3	Fox 2011
GUCY1A3-GUCY1B3	rs13139571	Intron	BP	A (0.20)	4q32.1	International Consortium 2011
HFE	rs1799945	Missense	BP	G (0.08)	6p22.2	International Consortium 2011
IPO7	rs12279202	Intron	BP	A (0.12)	11p15	Adeyemo 2009
JAG1	rs1327235	Not Available	BP	A (0.50)	20p12.2	International Consortium 2011
MAP4	rs319690	Intron	BP	T (0.51)	3p21.31	Wain 2011
MDS1	rs1918974	Not Available	BP	C (0.47)	3p26.2	Newton-Cheh 2009
MECOM	rs419076	Intron	BP	T (0.43)	3p26.2	International Consortium 2011
MOV10	rs2932538	Near Gene-5	BP	A (0.21)	1p13.2	International Consortium 2011
MTHFR	rs13306560	Near Gene-5	BP	A (0.04)	1p36.22	Tomaszewski 2010
MTHFR-NPPB	rs17367504	Intron	BP	G (0.17)	1p36.22	International Consortium 2011

Table 2. (Continued)

Gene[a]	Rs Number	Type of Variant	Phenotype	Minor Allele Frequency[b]	Chromosome Location	Reference
NPR3-C5orf23	rs1173771	Not Available	BP	A (0.35)	5p13.3	International Consortium 2011
PIK3CG	rs17477177	Not Available	BP	T (0.72)	7q22.3	Wain 2011
PLCD3	rs12946454	Intron	BP	T (0.27)	17q21.31	Newton-Cheh 2009
PLCE1	rs932764	Intron	BP	G (0.39)	10q23.33	International Consortium 2011
PLEKHA7	rs381815	Intron	BP	C (0.26)	11p15.1	Levy 2009
PMS1	rs5743185	Intron	BP	T (0.14)	2q31.1	Adeyemo 2009
PRRC2A, 3A, 4A, 5A	rs805303	Intron	BP	A (0.45)	6p21.33	International Consortium 2011
SH2B3	rs3184504	Missense	BP	T (0.48)	12q24.12	Levy 2009
SLC24A4	rs11160059	Intron	BP	A (0.18)	14q32.12	Adeyemo 2009
SLC39A8	rs13107325	Missense	BP	T (0.06)	4q24	International Consortium 2011
SLC4A7	rs13082711	Not Available	BP	C (0.11)	3p24.1	International Consortium 2011
STK39	rs6749447	Intron	BP	G (0.28)	2q24.3	Wang 2009
TBX3	rs2384550	Not Available	BP	A (0.34)	12q24.21	Levy 2009
TBX5-TBX3	rs10850411	Not Available	BP	C (0.42)	12q24.21	International Consortium 2011
ULK4	rs9815354	Intron	BP	A (0.23)	3p22.1	Levy 2009
YWHAZ	rs17365948	Intron	BP	A (0.11)	8q22.3	Adeyemo 2009
ZNF652	rs12940887	Intron	BP	T (0.21)	17q21.33	International Consortium 2011
ZNF652	rs16948048	Near Gene-5	BP	G (0.37)	17q21.33	Newton-Cheh 2009
3) Associated with Energy Metabolism and/or Body Composition						
ADIPOQ	rs2241766	Coding Synonymous	Energy Metabolism	G (0.14)	3q27.3	Zacharova 2005b

Gene[a]	Rs Number	Type of Variant	Phenotype	Minor Allele Frequency[b]	Chromosome Location	Reference
ADIPOQ	No rs Number	Intron	Body Composition	Not Available	3q27.3	Sutton 2005
ADIPOQ	No rs Number	3' Untranslated Region	Body Composition	Not Available	3q27.3	Sutton 2005
ADIPOQ	rs1501299	Intron	Body Composition	T (0.32)	3q27.3	Nakatani 2005
ADIPOQ	rs182052	Intron	Body Composition	A (0.43)	3q27.3	Sutton 2005
ADIPOQ	rs4632532	Not Available	Body Composition	T (0.49)	3q27.3	Sutton 2005
ADIPOQ	rs860291	Not Available	Body Composition	T (0.06)	3q27.3	Sutton 2005
AKT1	rs1130214	5' Untranslated Region	Energy Metabolism	T (0.28)	14q32.32	Devaney 2011
DRD2	rs1800497	Missense	Body Composition	T (0.20)	11q23.2	Thomas 2000
FTO	rs1121980	Intron	Body Composition	T (0.48)	16q12.2	Vimaleswaran 2009
FTO	rs1477196	Intron	Body Composition	A (0.34)	16q12.2	Rampersaud 2008
FTO	rs1861868	Intron	Body Composition	G (0.48)	16q12.2	Rampersaud 2008
FTO	rs8050136	Intron	Body Composition	A (0.46)	16q12.2	Mitchell 2010
FTO	rs9939609	Intron	Body Composition	A (0.46)	16q12.2	Andreasen 2008
GHRL	rs35682	Intron	Body Composition	G (0.45)	3p25.3	Chung 2009
GHRL	rs35683	Intron	Body Composition	A (0.45)	3p25.3	Chung 2009
HTR2C	rs6318	Missense	Body Composition	C (0.17)	Xq23	Pooley 2004
IGF2	rs3842759	Intron	Body Composition	T (0.11)	11p15.5	Heude 2007
IGF2	rs680	3' Untranslated Region	Body Composition	A (0.33)	11p15.5	Heude 2007
IL15	rs1589241	Intron	Body Composition	T (0.29)	4q31.21	Pistilli 2008
INSIG2	rs7566605	Not Available	Body Composition	C (0.30)	2q14.2	Franks 2008
LEP	rs17151919	Missense	Body Composition	A (0.03)	15q26.3	Friedlander 2010
LEP	rs2167270	5' Untranslated Region	Body Composition	A (0.35)	15q26.3	Friedlander 2010
LEP	rs28954369	Near Gene-5	Body Composition	T (0.06)	15q26.3	Friedlander 2010
LEP	rs4731413	Not Available	Body Composition	A (0.17)	15q26.3	De Krom 2007
LEP	rs4731427	Intron	Body Composition	C (0.07)	15q26.3	Friedlander 2010
LEP	rs7799039	Not Available	Body Composition	A (0.49)	15q26.3	Jiang 2004
LEPR	No rs Number	Not Available	Body Composition	A (0.35)	7q31.3	DeSilva 2001
LEPR	No rs Number[c]	3' Untranslated Region	Body Composition	Insertion (0.18)	7q31.3	Zacharova 2005
LEPR	rs1045895	Intron	Body Composition	A (0.39)	7q31.3	Gallichio 2009

Table 2. (Continued)

Gene[a]	Rs Number	Type of Variant	Phenotype	Minor Allele Frequency[b]	Chromosome Location	Reference
LEPR	rs1137101	Missense	Body Composition	A (0.45)	7q31.3	Gallichio 2009
LEPR	rs8179183	Missense	Body Composition	C (0.15)	7q31.3	Chagnon 2000
LIPE	No rs Number	Not Available	Body Composition	G (0.06)	19q13.2	Garenc 2002
LIPE	No rs Number[d]	Intron	Body Composition	X (0.43)	19q13.2	Lavebratt 2002
MC4R	rs17782313	Not Available	Body Composition	C (0.28)	18q21.32	Huang 2011b
MC4R	rs2229616	Missense	Body Composition	A (0.01)	18q21.32	Geller 2004
MC4R	rs7242169	Not Available	Body Composition	G (0.50)	18q21.32	Loos 2005
MTHFR	rs2066470	Coding Synonymous	Body Composition	T (0.10)	1p36.14	Liu 2008
MTHFR	rs3737964	Intron	Body Composition	A (0.31)	1p36.14	Liu 2008
MTHFR	rs4846048	Intron	Body Composition	G (0.34)	1p36.14	Liu 2008
NR3C1	rs41423247	Intron	Body Composition	G (0.37)	5q31.3	van Rossum 2003
NR3C1	rs6195	Missense	Body Composition	G (0.08)	5q31.3	Rosmond 2001
PPARD	rs1053049	3' Untranslated Region	Energy Metabolism	C (0.32)	6q21.31	Stefan 2007
PPARD	rs2016520	5' Untranslated Region	Body Composition	C (0.25)	6q21.31	Aberle 2006
PPARD	rs2076167	Coding Synonymous	Energy Metabolism	C (0.30)	6q21.31	Stefan 2007
PPARD	rs6902123	3' Untranslated Region	Energy Metabolism	C (0.32)	6q21.31	Stefan 2007
PPARG	rs1801282	Intron	Body Composition	G (0.08)	3p25.2	Robitaille 2003
PPARG	rs1152003	Not Available	Energy Metabolism	G (0.28)	3p25.2	Kilpelainen 2008
TNF	rs361525	Near Gene-5	Energy Metabolism	A (0.07)	6p21.3	Dalziel 2002
UCP1	no rs Number	Near Gene-5	Body Composition	G (0.24)	4q31.1	Kim 2005
UCP1	rs10011540	Near Gene-5	Energy Metabolism	G (0.08)	11q13.4	Mori 2001
UCP1	rs1800592	Not Available	Energy Metabolism	A (0.27)	11q13.4	Nagai 2003
UCP1	rs45539933	Missense	Body Composition	T (0.09)	11q13.4	Hermann 2003
UCP2	rs632862	Intron	Energy Metabolism	C (0.50)	11q13.4	Lee 2008
UCP2	rs659366	Near Gene-5	Energy Metabolism	A (0.50)	11q13.4	Lee 2008
UCP2	rs660339	Missense	Energy Metabolism	T (0.50)	11q13.4	Lee 2008
UCP3	rs1800849	Near Gene-5	Energy Metabolism	T (0.42)	11q13.4	Lee 2008
VDR	rs1544410	Intron	Energy Metabolism	A (0.49)	12q13.11	Boraska 2008
VDR	rs731236	Coding Synonymous	Energy Metabolism	C (0.45)	12q13.11	Boraska 2008

Gene[a]	Rs Number	Type of Variant	Phenotype	Minor Allele Frequency[b]	Chromosome Location	Reference
VDR	rs757343	Intron	Energy Metabolism	A (0.10)	12q13.11	Boraska 2008
VDR	rs10735810	Missense	Energy Metabolism	A (0.41)	12q13.11	Boraska 2008
4) Associated with Other Established and Emerging Cardiovascular Disease Risk Factors						
A. Lipids/Lipoproteins						
ABCA1	rs2249891	Not Available	Lipids/Lipoproteins	G (0.10)	9q31.1	Peloso 2010
ABCA1	rs212077	Intron	Lipids/Lipoproteins	G (0.21)	9q31.1	Peloso 2010
ABCC6	rs150468	Intron	Lipids/Lipoproteins	C (0.20)	16p13.11	Peloso 2010
APOA1	rs670	Near Gene-3	Lipids/Lipoproteins	A (0.10)	11q23.3	Souverein 2005
APOA2	rs3813627	Near Gene-5	Lipids/Lipoproteins	T (0.33)	1q23.3	Peloso 2010
APOB	rs1367117	Missense	Lipids/Lipoproteins	T (0.29)	2p24.1	Souverein 2005
APOB	rs531819	Intron	Lipids/Lipoproteins	C (0.14)	2p24.1	Benn 2008
APOC4	rs10413089	Not Available	Lipids/Lipoproteins	C (0.15)	19q13.32	Peloso 2010
APOE	rs439401	Intron	Lipids/Lipoproteins	T (0.38)	19q13.2	Kring 2010
APOE	rs429358	Missense	Lipids/Lipoproteins	C (0.21)	19q13.2	Ariza 2010
CETP	rs5882	Missense	Lipids/Lipoproteins	G (0.30)	16q21.1	Thompson 2008
CETP	rs1800775	Near Gene-5	Lipids/Lipoproteins	C (0.45)	16q21.1	Thompson 2008
CETP	rs1800776	Near Gene-5	Lipids/Lipoproteins	A (0.02)	16q21.1	Thompson 2008
CETP	rs1800777	Missense	Lipids/Lipoproteins	A (0.05)	16q21.1	Thompson 2008
CETP	rs708272	Intron	Lipids/Lipoproteins	A (0.44)	16q21.1	Nettleton 2006
CUBN	rs7893395	Intron	Lipids/Lipoproteins	T (0.18)	10p13	Peloso 2010
HTR5A	rs1436818	Not Available	Lipids/Lipoproteins	A (0.32)	7q36.2	Zhang 2010b
HTR5A	rs1730182	Not Available	Lipids/Lipoproteins	G (0.33)	7q36.2	Zhang 2010b
HTR5A	rs3734967	Not Available	Lipids/Lipoproteins	G (0.19)	7q36.2	Zhang 2010b
LIPC	rs723967	Not Available	Lipids/Lipoproteins	C (0.21)	15q21.3	Souverein 2005
LIPC	rs1800588	Near Gene-5	Lipids/Lipoproteins	T (0.21)	15q21.3	Nettleton 2006
LIPC	rs36041167	Near Gene-5	Lipids/Lipoproteins	A (0.03)	15q21.3	Chen 2009
LIPC	rs17269264	Intron	Lipids/Lipoproteins	G (0.49)	15q21.3	Felitosa 2009
LIPC	rs17190678	Intron	Lipids/Lipoproteins	C (0.48)	15q21.3	Felitosa 2009
LIPC	rs16940379	Intron	Lipids/Lipoproteins	G (0.24)	15q21.3	Felitosa 2009
LIPC	rs12594375	Intron	Lipids/Lipoproteins	A (0.02)	15q21.3	Boes 2009

Table 2. (Continued)

Gene[a]	Rs Number	Type of Variant	Phenotype	Minor Allele Frequency[b]	Chromosome Location	Reference
LIPC	rs3829462	Missense	Lipids/Lipoproteins	G (0.01)	15q21.3	Boes 2009
LIPC	rs1077834	Near Gene-5	Lipids/Lipoproteins	G (0.28)	15q21.3	Boes 2009
LIPC	rs8023503	Intron	Lipids/Lipoproteins	T (0.02)	15q21.3	Boes 2009
LIPC	rs11856322	Intron	Lipids/Lipoproteins	A (0.32)	15q21.3	Hodoglugil 2010
LIPC	rs4775065	Not Available	Lipids/Lipoproteins	A (0.22)	15q21.3	Peloso 2010
LPL	rs268	Missense	Lipids/Lipoproteins	G (0.04)	8p21.3	Wittrup 1999
LPL	rs1801177	Missense	Lipids/Lipoproteins	A (0.03)	8p21.3	Wittrup 1999
RETN	rs34861192	Near Gene-5	Lipids/Lipoproteins	A (0.22)	19p13.2	Asano 2009
RETN	rs3745368	3' Untranslated Region	Lipids/Lipoproteins	A (0.09)	19p13.2	Asano 2009
RETN	rs34124816	Near Gene-5	Lipids/Lipoproteins	C (0.05)	19p13.2	Asano 2009
RETN	rs1862513	Near Gene-5	Lipids/Lipoproteins	G (0.37)	19p13.2	Asano 2009
RXRA	rs11185660	Not Available	Lipids/Lipoproteins	C (0.17)	9q34.2	Peloso 2010
SELP	rs732314	Intron	Lipids/Lipoproteins	A (0.46)	1q24.2	Peloso 2010
SORT1	rs646776	3' Untranslated Region	Lipids/Lipoproteins	C (0.21)	1p13.3	Devaney 2011b
SORT1	rs12740374	3' Untranslated Region	Lipids/Lipoproteins	T (0.19)	1p13.3	Musunuru 2011
SORT1	rs599839	3' Untranslated Region	Lipids/Lipoproteins	G (0.34)	1p13.3	Musunuru 2011
SORT1	rs629301	3' Untranslated Region	Lipids/Lipoproteins	G (0.21)	1p13.3	Musunuru 2011
B. Inflamation/Thrombosis						
ADRB2	rs1042711	5' Untranslated Region	Inflammation	C (0.44)	5q32	Wessel 2007
ADRB2	rs1042713	Missense	Inflammation	A (0.34)	5q32	Wessel 2007
ADRB2	rs1042717	Coding Synonymous	Inflammation	A (0.20)	5q32	Wessel 2007
ADRB2	rs1042718	Coding Synonymous	Inflammation	A (0.18)	5q32	Wessel 2007
ADRB2	rs2053044	Near Gene-5	Inflammation	A (0.45)	5q32	Wessel 2007
ADRB2	rs41371044	Near Gene-5	Inflammation	A (0.35)	5q32	Wessel 2007
ADRB2	rs41432452	Near Gene-5	Inflammation	C (0.44)	5q32	Wessel 2007
ADRB2	rs1801704	5' Untranslated Region	Inflammation	C (0.49)	5q32	Wessel 2007
BDKRB2	rs1046248	Missense	Inflammation	T (0.11)	14q32.1	Asselbergs 2007
BDKRB2	rs5810761[c]	Intron	Inflammation	Deletion (0.46)	14q32.1	Asselbergs 2007
BDKRB2	rs1799722	5' Untranslated Region	Inflammation	T (0.41)	14q32.1	Asselbergs 2007

Gene[a]	Rs Number	Type of Variant	Phenotype	Minor Allele Frequency[b]	Chromosome Location	Reference
CRP	rs1800947	Coding Synonymous	Inflammation	C (0.04)	1q23.2	Carlson 2005
CRP	rs1205	3' Untranslated Region	Inflammation	A (0.32)	1q23.2	Wang 2006
CRP	rs1130864	3' Untranslated Region	Inflammation	A (0.31)	1q23.2	Wang 2006
CRP	rs1341665	Not Available	Inflammation	T (0.35)	1q23.2	Wang 2006
CRP	rs3093059	Near Gene-3	Inflammation	C (0.06)	1q23.2	Wang 2006
CRP	rs2794521	Near Gene-3	Inflammation	G (0.26)	1q23.2	Wang 2006
CRP	rs3091244	Near Gene-3	Inflammation	T (0.07)	1q23.2	Wang 2006
CRP	rs876538	Not Available	Inflammation	T (0.20)	1q23.2	Wang 2006
FGA	rs6050	Missense	Inflammation	G (0.25)	4q28	Reiner 2006
FGA	rs2070011	5' Untranslated Region	Inflammation	A (0.37)	4q28	Reiner 2006
FGB	rs1800790	Near Gene-5	Inflammation	A (0.14)	4q28	Reiner 2006
FGG	rs1049636	3' Untranslated Region	Inflammation	C (0.29)	4q31.3	Reiner 2006
HNMT	rs2071048	Near Gene-5	Inflammation	C (0.37)	2q22.1	Chen 2003
HNMT	rs45516894	Missense	Inflammation	T (0.09)	2q22.1	Chen 2003
HNMT	rs1455158	3' Untranslated Region	Inflammation	G (0.27)	2q22.1	Chen 2003
F7	rs6046	Missense	Inflammation	T (0.12)	13q34	Zee 2009
IL1B	rs1143634	Coding Synonymous	Inflammation	T (0.22)	2q13	Zee 2009
IL6	rs1800796	Near Gene-5	Inflammation	C (0.27)	7p15.3	Cheung 2011
IL6	rs2069837	Intron	Inflammation	G (0.11)	7p15.3	Cheung 2011
IL10	rs1800872	Near Gene-5	Inflammation	A (0.20)	1q32.1	Zee 2009
IL10	rs1800871	Near Gene-5	Inflammation	T (0.17)	1q32.1	Kuningas 2009
IL10	rs3024490	Intron	Inflammation	T (0.22)	1q32.1	Kuningas 2009
IL10	rs1554286	Intron	Inflammation	T (0.17)	1q32.1	Kuningas 2009
PAI-1	No rs Number[d]	Intron	Thrombosis	5G (0.48)	7q22.1	Bjorck 2011
PROC	rs2069901	Near Gene-5	Thrombosis	C (0.44)	2q14.3	Reiner 2008
PROCR	rs867186	Missense	Thrombosis	G (0.09)	20q11.22	Reiner 2008
PROS1	rs4857343	Intron	Thrombosis	C (0.18)	3q11.2	Reiner 2008
TLR4	rs10983755	Near Gene-5	Inflamation	A (0.03)	9q33.1	Chen 2010
TH	rs6356	Missense	Inflamation	A (0.38)	11p15.5	Wessel 2007
TH	rs10770140	Near Gene-3	Inflamation	G (0.35)	11p15.5	Wessel 2007

Table 2. (Continued)

Gene[a]	Rs Number	Type of Variant	Phenotype	Minor Allele Frequency[b]	Chromosome Location	Reference
TH	rs10840490	Near Gene-3	Inflamation	G (0.11)	11p15.5	Wessel 2007
TH	rs10734659	Near Gene-3	Inflamation	A (0.50)	11p15.5	Wessel 2007
5) From High Throughput Genotyping Studies of BP Meeting Arbitrary Statistical Significance						
ABCC4	rs9590141	Not Available	BP	A (0.12)	13q32	Adeyemo 2009
AC089987.26-201	rs17237198	Not Available	BP	A (0.03)	12q13.11	Hong 2010
AC089987.26-201	rs7312017	Not Available	BP	G (0.41)	12q13.11	Hong 2010
AC096631.2	rs12748299	Not Available	BP	C (0.13)	1q32.1	Adeyemo 2009
ACPP	rs11714139	Not Available	BP	T (0.08)	3q22.1	Adeyemo 2009
ADC	rs16835244	Missense	BP	T (0.07)	1p35.1	Hong 2010
ADD2	rs3755351	Intron	BP	A (0.36)	2p13.3	Kato 2008
ADH7	rs991316	Not Available	BP	T (0.45)	4q23	Adeyemo 2009
ADRA2A	rs11195417	Not Available	BP	A (0.09	10q25.2	Sober 2009
ADRA2A	rs11195419	3' Untranslated Region	BP	A (0.11)	10q25.2	Sober 2009
AL354747.12	rs7902529	Not Available	BP	A (0.14)	10p15.3	Adeyemo 2009
ALDH1A2	rs1550576	Not Available	BP	T (0.14)	15q21.3	Adeyemo 2009
AP000473.2	rs2823756	Not Available	BP	T (0.44)	21q21.2	Adeyemo 2009
ATP2B1	rs11105354	Intron	BP	G (0.18)	12q21.33	Levy 2009
ATXN2	rs10774625	Intron	BP	A (0.49)	12q24	Levy 2009
ATXN2	rs4766578	Intron	BP	T (0.49)	12q24	Levy 2009
C12orf30	rs17696736	Intron	BP	G (0.44)	12q24	Levy 2009
C12orf51	rs11066188	Intron	BP	A (0.43)	12q24	Levy 2009
C14orf118	rs2121070	Intron	BP	T (0.15)	14q24.3	Levy 2007
C18orf1	rs8096897	Intron	BP	G (0.01)	18p11.21	Levy 2009
C21orf91	rs243601	Not Available	BP	G (0.48)	21q21.1	Fox 2011
C21orf91	rs243603	Not Available	BP	C (0.50)	21q21.1	Fox 2011
C21orf91	rs243605	Near Gene-3	BP	C (0.50)	21q21.1	Fox 2011
C21orf91	rs243607	3' Untranslated Region	BP	C (0.50)	21q21.1	Fox 2011
C21orf91	rs243609	3' Untranslated Region	BP	T (0.49)	21q21.1	Fox 2011
C21orf91	rs2220511	3' Untranslated Region	BP	T (0.37)	21q21.1	Fox 2011

Gene[a]	Rs Number	Type of Variant	Phenotype	Minor Allele Frequency[b]	Chromosome Location	Reference
CAMK4	rs10493340	Not Available	BP	G (0.22)	5q21.3	Levy 2007
CASZ1	rs155524	Intron	BP	C (0.43)	1p36	Takeuchi 2010
CASZ1	rs284277	Intron	BP	C (0.35)	1p36.22	Levy 2009
CASZ1	rs880315	Intron	BP	C (0.35)	1p36.22	Levy 2009
CDH13	rs11646213	Not Available	BP	A (0.41)	16q24.3	Org 2009
CDYL2	rs4613079	Not Available	BP	T (0.18)	16q23.2	Adeyemo 2009
CYP17A1	rs12413409	Intron	BP	A (0.06)	10q24	Takeuchi 2010
CYP17A1	rs1328925	Not Available	BP	T (0.42)	4q32.1	Levy 2007
DCK	rs10512889	Not Available	BP	T (0.17)	5p15.31	Levy 2007
F13A1	rs13201744	Not Available	BP	A (0.16)	6p25	Adeyemo 2009
FAM155A	rs9301196	Not Available	BP	T (0.12)	13q33	Adeyemo 2009
FMNL2	rs13413144	Intron	BP	T (0.13)	2q23.3	Fox 2011
GPD2	rs592582	Not Available	BP	T (0.28)	2q24.1	Fox 2011
GPR98	rs1858309	Not Available	BP	C (0.28)	5q14.3	Fox 2011
GPR98	rs7709572	Not Available	BP	G (0.28)	5q14.3	Fox 2011
GPR98	rs7724489	Not Available	BP	A (0.28)	5q14.3	Fox 2011
IPO13	rs1990151	Intron	BP	A (0.01)	1p34.1	Fox 2011
ITGA9	rs743395	Intron	BP	T (0.40)	3p22.2	Levy 2009
ITGA9	rs7640747	Intron	BP	G (0.39)	3p22.2	Levy 2009
KCTD1	rs506038	Intron	BP	C (0.22)	18q11.2	Org 2009
KCTD1	rs9948310	Intron	BP	C (0.14)	18q11.2	Org 2009
LDHAL3	rs11692045	Not Available	BP	C (0.41)	2p21	Adeyemo 2009
LZTS1	rs11988036	Not Available	BP	T (0.24)	8p22	Adeyemo 2009
MC4R	rs11659639	Not Available	BP	C (0.10)	18q22	Adeyemo 2009
MDS1	rs1685374	Not Available	BP	C (0.04)	3q26	Adeyemo 2009
MSTN	rs13401889	Not Available	BP	C (0.21)	2q32	Levy 2009
MYADML	rs9308945	Not Available	BP	G (0.42)	2p22.3	Yang 2009
NRXN3	rs10135446	Not Available	BP	A (0.13)	14q31	Adeyemo 2009
NUCB2	rs214070	Intron	BP	A (0.24)	11p15.1	Fox 2011
OPN5	rs10485320	Intron	BP	C (0.29)	6p12.3	Levy 2007

Table 2. (Continued)

Gene[a]	Rs Number	Type of Variant	Phenotype	Minor Allele Frequency[b]	Chromosome Location	Reference
P4HA2	rs9791170	Not Available	BP	A (0.43)	5q31	Adeyemo 2009
PLD2	rs2286672	Missense	BP	A (0.39)	17p13.2	Hong 2010
PLEKHA7	rs11024074	Intron	BP	C (0.28)	11p15	Levy 2009
PLEKHA7	rs7926335	Intron	BP	C (0.26)	11p15.1	Levy 2009
PMS1	rs7571613	Not Available	BP	G (0.18)	2q31.1	Levy 2009
PRC1	rs1867226	Not Available	BP	C (0.46)	15q26	Adeyemo 2009
PTGER3	rs2268062	Intron	BP	C (0.38)	1p31.1	Sober 2009
PTPN14	rs11120313	Not Available	BP	A (0.16)	1q32	Adeyemo 2009
RHBG	rs12408339	Near Gene-3	BP	A (0.11)	1q22	Fox 2011
RP11-182B22.4	rs16848861	Not Available	BP	G (0.20)	1q43	Adeyemo 2009
RP11-182B22.4	rs2146204	Not Available	BP	C (0.09)	1q24.2	Adeyemo 2009
RP11-182B22.4	rs2183737	Not Available	BP	T (0.46)	9q21.11	Adeyemo 2009
RPL10L	rs11846013	Not Available	BP	A (0.14)	14q21.2	Adeyemo 2009
SLC25A42	rs6511018	Intron	BP	G (0.20)	19p13.11	Fox 2011
SLC25A42	rs12985799	Intron	BP	C (0.20)	19p13.11	Fox 2011
SLC25A42	rs2012318	Intron	BP	C (0.20)	19p13.11	Fox 2011
SLC25A42	rs11666627	Intron	BP	C (0.20)	19p13.11	Fox 2011
SLC25A42	rs10417974	3' Untranslated Region	BP	C (0.20)	19p13.11	Fox 2011
SLC2A1	rs1105297	Intron	BP	T (0.32)	1p34.2	Sober 2009
SLC4A2	rs2303934	Intron	BP	T (0.03)	7q36.2	Sober 2009
SLC8A1	rs394112	Intron	BP	A (0.08)	2p22.1	Sober 2009
SLC8A1	rs405884	Intron	BP	C (0.10)	2p22.1	Sober 2009
SLC8A1	rs406222	Intron	BP	G (0.08)	2p22.1	Sober 2009
SLC8A1	rs415695	Intron	BP	C (0.10)	2p22.1	Sober 2009
SLITRK3	rs6784190	Not Available	BP	T (0.25)	3q26.1	Org 2009
SMARCD2	rs2665797	Not Available	BP	G (0.10)	17q23.3	Adeyemo 2009
SV2B	rs8039294	Not Available	BP	G (0.48)	15q26	Adeyemo 2009
TMEM16C	rs1994547	Not Available	BP	T (0.13)	11p14.3	Org 2009
TRAFD1	rs17630235	Near Gene-3	BP	A (0.43)	12q	Levy 2009

Gene[a]	Rs Number	Type of Variant	Phenotype	Minor Allele Frequency[b]	Chromosome Location	Reference
UGT2A3	rs1841055	Not Available	BP	A (0.16)	4q13.2	Levy 2007
ULK4	rs6768438	Intron	BP	A (0.16)	3p22	Levy 2009
ULK4	rs9816772	Intron	BP	T (0.16)	3p22	Levy 2009
ULK4	rs9852991	Intron	BP	A (0.16)	3p22	Levy 2009
USH2A	rs2797221	Intron	BP	T (0.02)	1q41	Tomaszewski 2010
WRN	rs2553268	Intron	BP	C (0.28)	8p12	Vasan 2007
XRG9	rs7828552	Not Available	BP	C (0.31)	8q13.3	Vasan 2007
None	rs10491334	Intron	BP	T (0.20)	5q22.1	Levy 2007
None	rs10498500	Not Available	BP	G (0.13)	14q23.2	Levy 2007
None	rs10504389	Near Gene-5	BP	T (0.15)	8q13.1	Levy 2007
None	rs10506595	Not Available	BP	A (0.21)	12q15	Levy 2007
None	rs10510911	Not Available	BP	G (0.42)	3p14.1	Levy 2007
None	rs10520569	Not Available	BP	A (0.14)	15q25.2	Levy 2007
None	rs10744835	Not Available	BP	A (0.30)	12q24	Levy 2009
None	rs11065987	Not Available	BP	G (0.42)	12q24.21	Levy 2009
None	rs11105328	Not Available	BP	G (0.18)	12q21.33	Levy 2009
None	rs11105364	Not Available	BP	G (0.18)	12q21.33	Levy 2009
None	rs11105368	Not Available	BP	G (0.18)	12q21.33	Levy 2009
None	rs11105378	Not Available	BP	C (0.18)	12q21.33	Levy 2009
None	rs11110912	Intron	BP	G (0.17)	12q23	Welcomme Trust 2007
None	rs11895934	Not Available	BP	G (0.18)	2q32.2	Levy 2009
None	rs12230074	Not Available	BP	C (0.18)	12q21.33	Levy 2009
None	rs12579302	Near Gene-5	BP	G (0.18)	12q21.33	Levy 2009
None	rs1338657	Not Available	BP	T (0.36)	6q16.3	Levy 2007
None	rs1408113	Intron	BP	A (0.40)	9q32	Levy 2007
None	rs1408263	Intron	BP	T (0.26)	6p22.3	Levy 2007
None	rs1434939	Intron	BP	A (0.36)	8q13.2	Levy 2007
None	rs1519592	Not Available	BP	G (0.21)	6q24.1	Levy 2007

Table 2. (Continued)

Gene[a]	Rs Number	Type of Variant	Phenotype	Minor Allele Frequency[b]	Chromosome Location	Reference
None	rs1588260	Not Available	BP	G (0.22)	5q23.1	Levy 2007
None	rs1590919	Not Available	BP	T (0.22)	13q33.2	Levy 2007
None	rs17249754	Not Available	BP	G (0.18)	12q21.33	Levy 2009
None	rs1816088	Not Available	BP	T (0.20)	5p13.1	Levy 2007
None	rs1937506	Not Available	BP	A (0.29)	13q21	Welcomme Trust 2007
None	rs1963982	Not Available	BP	C (0.44)	8q13.3	Levy 2007
None	rs1991391	Not Available	BP	A (0.35)	12q24.21	Levy 2009
None	rs2035254	Not Available	BP	G (0.34)	3q13.11	Levy 2007
None	rs2322509	Not Available	BP	C (0.43)	8p21.2	Levy 2007
None	rs2398162	Intron	BP	G (0.26)	15q26	Welcomme Trust 2007
None	rs2509458	Not Available	BP	G (0.17)	6q15	Levy 2007
None	rs2820037	Not Available	BP	T (0.14)	1q43	Welcomme Trust 2007
None	rs3853241	Not Available	BP	T (0.08)	5q34	Levy 2007
None	rs4370013	Intron	BP	T (0.19)	3p26.3	Levy 2007
None	rs4514016	Intron	BP	C (0.09)	8q24.12	Levy 2007
None	rs4842666	Not Available	BP	C (0.18)	12q21.33	Levy 2009
None	rs629448	Not Available	BP	A (0.31)	9p21.2	Levy 2007
None	rs636864	Not Available	BP	T (0.25)	6q25.1	Levy 2007
None	rs6489992	Not Available	BP	A (0.37)	12q24.21	Levy 2009
None	rs6763833	Intron	BP	C (0.20)	3p14.1	Levy 2007
None	rs6940110	Not Available	BP	C (0.43)	6p24.3	Levy 2007
None	rs6950982	Not Available	BP	G (0.23)	7q22.1	Levy 2007
None	rs6997709	Not Available	BP	T (0.29)	8q24	Welcomme Trust 2007
None	rs715987	Not Available	BP	C (0.15)	10p15.1	Cho 2009

Gene[a]	Rs Number	Type of Variant	Phenotype	Minor Allele Frequency[b]	Chromosome Location	Reference
None	rs726698	Not Available	BP	T (0.49)	2p22.3	Levy 2007
None	rs729053	Not Available	BP	G (0.27)	18q21.2	Levy 2007
None	rs7564968	Not Available	BP	C (0.18)	2q32.2	Levy 2009
None	rs7961152	Intron	BP	A (0.42)	12p12	Welcomme Trust 2007
None	rs7963771	Not Available	BP	T (0.31)	12q24.21	Levy 2009
None	rs7977406	Not Available	BP	A (0.30)	12q24	Levy 2009
None	rs9311171	Intron	BP	G (0.18)	3p22.2	Levy 2007
None	rs9321764	Not Available	BP	T (0.21)	6q24.1	Levy 2007
None	rs935334	Not Available	BP	T (0.15)	14q24.3	Levy 2007
None	rs746463	Intron	BP	C (0.27)	11q22.3	Vasan 2007
None	rs2016718	Not Available	BP	T (0.48)	8q22.1	Vasan 2007
None	rs963328	Intron	BP	G (0.43)	1q32.3	Levy 2007

[a]Refers to the name of the gene for categories 1,3 and 4. Refers to the name of the nearest gene for categories 2 and 5.

[b]Allele frequencies takenfrom cited references whenavailable, otherwise fromInternational HapMapConsortium Northern andWesternEuropean-Derived AmericanCohort.

All variants are singlenucleotide polymorphismsunless reference sequencenumber indicated otherwise:[c]insertion-deletion,[d]variablenumber tandemrepeats.

Table 3. Genes and Variants Included in Our Prioritized Panel (Table 2) Summarized by Category

Category	Number of Genes	Number of Variants	Number of Chromosomes [a]
1- Associated with BP, the BP Response to Exercise or Antihypertensive Medication, and/or the Health-Related Fitness Phenotype Response to Exercise	60	162	19
Renal and Renin Angiotensin Systems	27	92	14
Sympathetic Nervous System	20	39	14
Nitric Oxide Synthase Pathway	4	14	4
Other Related BP Regulatory Pathways	9	17	7
2- From High Throughput Genotyping Studies of BP Meeting Statistical Significance After Bonferroni Correction for Multiple Testing[b]	-	55	17
3- Associated with Energy Metabolism and/or Body Composition[c]	22	61	15
4- Associated with Other Established and Emerging Cardiovascular Disease Risk Factors	30	86	16
Lipid Metabolism[d]	14	43	10
Inflammation/Thrombosis	16	43	11
5- From High Throughput Genotyping Studies of BP Meeting Arbitrary Statistical Significance Thresholds[b]	-	149	20
Total	102	513	23

BP - Blood Pressure.

[a] Indicates number of chromosomes containing at least one variant from this category. See Methods, Prioritized Panel Organization, Column Six for an explanation of chromosome location.

[b] The number of genes is not listed for these categories because many variants from high throughput genotyping studies are not located within established genes.

[c] The gene summary for this category does not include the leptin receptor gene (*LEPR*) as it is in category 1.

[d] The gene summary for this category does not include the apolipoprotein (*APOE*) or lipoprotein lipase (*LPL*) genes as they are in category 1.

A delimitation of our panel is that, unlike previous panels in the literature [41-43], we did not include variants on the basis of LD. We employed this strategy in order to limit our panel to variants with direct evidence for association with health-related phenotypes. Future studies could expand the panel to include variants in LD, by inputting the variants currently included to an algorithm designed to find LD variants such as TAGGER [54]. The inclusion of LD variants would allow us to include a greater number of variants in strong candidate genes likely to associate with our phenotype [44,55,56].

Despite the many advantages of a GWAS that include the discovery of previously unexplored variants associated with phenotypes, a systematic and hypothesis-free approach, and the mitigation of selection bias with regard to variants explored, there are also limitations.These limitations include detecting small effect sizes, meeting the high statistical

significance needed to test the large the number of variants examined, enrolling large samples, and ensuring quality controlling of the genotype and phenotype assessments. Thus, our prioritized panel of 513 genetic variants can be to be used in conjunction with high throughput genotyping studies such as GWAS in future studies to help address these limitations.

Table 4. Genetic Variants Summarized by Type of Variant[a]

Type of Variant	Number of Variants	Percentage of Total Panel Variants
Intron	188	36.6%
Not Available	146	28.5%
Missense	59	11.5%
Near Gene Regions	51	9.9%
Near Gene-5	36	7.0%
Near Gene-3	15	2.9%
Untranslated Regions	45	8.8%
3’ Untranslated Region	33	6.4%
5’ Untranslated Region	12	2.3%
Coding Synonymous	22	4.3%
Nonsense	2	0.4%
Total	513	100.0%

[a] See Table 1 for the definitions of terms used in this table.

For example, subjects could be genotyped using GWAS high throughput genotyping and then be phenotyped for their BP response to exercise, i.e., before and after a standardized, structured exercise intervention. To explore genotype BP phenotype associations from the panel, we would then use the GWAS genotyping data and compare it to the panel variants in the order of the prioritized categories from category 1 through category 5. The variants showing significant association with the BP phenotype in both the GWAS and panel would be identified as significant genetic determinants of the BP response to exercise. In the event a panel variant was not included in the GWAS, its genotype could be determined by *imputation* based on GWAS data using LD information from the HapMap [61,66]. Lastly, as new genetic variants are identified in the emerging literature as relevant to the BP response to exercise, we would statistically examine them as confirmation of their importance. If statistically significant associations are found, they then would also be included on our panel for future replication studies. Updated versions of the panel including these new variants will be published annually in online supplementary material for this chapter at www. novapublishers.com.

In summary, this chapter provides genomic information for genetic variants in our prioritized panel (Table 2), and can serve as a reference for future studies seeking to utilize this panel to study BP response to exercise. It can also serve as a time saving exercise genomics reference for researchers and clinicians. Lastly, it can serve as a model for future prioritized panels to investigate the response of other health-related fitness phenotypes to exercise.

APPENDIX A. GENE NAME ABBREVIATIONS

1) From Candidate Gene Studies (Categories 1, 3, and 4 of Table 2)	
Gene Abbreviation	Gene Name
ABCA1	ATP-Binding Cassette, Sub-Family A, Member 1
ABCC6	ATP-Binding Cassette, Sub-Family C, Member 6
ACE	Angiotensin 1 Converting Enzyme
ADD1	Adducin 1 (Alpha)
ADD2	Adducin 2 (Beta)
ADD3	Adducin 3 (Gamma)
ADIPOQ	Adiponectin, C1Q and Collagen Domain Containing
ADRA1A	Adrenergic Alpha 1A Receptor
ADRA1D	Adrenergic Alpha 1D Receptor
ADRA2A	Adrenergic Alpha 2A Receptor
ADRB1	Adrenergic Beta 1 Receptor
ADRB2	Adrenergic Beta 2 Receptor
AGT	Angiotensinogen
AGTR1	Angiotensin II Receptor Type I
AGTR2	Angiotensin II Receptor Type II
AKT1	V-Akt Murine Thymoma Viral Oncogene Homolog 1
AMPD1	Adenosine Monophosphate Deaminase 1
APLNR	Apelin Receptor
APOA1	Apolipoprotein A1
APOA2	Apolipoprotein A-II
APOB	Apolipoprotein B
APOC4	Apolipoprotein C-IV
APOE	Apolipoprotein E
ATP2B1	ATPase, Ca++ Transporting, Plasma Membrane 1
AVPR1A	Arginine Vasopressin VA1 Receptor
BDKRB2	Bradykinin B2 Receptor
CA1	Carbonic Anhydrase
CACNA1A	Calcium Channel, Voltage-Dependent, P/Q Type, Alpha 1A Subunit
CACNA1C	Calcium Channel, Voltage-Dependent, L Type, Alpha 1C Subunit
CASR	Calcium Sensing Receptor
CETP	Cholesteryl Ester Transfer Protein, Plasma
CHRM2	Cholenergic Receptor, Muscarinic 2
COMT	Catechol-O-Methyltransferase Activity
CRP	C-Reactive Protein
CUBN	Cubulin
CYBA	Cytochrome b-245, Alpha Polypeptide
CYP11B2	Aldosterone Synthase
CYP17A1	Cytochrome P450, Family 17, Subfamily A, Polypeptide 1
CYP2D6	Cytochrome P450, Family 2, Subfamily D, Polypeptide 6
CYP3A5	Cytochrome P450, Family 3, Subfamily A, Polypeptide 5
DRD2	Dopamine Receptor D2

EDN1	Endothelin-1
EMILIN1	Elastin Microfibril Interfacer 1
F7	Coagulation Factor VII
FABP2	Fatty Acid Binding Protein 2
FGA	Fibrinogen Alpha
FGB	Fibrinogen Beta
FGG	Fibrinogen Gamma
FTO	Fat Mass and Obesity Associated
GHRL	Ghrelin
GNAS	Guanine Nucleotide Binding Protein
GNB3	G Protein Beta 3
HNMT	Histamine N-Methyltransferase
HSD11B1	11-Beta-Hydroxysteroid Dehydrogenase, Type 1
HSD11B2	11-Beta-Hydroxysteroid Dehydrogenase, Type 2
HTR2C	5-Hydroxytryptamine Receptor 2C
HTR5A	5-Hydroxytryptamine Receptor 5A
IGF2	Insulin Growth Factor 2
IL10	Interleukin 10
IL15	Interleukin 15
IL1B	Interleukin-1 Beta
IL6	Interleukin 6 (Interferon, Beta 2)
INSIG2	Insulin Induced Gene 2
KLK1	Kallikrein 1
LEP	Leptin
LEPR	Leptin Receptor
LIPC	Hepatic Lipase
LIPE	Lipase, Hormone-Sensitive
LPL	Lipoprotein Lipase
MC4R	Melanocortin-4 Receptor
MMP3	Matrix Metalloproteinase
MTHFR	Methylenetetrahydrofolate Reductase
NEDD4L	Neural Precursor Cell Expressed, Developmentally Down-Regulated 4-Like
NOS3	Endothelial Nitric Oxide Synthase
NPPA	Natriuretic Peptide Precursor A
NR3C1	Nuclear Receptor Subfamily 3, Group C, Member 1
NR3C2	Nuclear Receptor Subfamily 3, Group C, Member 2
PAI-1	Serpin Peptidase Inhibitor, Clade E, Member 1; Serpine1
PNMT	Phenylethanolamine N-Methyltransferase
PPARD	Peroxisome Proliferative Receptor Delta
PPARG	Peroxisome Proliferative Receptor Gamma
PROC	Protein C
PROCR	Protein C Receptor, Endothelial
PROS1	Protein S
RABGAP1L	Rab Gtpase Activating Protein 1-Like

Appendix A. (Continued)

REN	Renin
RETN	Resistin
RXRA	Retinoid X Receptor, Alpha
SCNN1A	Sodium Channel, Nonvoltage-Gated 1 Alpha
SCNN1B	Sodium Channel, Nonvoltage-Gated 1 Beta
SCNN1G	Y-Subunit Epithelial Sodium Channel
SDK1	Sidekick 1
SELP	Selectin P
SLC12A3	Solute Carrier Family 12 (Sodium/Chloride Transporters), Member 3
SLC4A5	Solute Carrier Family 4, Sodium Bicarbonate Cotransporter, Member 5
SLC6A2	Solute Carrier Family 6 (Neurotransmitter Transporter, Noradrenalin), Member 2
SLC9A1	Solute Carrier Family 9 (Sodium/Hydrogen Exchanger), Member 1
SORT1	Sortilin
TBXA2R	Thromboxane A2 Receptor, Platelet
TGFB1	Transforming Growth Factor, B1
TH	Tyrosine Hydroxylase
TLR4	Toll-Like Receptor 4
TNF	Tumour Necrosis Factor
UCP1	Mitochondrial Uncoupling Protein 1
UCP2	Mitochondrial Uncoupling Protein 2
UCP3	Mitochondrial Uncoupling Protein 3
VDR	Vitamin D Receptor
WNK1	Protein Kinase, Lysine-Deficient 1
WNK4	Protein Kinase, Lysine-Deficient 4
2) From High Throughput Genotyping Studies (Categories 2 and 5 of Table 2)	
Gene Abbreviation	Gene Name
ABCC4	Atp-Binding Cassette, Sub-Family C (Cftr/Mrp), Member 4
AC089987.26-201	AC089987.26-201
AC096631.2	AC096631.2
ACPP	Acid Phosphatase, Prostate
ADAMTS8	A Disintegrin-Like and Metalloproteinase with Thrombospondin Type 1 Motif, 8
ADC	Arginine Decarboxylase
ADH7	Alcohol Dehydrogenase 7
ADM	Adrenomedullin
ADRB1	Adrenergic Beta 1 Receptor
AL354747.12	AL354747.12
AL365265.23	AL365265.23
ALDH1A2	Aldehyde Dehydrogenase 1 Family, Member A2

AP000473.2	AP000473.2
ARHGAP42	Rho GTPase Activating Protein 42
ARRDC3	Arrestin Domain Containing 3
ATP2B1	Atpase, Ca++ Transporting, Plasma Membrane 1
ATXN2	Ataxin 2
c10orf107	Chromosome 10 Open Reading Frame 107
C12orf30	Chromosome 12 Open Reading Frame 30
C12orf51	Chromosome 12 Open Reading Frame 51
C14orf118	Chromosome 14 Open Reading Frame 118
C18orf1	Chromosome 18 Open Reading Frame 1
C21orf91	Chromosome 21 Open Reading Frame 91
C5orf23	Chromosome 5 Open Reading Frame 23
CACNA1H	Calcium Channel, Voltage-Dependent, T Type, Alpha-1H Subunit
CACNB2	Calcium Channel, Voltage=Dependent, Beta-2 Subunit
CAMK4	Calcium/Calmodulin-Dependent Protein Kinase IV
CASZ1	Castor Zinc Finger 1
CDH13	H-Cahedrin
CDYL2	Chromodomain Protein, Y-Like 2
CHIC2	Cysteine-Rich Hydrophobic Domain 2
CSK	C-Src Tyrosine Kinase
DCK	Deoxycytidine Kinase
EBF1	Early B-Cell, Factor 1
EDN3	Endothelin-3
F13A1	Coagulation Factor XIII, A1 Polypeptide
FAM155A	Family With Sequence Similarity 155, Member A
FES	Feline Sarcoma Oncogene
FGF5	Fibroblast Growth Factor 5
FIGN	Fidgetin
FMNL2	Formin-Like 2
FURIN	Furin
GPD2	Glycerol-3 Phosphate Dehydrogenase 2
GNAS	Guanine Nucleotide Binding Protein
GOSR2	Golgi Snap Receptor Complex Member 2
GPR98	G Protein-Coupled Receptor 98
GUCY1A3	Guanylate Cyclase 1, Soluble, Alpha-3
GUCY1B3	Gluanlyate Cyclase 1, Soluble, Beta-3
HFE	HFE Gene
IPO7	Importin 7
IPO13	Importin 13
ITGA9	Integrin, Alpha 9
JAG1	Jagged 1
KCTD1	Potassium Channel Tetramerisation Domain
LDHAL3	Lactate Dehydrogenase A-Like 3
LZTS1	Leucine Zipper, Putative Tumor Suppressor 1
MAP4	Microtubule-Associated Protein 4

Appendix A. (Continued)

MC4R	Melanocortin 4 Receptor
MDS1	Myelodysplasia Syndrome 1
MECOM	Ecotropic Viral Integration Site 1
MOV10	MOV10-Like 1
MSTN	Myostatin
MTHFR	Methylenetetrahydrofolate Reductase
MYADML	Myeloid-Associated Differentiation Marker-Like
NPPB	Natriuretic Peptide Precursor B
NPR3	Natriuretic Peptide Receptor C
NRXN3	Neurexin 3
NUCB2	Nucleobindin 2
OPN5	Opsin 5
P4HA2	Prolyl 4-Hydroxylase, Alpha Polypeptide II
PIK3CG	Phosphatidylinositol 3-Kinase, Catalytic, Gamma
PLCD3	Phospholipase C, Delta 3
PLCE1	Phospholipase C, Epsilon 1
PLD2	Phospholipase D2
PLEKHA7	Pleckstrin Homology Domain Containing, Family A Member 7
PMS1	Pms1 Postmeiotic Segregation Increased 1 (S. Cerevisiae)
PRC1	Protein Regulator Of Cytokinesis 1
PRRC2A, 3A, 4A, 5A	Proline-Rich Coiled-Coil Protein 2A, 3A, 4A, 5A
PTGER3	Prostaglandin E Receptor 3 (Subtype Ep3)
PTPN14	Protein Tyrosine Phosphatase, Non-Receptor Type 14
RHBG	Rh Family, B Glycoprotein
RP11-182B22.4	Retinitis Pigmentosa 11
RPL10L	Ribosomal Protein L10-Like
SH2B3	Sh2B Adaptor Protein 3
SLC24A4	Sodium/Potassium/Calcium Exchanger
SLC2A1	Solute Carrier Family 2 (Facilitated Glucose Transporter), Member 1
SLC25A42	Solute Carrier Family 25, Member 42
SLC39A8	Solute Carrier Family 39 (Zinc Transporter), Member 8
SLC4A2	Solute Carrier Family 4, Anion Exchanger, Member 2 (Erythrocyte Membrane Protein Band 3-Like 1)
SLC4A7	Solute Carrier Family 4 (Sodium Bicarbonate Cotransporter), Member 7
SLC8A1	Solute Carrier Family 8 (Sodium/Calcium Exchanger), Member 1
SLITRK3	Slitrk
SMARCD2	Swi/Snf Related, Matrix Associated, Actin Dependent Regulator Of Chromatin, Subfamily D, Member 2
STK39	Serine Threonine Kinase 39
SV2B	Synaptic Vesicle Glycoprotein 2
TBX3	T-Box 3
TBX5	T-Box 5

TMEM16C	Transmembrane Protein 16C
TRAFD1	Traf-Type Zinc Finger Domain Containing 1
UGT2A3	Udp Glucuronosyltransferase 2 Family, Polypeptide A3
ULK3	Unc-51-Like Kinase 3
ULK4	Unc-51-Like Kinase 4
USH2A	Usher Syndrome 2A
WRN	Werner Syndrome, RecQ Helicase-Like
XKR9	XK, Kell Blood Group Complex Subunit-Related Family, Member 9
YWHAZ	Tyrosine 3-Monooxygenase/Tryptophan 5-Monooxygenase Activation Protein, Zeta Polypeptide
ZNF652	Zinc Finger Protein 652

APPENDIX B. (REFERENCES FOR TABLE 2)

Aberle, J., Hopfer, I., Beil, F. U., Seedorf, U. Association of peroxisome proliferator-activated receptor delta +294T/C with body mass index and interaction with peroxisome proliferator-activated receptor alpha L162V.*Int. J. Obes.* (Lond.), Dec., 2006, 30, 1709-1713.

Adeyemo, A., Gerry, N., Chen, G., Herbert, A., Doumatey, A., Huang, H. et al. A genome-wide association study of hypertension and blood pressure in African Americans. *PLoS Genet.*, Jul., 2009, 5, e1000564.

Andreasen, C. H., Stender-Petersen, K. L., Mogensen, M. S., Torekov, S. S., Wegner, L., Andersen, G. et al. Low physical activity accentuates the effect of the FTO rs9939609 polymorphism on body fat accumulation. *Diabetes*, Jan., 2008, 57, 95-101.

Ariza, M. J., Sanchez-Chaparro, M. A., Baron, F. J., Hornos, A. M., Calvo-Bonacho, E., Rioja, J. et al. Additive effects of LPL, APOA5 and APOE variant combinations on triglyceride levels and hypertriglyceridemia: results of the ICARIA genetic sub-study. *BMC Med. Genet*., Apr. 29, 2010, 11, 66.

Asano, H., Izawa, H., Nagata, K., Nakatochi, M., Kobayashi, M., Hirashiki, A. et al. Plasma resistin concentration determined by common variants in the resistin gene and associated with metabolic traits in an aged Japanese population. *Diabetologia*, Feb., 2010, 53, 234-246.

Asselbergs, F. W., Williams, S. M., Hebert, P. R., Coffey, C. S., Hillege, H. L., Navis, G. et al. Epistatic effects of polymorphisms in genes from the renin-angiotensin, bradykinin, and fibrinolytic systems on plasma t-PA and PAI-1 levels. *Genomics*, Mar., 2007, 89, 362-369.

Augeri, A. L., Tsongalis, G. J., Van Heest, J. L., Maresh, C. M., Thompson, P. D., Pescatello, L. S. The endothelial nitric oxide synthase −786 T>C polymorphism and the exercise-induced blood pressure and nitric oxide responses among men with elevated blood pressure.*Atherosclerosis*, 6, 2009, 204, e28-e34.

Benn, M., Stene, M. C., Nordestgaard, B. G., Jensen, G. B., Steffensen, R., Tybjaerg-Hansen, A. Common and rare alleles in apolipoprotein B contribute to plasma levels of low-density lipoprotein cholesterol in the general population. *J. Clin. Endocrinol.Metab*., Mar., 2008, 93, 1038-1045.

Bianchi, G., Ferrari, P., Staessen, J. A. Adducin polymorphism: detection and impact on hypertension and related disorders. *Hypertension*, Mar., 2005, 45, 331-340.

Bjorck, H. M., Eriksson, P., Alehagen, U., De Basso, R., Ljungberg, L. U., Persson, K. et al. Gender-specific association of the plasminogen activator inhibitor-1 4G/5G polymorphism with central arterial blood pressure. *Am. J. Hypertens.*, Jul., 2011, 24, 802-808.

Blanchard, B. E, Tsongalis, G. J, Guidry, M., LaBelle, L. A., Poulin, M., Taylor, A. L. et al. RAAS polymorphisms alter the acute blood pressure response to aerobic exercise among men with hypertension. *Eur. J. Appl. Physiol.*, May, 2006, 97, 26-33.

Boes, E., Coassin, S., Kollerits, B., Heid, I. M., Kronenberg, F. Genetic-epidemiological evidence on genes associated with HDL cholesterol levels: a systematic in-depth review. *Exp. Gerontol.*, Mar., 2009, 44, 136-160.

Boraska, V., Skrabic, V., Zeggini, E., Groves, C. J., Buljubasic, M., Peruzovic, M. et al. Family-based analysis of vitamin D receptor gene polymorphisms and type 1 diabetes in the population of South Croatia. *J. Hum. Genet.*, 2008, 53, 210-214.

Bouzekri, N., Zhu, X., Jiang, Y., McKenzie, C. A., Luke, A., Forrester, T. et al. Angiotensin I-converting enzyme polymorphisms, ACE level and blood pressure among Nigerians, Jamaicans and African-Americans. *Eur. J. Hum. Genet.*, Jun., 2004, 12, 460-468.

Bozkurt, O., Verschuren, W. M., Van Wieren-de Wijer, B. M., Knol, M. J., De Boer, A., Grobbee, D. E. et al. Genetic variation in the renin-angiotensin system modifies the beneficial effects of ACE inhibitors on the risk of diabetes mellitus among hypertensives. *J. Hum. Hypertens.*, Nov., 2008, 22, 774-780.

Busst, C. J., Scurrah, K. J., Ellis, J. A., Harrap, S. B. Selective genotyping reveals association between the epithelial sodium channel gamma-subunit and systolic blood pressure. *Hypertension*, Oct., 2007, 50, 672-678.

Carlson, C. S., Aldred, S. F., Lee, P. K., Tracy, R. P., Schwartz, S. M., Rieder, M. et al. Polymorphisms within the C-reactive protein (CRP) promoter region are associated with plasma CRP levels. *Am. J. Hum. Genet.*, Jul., 2005, 77, 64-77.

Chagnon, Y. C., Chung, W. K., Perusse, L., Chagnon, M., Leibel, R. L., Bouchard, C. Linkages and associations between the leptin receptor (LEPR) gene and human body composition in the Quebec Family Study. *Int. J. Obes. Relat.Metab.Disord.*, Mar., 1999, 23, 278-286.

Charu, R, Stobdan, T., Ram, R. B., Khan, A. P., Qadar Pasha, M. A., Norboo, T. et al. Susceptibility to high altitude pulmonary oedema: role of ACE and ET-1 polymorphisms. *Thorax.*,Nov., 2006, 61, 1011-1012.

Chen, G. L., Wang, H., Wang, W., Xu, Z. H., Zhou, G., He, F. et al. Histamine N-methyltransferase gene polymorphisms in Chinese and their relationship with enzyme activity in erythrocytes. *Pharmacogenetics*, Jul., 2003, 13, 389-397.

Chen, K., Wang, Y. T., Gu, W., Zeng, L., Jiang, D. P., Du, D. Y. et al. Functional significance of the Toll-like receptor 4 promoter gene polymorphisms in the Chinese Han population. *Crit. Care Med.*, May, 2010, 38, 1292-1299.

Chen, S. N., Cilingiroglu, M., Todd, J., Lombardi, R., Willerson, J. T., Gotto, A. M.,Jr. et al. Candidate genetic analysis of plasma high-density lipoprotein-cholesterol and severity of coronary atherosclerosis. *BMC Med. Genet.*, Oct. 30, 2009, 10, 111.

Cheung, B. M., Ong, K. L., Tso, A. W., Leung, R. Y., Cherny, S. S., Sham, P. C., et al. Relationship of Plasma Interleukin-6 and Its Genetic Variants With Hypertension in Hong Kong Chinese. *Am. J. Hypertens.*, Aug. 11, 2011,

Cho, Y. S., Go, M. J., Kim, Y. J., Heo, J. Y., Oh, J. H., Ban, H. J. et al. A large-scale genome-wide association study of Asian populations uncovers genetic factors influencing eight quantitative traits. *Nat. Genet.*, May, 2009, 41, 527-534.

Chung, W. K., Patki, A., Matsuoka, N., Boyer, B. B., Liu, N., Musani, S. K. et al. Analysis of 30 genes (355 SNPS) related to energy homeostasis for association with adiposity in European-American and Yup'ik Eskimo populations. *Hum. Hered.*,2009, 67, 193-205.

Dalziel, B., Gosby, A. K., Richman, R. M., Bryson, J. M., Caterson, I. D. Association of the TNF-alpha -308 G/A promoter polymorphism with insulin resistance in obesity. *Obes. Res.*, May, 2002, 10, 401-407.

De Krom, M., Van der Schouw, Y. T., Hendriks, J., Ophoff, R. A., Van Gils, C. H., Stolk, R. P. et al. Common genetic variations in CCK, leptin, and leptin receptor genes are associated with specific human eating patterns. *Diabetes*, Jan., 2007, 56, 276-280.

De Luis, D. A., Aller, R., Izaola, O., Sagrado, M. G., Conde, R. Influence of ALA54THR polymorphism of fatty acid binding protein 2 on lifestyle modification response in obese subjects. *Ann. Nutr. Metab*.,2006, 50, 354-360.

De Silva, A. M., Walder, K. R., Boyko, E. J., Whitecross, K. F., Nicholson, G., Kotowicz, M. et al. Genetic variation and obesity in Australian women: a prospective study. *Obes. Res.*, Dec., 2001, 9, 733-740.

Devaney, J. M., Gordish-Dressman, H., Harmon, B. T., Bradbury, M. K., Devaney, S. A., Harris, T. B. et al. AKT1 polymorphisms are associated with risk for metabolic syndrome. *Hum. Genet.*, Feb., 2011, 129, 129-139.

Devaney, J. M., Thompson, P. D., Visich, P. S., Saltarelli, W. A., Gordon, P. M., Orkunoglu-Suer, E. F. et al. The 1p13.3 LDL (C)-associated locus shows large effect sizes in young populations. *Pediatr. Res.*, Jun., 2011, 69, 538-543.

Dong, Y., Wang, X., Zhu, H., Treiber, F. A., Snieder, H. Endothelin-1 gene and progression of blood pressure and left ventricular mass: longitudinal findings in youth. *Hypertension*, Dec., 2004, 44, 884-890.

Feairheller, D. L., Brown, M. D., Park, J. Y., Brinkley, T. E., Basu, S., Hagberg, J. M. et al. Exercise training, NADPH oxidase p22phox gene polymorphisms, and hypertension.*Med. Sci. Sports Exerc.*, Jul., 2009, 41, 1421-1428.

Feitosa, M. F., Myers, R. H., Pankow, J. S., Province, M. A., Borecki, I. B. LIPC variants in the promoter and intron 1 modify HDL-C levels in a sex-specific fashion. *Atherosclerosis*, May, 2009, 204, 171-177.

Flavell, D. M., Wootton, P. T., Myerson, S. G., World, M. J., Pennell, D. J., Humphries, S. E. et al. Variation in the lipoprotein lipase gene influences exercise-induced left ventricular growth. *J. Mol. Med.* (Berl.), Feb., 2006, 84, 126-131.

Fox, E. R., Young, J. H., Li, Y., Dreisbach, A. W., Keating, B. J., Musani, S. K. et al. Association of genetic variation with systolic and diastolic blood pressure among African Americans: the Candidate Gene Association Resource study. *Hum. Mol. Genet., Jun.* 1, 2011, 20, 2273-2284.

Franks, P. W., Jablonski, K. A., Delahanty, L. M., McAteer, J. B., Kahn, S. E., Knowler, W. C. et al. Assessing gene-treatment interactions at the FTO and INSIG2 loci on obesity-

related traits in the Diabetes Prevention Program. *Diabetologia*, Dec., 2008, 51, 2214-2223.

Franks, P. W., Ravussin, E., Hanson, R. L., Harper, I. T., Allison, D. B., Knowler, W. C. et al. Habitual physical activity in children: the role of genes and the environment. *Am. J. Clin. Nutr*., Oct., 2005, 82, 901-908.

Friedlander, Y., Li, G., Fornage, M., Williams, O. D., Lewis, C. E., Schreiner, P. et al. Candidate molecular pathway genes related to appetite regulatory neural network, adipocyte homeostasis and obesity: results from the CARDIA Study. *Ann. Hum. Genet*., Sep. 1, 2010, 74, 387-398.

Gallicchio, L., Chang, H. H., Christo, D. K., Thuita, L., Huang, H. Y., Strickland, P. et al. Single nucleotide polymorphisms in obesity-related genes and all-cause and cause-specific mortality: a prospective cohort study. *BMC Med. Genet., Oct.* 9, 2009, 10, 103.

Garenc, C., Perusse, L., Chagnon, Y. C., Rankinen, T., Gagnon, J., Borecki, I. B. et al. The hormone-sensitive lipase gene and body composition: the HERITAGE Family Study. *Int. J. Obes. Relat.Metab.Disord*., Feb., 2002, 26, 220-227.

Geller, F., Reichwald, K., Dempfle, A., Illig, T., Vollmert, C., Herpertz, S. et al. Melanocortin-4 receptor gene variant I103 is negatively associated with obesity. *Am. J. Hum. Genet*., Mar., 2004, 74, 572-581.

Gu, D., Su, S., Ge, D., Chen, S., Huang, J., Li, B. et al. Association study with 33 single-nucleotide polymorphisms in 11 candidate genes for hypertension in Chinese. *Hypertension*, Jun., 2006, 47, 1147-1154.

Hagberg, J. M., Ferrell, R. E., Dengel, D. R., Wilund, K. R. Exercise training-induced blood pressure and plasma lipid improvements in hypertensives may be genotype dependent. *Hypertension*, Jul., 1999, 34, 18-23.

Hautala, A. J., Rankinen, T., Kiviniemi, A. M., Makikallio, T. H., Huikuri, H. V., Bouchard, C. et al. Heart rate recovery after maximal exercise is associated with acetylcholine receptor M2 (CHRM2) gene polymorphism. *Am. J. Physiol. Heart Circ. Physiol.,* Jul., 2006, 291, H459-66.

He, J., Gu, D., Kelly, T. N., Hixson, J. E., Rao, D. C., Jaquish, C. E. et al. Genetic variants in the renin-angiotensin-aldosterone system and blood pressure responses to potassium intake. *J. Hypertens*., Sep., 2011, 29, 1719-1730.

Herrmann, S. M., Wang, J. G., Staessen, J. A., Kertmen, E., Schmidt-Petersen, K., Zidek, W. et al. Uncoupling protein 1 and 3 polymorphisms are associated with waist-to-hip ratio. *J. Mol. Med*. (Berl.), May, 2003, 81, 327-332.

Heude, B., Ong, K. K., Luben, R., Wareham, N. J., Sandhu, M. S. Study of association between common variation in the insulin-like growth factor 2 gene and indices of obesity and body size in middle-aged men and women. *J. Clin. Endocrinol.Metab*., Jul., 2007, 92, 2734-2738.

Hodoglugil, U., Williamson, D. W., Mahley, R. W. Polymorphisms in the hepatic lipase gene affect plasma HDL-cholesterol levels in a Turkish population. *J. Lipid Res*., Feb., 2010, 51, 422-430.

Hong, K. W., Jin, H. S., Lim, J. E., Cho, Y. S., Go, M. J., Jung, J. et al. Non-synonymous single-nucleotide polymorphisms associated with blood pressure and hypertension. *J. Hum. Hypertens*., Nov., 2010, 24, 763-774.

Htun, N. C., Miyaki, K., Song, Y., Ikeda, S., Shimbo, T., Muramatsu, M. Association of the catechol-O-methyl transferase gene Val158Met polymorphism with blood pressure and

prevalence of hypertension: interaction with dietary energy intake. *Am. J. Hypertens.*, Sep., 2011, 24, 1022-1026.

Huang, C., Zhang, S., Hu, K., Ma, Q., Yang, T. Phenylethanolamine N-methyltransferase gene promoter haplotypes and risk of essential hypertension.*Am. J. Hypertens.*, Nov., 2011, 24, 1222-1226.

Huang, W., Sun, Y., Sun, J. Combined effects of FTO rs9939609 and MC4R rs17782313 on obesity and BMI in Chinese Han populations. *Endocrine*, Feb., 2011, 39, 69-74.

Ingelsson, E., Larson, M. G., Vasan, R. S., O'Donnell, C. J., Yin, X., Hirschhorn, J. N. et al. Heritability, linkage, and genetic associations of exercise treadmill test responses. *Circulation*, Jun. 12, 2007, 115, 2917-2924.

International Consortium for Blood Pressure Genome-Wide Association Studies; Ehret, G. B., Munroe, P. B., Rice, K. M., Bochud, M., Johnson, A. D. et al. Genetic variants in novel pathways influence blood pressure and cardiovascular disease risk. *Nature*, Sep. 11, 2011, 478, 103-109.

Jiang, Y., Wilk, J. B., Borecki, I., Williamson, S., DeStefano, A. L., Xu, G. et al. Common variants in the 5' region of the leptin gene are associated with body mass index in men from the National Heart, Lung, and Blood Institute Family Heart Study. *Am. J. Hum. Genet.*, Aug., 2004, 75, 220-230.

Johnson, A. D., Newton-Cheh, C., Chasman, D. I., Ehret, G. B., Johnson, T., Rose, L. et al. Association of hypertension drug target genes with blood pressure and hypertension in 86,588 individuals. *Hypertension*, May, 2011, 57, 903-910.

Jung, J., Foroud, T. M., Eckert, G. J., Flury-Wetherill, L., Edenberg, H. J., Xuei, X. et al. Association of the calcium-sensing receptor gene with blood pressure and urinary calcium in African-Americans. *J. Clin. Endocrinol.Metab.*, Mar., 2009, 94, 1042-1048.

Kardia, S. L., Sun, Y. V., Hamon, S. C., Barkley, R. A., Boerwinkle, E., Turner, S. T. Interactions between the adducin 2 gene and antihypertensive drug therapies in determining blood pressure in people with hypertension. *BMC Med. Genet.*, Sep. 13, 2007, 8, 61.

Kato, N., Miyata, T., Tabara, Y., Katsuya, T., Yanai, K., Hanada, H. et al. High-density association study and nomination of susceptibility genes for hypertension in the Japanese National Project. *Hum. Mol. Genet.*, Feb. 15, 2008, 17, 617-627.

Keszei, A. P., Tisler, A., Backx, P. H., Andrulis, I. L., Bull, S. B., Logan, A. G. Molecular variants of the thiazide-sensitive Na+-Cl- cotransporter in hypertensive families. *J. Hypertens.*, Oct., 2007, 25, 2074-2081.

Kilpelainen, T. O., Lakka, T. A., Laaksonen, D. E., Lindstrom, J., Eriksson, J. G., Valle, T. T. et al. SNPs in PPARG associate with type 2 diabetes and interact with physical activity. *Med. Sci. Sports Exerc.*, Jan., 2008, 40, 25-33.

Kilpelainen, T. O., Lakka, T. A., Laaksonen, D. E., Mager, U., Salopuro, T., Kubaszek, A. et al. Interaction of single nucleotide polymorphisms in ADRB2, ADRB3, TNF, IL6, IGF1R, LIPC, LEPR, and GHRL with physical activity on the risk of type 2 diabetes mellitus and changes in characteristics of the metabolic syndrome: The Finnish Diabetes Prevention Study. *Metabolism*, Mar., 2008, 57, 428-436.

Kim, K. S., Cho, D. Y., Kim, Y. J., Choi, S. M., Kim, J. Y., Shin, S. U. et al. The finding of new genetic polymorphism of UCP-1 A-1766G and its effects on body fat accumulation.*Biochim.Biophys.* Acta, Jun. 30, 2005, 1741, 149-155.

Kring, S. I., Brummett, B. H., Barefoot, J., Garrett, M. E., Ashley-Koch, A. E., Boyle, S. H. et al. Impact of psychological stress on the associations between apolipoprotein E variants and metabolic traits: findings in an American sample of caregivers and controls. *Psychosom. Med.*, Jun., 2010, 72, 427-433.

Kumar, N. N., Benjafield, A. V., Lin, R. C., Wang, W. Y., Stowasser, M., Morris, B. J. Haplotype analysis of aldosterone synthase gene (CYP11B2) polymorphisms shows association with essential hypertension. *J. Hypertens.*, Jul., 2003, 21, 1331-1337.

Kuningas, M., May, L., Tamm, R., Van Bodegom, D., Van den Biggelaar, A. H., Meij, J. J. et al. Selection for genetic variation inducing pro-inflammatory responses under adverse environmental conditions in a Ghanaian population. *PLoS One*, Nov. 11, 2009, 4, e7795.

Laaksonen, D. E., Siitonen, N., Lindstrom, J., Eriksson, J. G., Reunanen, P., Tuomilehto, J. et al. Physical activity, diet, and incident diabetes in relation to an ADRA2B polymorphism. *Med. Sci. Sports Exerc.*, Feb., 2007, 39, 227-232.

Lavebratt, C., Ryden, M., Schalling, M., Sengul, S., Ahlberg, S., Hoffstedt, J. The hormone-sensitive lipase i6 gene polymorphism and body fat accumulation. *Eur. J. Clin. Invest.*, Dec., 2002, 32, 938-942.

Lee, H. J., Ryu, H. J., Shin, H. D., Park, B. L., Kim, J. Y., Cho, Y. M. et al. Associations between polymorphisms in the mitochondrial uncoupling proteins (UCPs) with T2DM. *Clin.Chim.Acta.*, Dec., 2008, 398, 27-33.

Lee, J., Aziz, H., Liu, L., Lipkowitz, M., O'Connor, D. T., Richard, E. et al. beta(1)-adrenergic receptor polymorphisms and response to beta-blockade in the African-American study of kidney disease and hypertension (AASK). *Am. J. Hypertens.*, Jun., 2011, 24, 694-700.

Leineweber, K., Bruck, H., Temme, T., Heusch, G., Philipp, T., Brodde, O. E. The Arg389Gly beta1-adrenoceptor polymorphism does not affect cardiac effects of exercise after parasympathetic inhibition by atropine. *Pharmacogenet. Genomics*, Jan., 2006, 16, 9-13.

Levy, D., Ehret, G. B., Rice, K., Verwoert, G. C., Launer, L. J., Dehghan, A. et al. Genome-wide association study of blood pressure and hypertension. *Nat. Genet.*, Jun., 2009, 41, 677-687.

Levy, D., Larson, M. G., Benjamin, E. J., Newton-Cheh, C., Wang, T. J., Hwang, S. J. et al. Framingham Heart Study 100K Project: genome-wide associations for blood pressure and arterial stiffness. *BMC Med. Genet.*, Sep. 19, 2007, 8 Suppl. 1, S3.

Liljedahl, U., Karlsson, J., Melhus, H., Kurland, L., Lindersson, M., Kahan, T. et al.A microarray minisequencing system for pharmacogenetic profiling of antihypertensive drug response.*Pharmacogenetics*, Jan., 2003, 13, 7-17.

Liu, C., Li, H., Qi, Q., Lu, L., Gan, W., Loos, R. J. et al. Common variants in or near FGF5, CYP17A1 and MTHFR genes are associated with blood pressure and hypertension in Chinese Hans. *J. Hypertens.*, Jan., 2011, 29, 70-75.

Liu, X., Zhao, L. J., Liu, Y. J., Xiong, D. H., Recker, R. R., Deng, H. W. The MTHFR gene polymorphism is associated with lean body mass but not fat body mass. *Hum. Genet.*, Mar., 2008, 123, 189-196.

Loos, R. J., Rankinen, T., Tremblay, A., Perusse, L., Chagnon, Y., Bouchard, C. Melanocortin-4 receptor gene and physical activity in the Quebec Family Study.*Int. J. Obes.* (Lond.), Apr., 2005, 29, 420-428.

Lorentzon, M., Lorentzon, R., Lerner, U. H., Nordstrom, P. Calcium sensing receptor gene polymorphism, circulating calcium concentrations and bone mineral density in healthy adolescent girls. *Eur. J. Endocrinol*., Mar., 2001, 144, 257-261.

Luo, F., Wang, Y., Wang, X., Sun, K., Zhou, X., Hui, R. A functional variant of NEDD4L is associated with hypertension, antihypertensive response, and orthostatic hypotension. *Hypertension*, Oct., 2009, 54, 796-801.

Lynch, A. I., Boerwinkle, E., Davis, B. R., Ford, C. E., Eckfeldt, J. H., Leiendecker-Foster, C. et al. Pharmacogenetic association of the NPPA T2238C genetic variant with cardiovascular disease outcomes in patients with hypertension. *JAMA*, Jan. 23, 2008, 299, 296-307.

Macho-Azcarate, T., Marti, A., Calabuig, J., Martinez, J. A. Basal fat oxidation and after a peak oxygen consumption test in obese women with a beta2 adrenoceptor gene polymorphism.*J. Nutr. Biochem*., May, 2003, 14, 275-279.

Masuki, S., Mori, M., Tabara, Y., Miki, T., Sakurai, A., Morikawa, M. et al. Vasopressin V1a receptor polymorphism and interval walking training effects in middle-aged and older people. *Hypertension*, Mar., 2010, 55, 747-754.

Mitchell, J. A., Church, T. S., Rankinen, T., Earnest, C. P., Sui, X., Blair, S. N. FTO genotype and the weight loss benefits of moderate intensity exercise. *Obesity* (Silver Spring), Mar., 2010, 18, 641-643.

Mong, J. L., Ng, M. C., Guldan, G. S., Tam, C. H., Lee, H. M., Ma, R. C. et al. Associations of insulin-like growth factor binding protein-3 gene polymorphisms with IGF-I activity and lipid parameters in adolescents. *Int. J. Obes*. (Lond.), Dec., 2009, 33, 1446-1453.

Montasser, M. E., Gu, D., Chen, J., Shimmin, L. C., Gu, C., Kelly, T. N. et al. Interactions of genetic variants with physical activity are associated with blood pressure in Chinese: the GenSalt study. *Am. J. Hypertens*., Sep., 2011, 24, 1035-1040.

Moore, N., Dicker, P., O'Brien, J. K., Stojanovic, M., Conroy, R. M., Treumann, A. et al. Renin gene polymorphisms and haplotypes, blood pressure, and responses to renin-angiotensin system inhibition. *Hypertension*, Aug., 2007, 50, 340-347.

Mori, H., Okazawa, H., Iwamoto, K., Maeda, E., Hashiramoto, M., Kasuga, M. A polymorphism in the 5' untranslated region and a Met229-->Leu variant in exon 5 of the human UCP1 gene are associated with susceptibility to type II diabetes mellitus. *Diabetologia*, Mar., 2001, 44, 373-376.

Musunuru, K., Strong, A., Frank-Kamenetsky, M., Lee, N. E., Ahfeldt, T., Sachs, K. V. et al.From noncoding variant to phenotype via SORT1 at the 1p13 cholesterol locus.*Nature*, Aug. 5, 2010, 466, 714-719.

Nagai, N., Sakane, N., Ueno, L. M., Hamada, T., Moritani, T. The -3826 A-->G variant of the uncoupling protein-1 gene diminishes postprandial thermogenesis after a high fat meal in healthy boys. *J. Clin. Endocrinol.Metab.*, Dec., 2003, 88, 5661-5667.

Nakatani, K., Noma, K., Nishioka, J., Kasai, Y., Morioka, K., Katsuki, A. et al. Adiponectin gene variation associates with the increasing risk of type 2 diabetes in non-diabetic Japanese subjects. *Int. J. Mol. Med*., Jan., 2005, 15, 173-177.

Nettleton, J. A., Steffen, L. M., Ballantyne, C. M., Boerwinkle, E., Folsom, A. R. Associations between HDL-cholesterol and polymorphisms in hepatic lipase and lipoprotein lipase genes are modified by dietary fat intake in African American and White adults. *Atherosclerosis*, Oct., 2007, 194, e131-40.

Newton-Cheh, C., Johnson, T., Gateva, V., Tobin, M. D., Bochud, M., Coin, L. et al. Genome-wide association study identifies eight loci associated with blood pressure. *Nat. Genet*., Jun., 2009, 41, 666-676.

Nielsen, S. J., Jeppesen, J., Torp-Pedersen, C., Hansen, T. W., Linneberg, A., Fenger, M. Tyrosine hydroxylase polymorphism (C-824T) and hypertension: a population-based study. *Am. J. Hypertens*., Dec., 2010, 23, 1306-1311.

Nonen, S., Okamoto, H., Fujio, Y., Takemoto, Y., Yoshiyama, M., Hamaguchi, T. et al. Polymorphisms of norepinephrine transporter and adrenergic receptor alpha1D are associated with the response to beta-blockers in dilated cardiomyopathy. *Pharmacogenomics J.* Feb., 2008, 8, 78-84.

Nossent, A. Y., Hansen, J. L., Doggen, C., Quax, P. H., Sheikh, S. P., Rosendaal, F. R. SNPs in microRNA binding sites in 3'-UTRs of RAAS genes influence arterial blood pressure and risk of myocardial infarction. *Am. J. Hypertens., Sep*., 2011, 24, 999-1006.

Oguri, M., Kato, K., Yokoi, K., Yoshida, T., Watanabe, S., Metoki, N. et al. Assessment of a Polymorphism of SDK1 With Hypertension in Japanese Individuals. *Am. J. Hypertens*., Jan., 2010, 23, 70-77.

Org, E., Eyheramendy, S., Juhanson, P., Gieger, C., Lichtner, P., Klopp, N. et al. Genome-wide scan identifies CDH13 as a novel susceptibility locus contributing to blood pressure determination in two European populations. *Hum. Mol. Genet*., Jun. 15, 2009, 18, 2288-2296.

Peloso, G. M., Demissie, S., Collins, D., Mirel, D. B., Gabriel, S. B., Cupples, L. A. et al. Common genetic variation in multiple metabolic pathways influences susceptibility to low HDL-cholesterol and coronary heart disease. *J. Lipid. Res*., Dec., 2010, 51, 3524-3532.

Pereira, T. V., Nunes, A. C., Rudnicki, M., Yamada, Y., Pereira, A. C., Krieger, J. E. Meta-analysis of the association of 4 angiotensinogen polymorphisms with essential hypertension: a role beyond M235T? *Hypertension*, Mar., 2008, 51, 778-783.

Pereira, T. V., Rudnicki, M., Cheung, B. M., Baum, L., Yamada, Y., Oliveira, P. S. et al. Three endothelial nitric oxide (NOS3) gene polymorphisms in hypertensive and normotensive individuals: meta-analysis of 53 studies reveals evidence of publication bias. *J. Hypertens.*, Sep., 2007, 25, 1763-1774.

Pescatello, L. S., Blanchard, B. E., Tsongalis, G. J., Maresh, C. M., Griffiths, B., Thompson, P. D. The GNAS 393 T>C polymorphism and the blood pressure response immediately following aerobic exercise among men with elevated blood pressure. *Vasc. Dis. Prev*., 2009, 56-64.

Pescatello, L. S., Blanchard, B. E., Tsongalis, G. J., Maresh, C. M., O'Connell, A., Thompson, P. D. The alpha-adducin Gly460Trp polymorphism and the antihypertensive effects of exercise among men with high blood pressure.*Clin. Sci*. (Lond.), Sep., 2007, 113, 251-258.

Pescatello, L. S., Kostek, M. A., Gordish-Dressman, H., Thompson, P. D., Seip, R. L., Price, T. B. et al. ACE ID genotype and the muscle strength and size response to unilateral resistance training. *Med. Sci. Sports. Exerc.*, Jun., 2006, 38, 1074-1081.

Pistilli, E. E., Devaney, J. M., Gordish-Dressman, H., Bradbury, M. K., Seip, R. L., Thompson, P. D. et al. Interleukin-15 and interleukin-15R alpha SNPs and associations with muscle, bone, and predictors of the metabolic syndrome. *Cytokine*, Jul., 2008, 43, 45-53.

Rampersaud, E., Mitchell, B. D., Pollin, T. I., Fu, M., Shen, H., O'Connell, J. R. et al. Physical activity and the association of common FTO gene variants with body mass index and obesity. *Arch. Intern. Med.*, Sep. 8, 2008, 168, 1791-1797.

Rana, B. K., Insel, P. A., Payne, S. H., Abel, K., Beutler, E., Ziegler, M. G. et al. Population-based sample reveals gene-gender interactions in blood pressure in White Americans. *Hypertension*, Jan., 2007, 49, 96-106.

Rankinen, T., Church, T., Rice, T., Markward, N., Leon, A. S., Rao, D. C. et al. Effect of endothelin 1 genotype on blood pressure is dependent on physical activity or fitness levels. *Hypertension*, Dec., 2007, 50, 1120-1125.

Rankinen, T., Rice, T., Leon, A. S., Skinner, J. S., Wilmore, J. H., Rao, D. C. et al. G protein beta 3 polymorphism and hemodynamic and body composition phenotypes in the HERITAGE Family Study. *Physiol. Genomics*, Feb. 28, 2002, 8, 151-157.

Reiner, A. P., Carty, C. L., Carlson, C. S., Wan, J. Y., Rieder, M. J., Smith, J. D. et al. Association between patterns of nucleotide variation across the three fibrinogen genes and plasma fibrinogen levels: the Coronary Artery Risk Development in Young Adults (CARDIA) study. *J. Thromb. Haemost.*, Jun., 2006, 4, 1279-1287.

Reiner, A. P., Carty, C. L., Jenny, N. S., Nievergelt, C., Cushman, M., Stearns-Kurosawa, D. J. et al. PROC, PROCR and PROS1 polymorphisms, plasma anticoagulant phenotypes, and risk of cardiovascular disease and mortality in older adults: the Cardiovascular Health Study. *J. Thromb. Haemost.*, Oct., 2008, 6, 1625-1632.

Riechman, S. E., Balasekaran, G., Roth, S. M., Ferrell, R. E. Association of interleukin-15 protein and interleukin-15 receptor genetic variation with resistance exercise training responses. *J. Appl. Physiol.*, Dec., 2004, 97, 2214-2219.

Rivera, M. A., Echegaray, M., Rankinen, T., Perusse, L., Rice, T., Gagnon, J. et al. TGF-beta(1) gene-race interactions for resting and exercise blood pressure in the HERITAGE Family Study. *J. Appl. Physiol.*, Oct., 2001, 91, 1808-1813.

Robitaille, J., Despres, J. P., Perusse, L., Vohl, M. C. The PPAR-gamma P12A polymorphism modulates the relationship between dietary fat intake and components of the metabolic syndrome: results from the Quebec Family Study. *Clin.Genet., Feb.*, 2003, 63, 109-116.

Rosmond, R., Bouchard, C., Bjorntorp, P. Tsp509I polymorphism in exon 2 of the glucocorticoid receptor gene in relation to obesity and cortisol secretion: cohort study. *BMJ*, Mar. 17, 2001, 322, 652-653.

Rubio, J. C., Martin, M. A., Rabadan, M., Gomez-Gallego, F., San Juan, A. F., Alonso, J. M. et al. Frequency of the C34T mutation of the AMPD1 gene in world-class endurance athletes: does this mutation impair performance? *J. Appl. Physiol., Jun.*, 2005, 98, 2108-2112.

Sanada, K., Iemitsu, M., Murakami, H., Tabata, I., Yamamoto, K., Gando, Y. et al. PPARgamma2 C1431T genotype increases metabolic syndrome risk in young men with low cardiorespiratory fitness. *Physiol. Genomics.*, Feb. 11, 2011, 43, 103-109.

Sherva, R., Ford, C. E., Eckfeldt, J. H., Davis, B. R., Boerwinkle, E.,Arnett, D. K. Pharmacogenetic effect of the stromelysin (MMP3) polymorphism on stroke risk in relation to antihypertensive treatment: the genetics of hypertension associated treatment study. *Stroke*, Feb., 2011, 42, 330-335.

Shimodaira, M., Nakayama, T., Sato, N., Naganuma, T., Yamaguchi, M., Aoi, N. et al. Association study of the elastin microfibril interfacer 1 (EMILIN1) gene in essential hypertension.*Am. J. Hypertens.*, May, 2010, 23, 547-555.

Simino, J., Shi, G., Kume, R., Schwander, K., Province, M. A., Gu, C. C. et al. Five blood pressure loci identified by an updated genome-wide linkage scan: meta-analysis of the Family Blood Pressure Program. *Am. J. Hypertens.*, Mar., 2011, 24, 347-354.

Sober, S., Org, E., Kepp, K., Juhanson, P., Eyheramendy, S., Gieger, C. et al. Targeting 160 candidate genes for blood pressure regulation with a genome-wide genotyping array. *PLoS One*, Jun. 29, 2009, 4, e6034.

Soranzo, N., Sanna, S., Wheeler, E., Gieger, C., Radke, D., Dupuis, J. et al. Common variants at 10 genomic loci influence hemoglobin A(C) levels via glycemic and nonglycemic pathways. *Diabetes*, Dec., 2010, 59, 3229-3239.

Souverein, O. W., Jukema, J. W., Boekholdt, S. M., Zwinderman, A. H. Tanck, M. W. Polymorphisms in APOA1 and LPL genes are statistically independently associated with fasting TG in men with CAD. *Eur. J. Hum. Genet.*,Apr., 2005, 13, 445-451.

Stefan, N., Thamer, C., Staiger, H., Machicao, F., Machann, J., Schick, F. et al. Genetic variations in PPARD and PPARGC1A determine mitochondrial function and change in aerobic physical fitness and insulin sensitivity during lifestyle intervention. *J. Clin. Endocrinol.Metab*., May, 2007, 92, 1827-1833.

Sutton, B. S., Weinert, S., Langefeld, C. D., Williams, A. H., Campbell, J. K., Saad, M. F. et al. Genetic analysis of adiponectin and obesity in Hispanic families: the IRAS Family Study. *Hum. Genet*., Jul., 2005, 117, 107-118.

Svetkey, L. P., Harris, E. L., Martin, E., Vollmer, W. M., Meltesen, G. T., Ricchiuti, V. et al. Modulation of the BP response to diet by genes in the renin-angiotensin system and the adrenergic nervous system. *Am. J. Hypertens.*, Feb., 2011, 24, 209-217.

Tabara, Y., Kohara, K., Kita, Y., Hirawa, N., Katsuya, T., Ohkubo, T. et al. Common variants in the ATP2B1 gene are associated with susceptibility to hypertension: the Japanese Millennium Genome Project. *Hypertension*, Nov., 2010, 56, 973-980.

Takeuchi, F., Isono, M., Katsuya, T., Yamamoto, K., Yokota, M., Sugiyama, T., et al. Blood pressure and hypertension are associated with 7 loci in the Japanese population. *Circulation*, Jun. 1, 2010, 121, 2302-2309.

Taylor, J. Y., Maddox, R., Wu, C. Y. Genetic and environmental risks for high blood pressure among African American mothers and daughters. *Biol. Res. Nurs.*, Jul., 2009, 11, 53-65.

Thomas, G. N., Tomlinson, B., Critchley, J. A. Modulation of blood pressure and obesity with the dopamine D2 receptor gene TaqI polymorphism. *Hypertension*, Aug., 2000, 36, 177-182.

Thompson, A., Di Angelantonio, E., Sarwar, N., Erqou, S., Saleheen, D., Dullaart, R. P. et al. Association of cholesteryl ester transfer protein genotypes with CETP mass and activity, lipid levels, and coronary risk. *JAMA*, Jun. 18, 2008, 299, 2777-2788.

Thompson, P. D., Tsongalis, G. J., Seip, R. L., Bilbie, C., Miles, M., Zoeller, R. et al. Apolipoprotein E genotype and changes in serum lipids and maximal oxygen uptake with exercise training. *Metabolism*, Feb., 2004, 53, 193-202.

Tobin, M. D., Raleigh, S. M., Newhouse, S., Braund, P., Bodycote, C., Ogleby, J. et al. Association of WNK1 gene polymorphisms and haplotypes with ambulatory blood pressure in the general population. *Circulation*, Nov. 29, 2005, 112, 3423-3429.

Tomaszewski, M., Debiec, R., Braund, P. S., Nelson, C. P., Hardwick, R., Christofidou, P. et al. Genetic architecture of ambulatory blood pressure in the general population: insights from cardiovascular gene-centric array. *Hypertension*, Dec., 2010, 56, 1069-1076.

Van Rossum, E. F., Koper, J. W., Van den Beld, A. W., Uitterlinden, A. G., Arp, P., Ester, W. et al. Identification of the BclI polymorphism in the glucocorticoid receptor gene: association with sensitivity to glucocorticoids in vivo and body mass index. *Clin.Endocrinol*. (Oxf), Nov., 2003, 59, 585-592.

Vasan, R. S., Larson, M. G., Aragam, J., Wang, T. J., Mitchell, G. F., Kathiresan, S. et al. Genome-wide association of echocardiographic dimensions, brachial artery endothelial function and treadmill exercise responses in the Framingham Heart Study. *BMC Med. Genet*., Sep. 19, 2007, 8 Suppl. 1, S2.

Vimaleswaran, K. S., Li, S., Zhao, J. H., Luan, J., Bingham, S. A., Khaw, K. T. et al. Physical activity attenuates the body mass index-increasing influence of genetic variation in the FTO gene. *Am. J. Clin. Nutr*., Aug., 2009, 90, 425-428.

Wain, L. V., Verwoert, G. C., O'Reilly, P. F., Shi, G., Johnson, T., Johnson, A. D. et al. Genome-wide association study identifies six new loci influencing pulse pressure and mean arterial pressure. *Nat. Genet.*, Sep. 11, 2011, 43, 1005-1011.

Wang, Q., Hunt, S. C., Xu, Q., Chen, Y. E., Province, M. A., Eckfeldt, J. H. et al. Association study of CRP gene polymorphisms with serum CRP level and cardiovascular risk in the NHLBI Family Heart Study. *Am. J. Physiol. Heart Circ. Physiol*., Dec., 2006, 291, H2752-7.

Wang, Y., O'Connell, J. R., McArdle, P. F., Wade, J. B., Dorff, S. E., Shah, S. J. et al. From the Cover: Whole-genome association study identifies STK39 as a hypertension susceptibility gene. *Proc. Natl. Acad. Sci*. U S A, Jan. 6, 2009, 106, 226-231.

Watkins, W. S., Hunt, S. C., Williams, G. H., Tolpinrud, W., Jeunemaitre, X., Lalouel, J. M. et al. Genotype-phenotype analysis of angiotensinogen polymorphisms and essential hypertension: the importance of haplotypes. *J. Hypertens*., Jan., 2010, 28, 65-75.

Wei, Z., Biswas, N., Wang, L., Courel, M., Zhang, K., Soler-Jover, A. et al. A common genetic variant in the 3'-UTR of vacuolar H+-ATPase ATP6V0A1 creates a micro-RNA motif to alter chromogranin A processing and hypertension risk. *Circ. Cardiovasc. Genet*., Aug. 1, 2011, 4, 381-389.

Wellcome Trust Case Control Consortium. Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls. *Nature*, Jun. 7, 2007, 447, 661-678.

Wessel, J., Moratorio, G., Rao, F.,Mahata, M., Zhang, L., Greene, W. et al. C-reactive protein, an 'intermediate phenotype' for inflammation: human twin studies reveal heritability, association with blood pressure and the metabolic syndrome, and the influence of common polymorphism at catecholaminergic/beta-adrenergic pathway loci. *J. Hypertens*., Feb., 2007, 25, 329-343.

Wessel, J., Moratorio, G., Rao, F., Mahata, M., Zhang, L., Greene, W. et al. C-reactive protein, an 'intermediate phenotype' for inflammation: human twin studies reveal heritability, association with blood pressure and the metabolic syndrome, and the influence of common polymorphism at catecholaminergic/beta-adrenergic pathway loci. *J. Hypertens.*, Feb., 2007, 25, 329-343.

Wittrup, H. H., Tybjaerg-Hansen, A., Nordestgaard, B. G. Lipoprotein lipase mutations, plasma lipids and lipoproteins, and risk of ischemic heart disease.A meta-analysis.*Circulation*, Jun. 8, 1999, 99, 2901-2907.

Yang, H. C., Liang, Y. J., Wu, Y. L., Chung, C. M., Chiang, K. M., Ho, H. Y. et al. Genome-wide association study of young-onset hypertension in the Han Chinese population of Taiwan. *PLoS One*, 2009, 4, e5459.

Yang, Y. Y., Lin, H. C., Lin, M. W., Chu, C. J., Lee, F. Y., Hou, M. C. et al. Identification of diuretic non-responders with poor long-term clinical outcomes: a 1-year follow-up of 176 non-azotaemic cirrhotic patients with moderate ascites. *Clin. Sci.* (Lond.), Dec., 2011, 121, 509-521.

Yazdanpanah, M., Aulchenko, Y. S., Hofman, A., Janssen, J. A., Sayed-Tabatabaei, F. A., Van Schaik, R. H. et al. Effects of the renin-angiotensin system genes and salt sensitivity genes on blood pressure and atherosclerosis in the total population and patients with type 2 diabetes. *Diabetes*, Jul., 2007, 56, 1905-1912.

Zacharova, J., Chiasson, J. L., Laakso, M. Leptin receptor gene variation predicts weight change in subjects with impaired glucose tolerance. *Obes. Res.*, Mar., 2005, 13, 501-506.

Zacharova, J., Chiasson, J. L., Laakso, M., STOP-NIDDM Study Group. The common polymorphisms (single nucleotide polymorphism [SNP] +45 and SNP +276) of the adiponectin gene predict the conversion from impaired glucose tolerance to type 2 diabetes: the STOP-NIDDM trial. *Diabetes*, Mar., 2005, 54, 893-899.

Zateyshchikov, D. A., Minushkina, L. O., Brovkin, A. N., Savel'eva, E. G., Zateyshchikova, A. A., Manchaeva, B. B. et al. Association of CYP2D6 and ADRB1 genes with hypotensive and antichronotropic action of betaxolol in patients with arterial hypertension. *Fundam Clin. Pharmacol.*, Aug., 2007, 21, 437-443.

Zee, R. Y., Glynn, R. J., Cheng, S., Steiner, L., Rose, L., Ridker, P. M. An evaluation of candidate genes of inflammation and thrombosis in relation to the risk of venous thromboembolism: The Women's Genome Health Study. *Circ. Cardiovasc. Genet.*, Feb., 2009, 2, 57-62.

Zhang, L., Miyaki, K., Wang, W., Muramatsu, M. CYP3A5 polymorphism and sensitivity of blood pressure to dietary salt in Japanese men.*J. Hum. Hypertens.*, May, 2010, 24, 345-350.

Zhang, Y., Smith, E. M., Baye, T. M., Eckert, J. V., Abraham, L. J., Moses, E. K. et al. Serotonin (5-HT) receptor 5A sequence variants affect human plasma triglyceride levels. *Physiol. Genomics*, Jul. 7, 2010, 42, 168-176.

Zhao, Q.,Gu, D., Hixson, J. E., Liu, D. P., Rao, D. C., Jaquish, C. E. et al. Common variants in epithelial sodium channel genes contribute to salt sensitivity of blood pressure: The GenSalt study. *Circ. Cardiovasc. Genet.*,Aug. 1, 2011, 4, 375-380.

Zhou, J. B. and Yang, J. K. Meta-analysis of association of ACE2 G8790A polymorphism with Chinese Han essential hypertension.*J. Renin. Angiotensin. Aldosterone Syst.*, Mar., 2009, 10, 31-34.

REFERENCES

[1] Pescatello, L. S., Franklin, B. A., Fagard, R., Farquhar, W. B., Kelley, G. A., Ray, C. A. et al. American College of Sports Medicine position stand. Exercise and hypertension. *Med. Sci. Sports Exerc.*, Mar., 2004, 36, 533-553.

[2] Chobanian, A. V., Bakris, G. L., Black, H. R., Cushman, W. C., Green, L. A., Izzo, J. L., Jr. et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension*, Dec., 2003, 42, 1206-1252.

[3] Hagberg, J. M., Park, J. J., Brown, M. D. The role of exercise training in the treatment of hypertension: an update. *Sports Med., Sep*., 2000, 30, 193-206.

[4] Cornelissen, V. A. and Fagard, R. H. Effects of endurance training on blood pressure, blood pressure-regulating mechanisms, and cardiovascular risk factors. *Hypertension*, Oct., 2005, 46, 667-675.

[5] Hagberg, J. M. Interactive Effects of Genetics and Acute Exercise and Exercise Training on Plasma Lipoprotein Lipid and Blood Pressure Phenotypes. In: Pescatello, L. S. and Roth, S. M., editors. Exercise Genomics. New York, NY: *Springer*; 2011; 129-156.

[6] Hagberg, J. M. and Brown, M. D. Does exercise training play a role in the treatment of essential hypertension? *J. Cardiovasc. Risk*, Aug., 1995, 2, 296-302.

[7] Pescatello, L. S. and Kulikowich, J. M. The aftereffects of dynamic exercise on ambulatory blood pressure. *Med. Sci. Sports Exerc*., Nov., 2001, 33, 1855-1861.

[8] Whelton, S. P., Chin, A., Xin, X., He, J. Effect of aerobic exercise on blood pressure: a meta-analysis of randomized, controlled trials. *Ann. Intern. Med*., Apr. 2, 2002, 136, 493-503.

[9] Fagard, R. H. Physical activity in the prevention and treatment of hypertension in the obese. *Med. Sci. Sports Exerc.*, Nov., 1999, 31, S624-30.

[10] Pescatello, L. S., Blanchard, B. E., Tsongalis, G. J., O'Connell, A. A., Gordish-Dressman, H., Maresh, C. M. et al. A comparison of the genetic and clinical profile of men that respond and do not respond to the immediate antihypertensive effects of aerobic exercise. *Application of Clinical Genetics*, 2008, 1, 7-17.

[11] Pescatello, L. S., Roth, S. M. Exercise Genomics. New York, NY: *Springer* 2011.

[12] Baldwin, K. M. and Haddad, F. Research in the exercise sciences: where we are and where do we go from here--Part II. *Exerc. Sport Sci. Rev*., Apr., 2010, 38, 42-50.

[13] Pescatello, L. S., Blanchard, B. E., Tsongalis, G. J., Maresh, C. M., O'Connell, A., Thompson, P. D. The alpha-adducin Gly460Trp polymorphism and the antihypertensive effects of exercise among men with high blood pressure. *Clin. Sci.* (Lond.), Sep., 2007, 113, 251-258.

[14] Augeri, A. L., Tsongalis, G. J., Van Heest, J. L., Maresh, C. M., Thompson, P. D., Pescatello, L. S. The endothelial nitric oxide synthase -786 T>C polymorphism and the exercise-induced blood pressure and nitric oxide responses among men with elevated blood pressure. *Atherosclerosis*, Jun., 2009, 204, e28-34.

[15] Pescatello, L., Blanchard, B. E., Tsongalis, G. J., Maresh, C. M., Griffiths, B., Thompson, P. D. The GNAS 393 T>C polymorphism and the blood pressure response immediately following aerobic exercise among men with elevated blood pressure. *Vasc. Dis. Prev*., 2009, 56-64.

[16] Blanchard, B. E., Tsongalis, G. J., Guidry, M. A., LaBelle, L. A., Poulin, M., Taylor, A. L. et al. RAAS polymorphisms alter the acute blood pressure response to aerobic exercise among men with hypertension. *Eur. J. Appl. Physiol*., May, 2006, 97, 26-33.

[17] Rankinen, T., Church, T., Rice, T., Markward, N., Leon, A. S., Rao, D. C. et al. Effect of endothelin 1 genotype on blood pressure is dependent on physical activity or fitness levels. *Hypertension*, Dec., 2007, 50, 1120-1125.

[18] Franks, P. W., Bhattacharyya, S., Luan, J., Montague, C., Brennand, J., Challis, B. et al. Association between physical activity and blood pressure is modified by variants in the G-protein coupled receptor 10. *Hypertension*, Feb., 2004, 43, 224-228.

[19] Grove, M. L., Morrison, A., Folsom, A. R., Boerwinkle, E., Hoelscher, D. M., Bray, M. S. Gene-environment interaction and the GNB3 gene in the Atherosclerosis Risk in Communities study. *Int. J. Obes*. (Lond.), Jun., 2007, 31, 919-926.

[20] De Luis, D. A., Aller, R., Izaola, O., Sagrado, M. G., Conde, R. Influence of ALA54THR polymorphism of fatty acid binding protein 2 on lifestyle modification response in obese subjects. *Ann. Nutr. Metab*., 2006, 50, 354-360.

[21] Delmonico, M. J., Ferrell, R. E., Meerasahib, A., Martel, G. F., Roth, S. M., Kostek, M. C. et al. Blood pressure response to strength training may be influenced by angiotensinogen A-20C and angiotensin II type I receptor A1166C genotypes in older men and women. *J. Am. Geriatr. Soc*., Feb., 2005, 53, 204-210.

[22] Hagberg, J. M., Ferrell, R. E., Dengel, D. R., Wilund, K. R. Exercise training-induced blood pressure and plasma lipid improvements in hypertensives may be genotype dependent. *Hypertension*, Jul., 1999, 34, 18-23.

[23] Rauramaa, R., Kuhanen, R., Lakka, T. A., Vaisanen, S. B., Halonen, P., Alen, M. et al. Physical exercise and blood pressure with reference to the angiotensinogen M235T polymorphism. *Physiol. Genomics*, Aug. 14, 2002, 10, 71-77.

[24] Rankinen, T., Rice, T., Leon, A. S., Skinner, J. S., Wilmore, J. H., Rao, D. C. et al. G protein beta 3 polymorphism and hemodynamic and body composition phenotypes in the HERITAGE Family Study. *Physiol. Genomics*, Feb. 28, 2002, 8, 151-157.

[25] Zhang, B., Sakai, T., Miura, S., Kiyonaga, A., Tanaka, H., Shindo, M. et al. Association of angiotensin-converting-enzyme gene polymorphism with the depressor response to mild exercise therapy in patients with mild to moderate essential hypertension. *Clin. Genet*., Oct., 2002, 62, 328-333.

[26] Feairheller, D. L., Brown, M. D., Park, J. Y., Brinkley, T. E., Basu, S., Hagberg, J. M. et al. Exercise training, NADPH oxidase p22phox gene polymorphisms, and hypertension. *Med. Sci. Sports Exerc.*, Jul., 2009, 41, 1421-1428.

[27] Zateyshchikov, D. A., Minushkina, L. O., Brovkin, A. N., Savel'eva, E. G., Zateyshchikova, A. A., Manchaeva, B. B. et al. Association of CYP2D6 and ADRB1 genes with hypotensive and antichronotropic action of betaxolol in patients with arterial hypertension. *Fundam. Clin. Pharmacol.*, Aug., 2007, 21, 437-443.

[28] Hautala, A. J., Rankinen, T., Kiviniemi, A. M., Makikallio, T. H., Huikuri, H. V., Bouchard, C. et al. Heart rate recovery after maximal exercise is associated with acetylcholine receptor M2 (CHRM2) gene polymorphism. *Am. J. Physiol. Heart Circ. Physiol*., Jul., 2006, 291, H459-66.

[29] Kilpelainen, T. O., Lakka, T. A., Laaksonen, D. E., Mager, U., Salopuro, T., Kubaszek, A. et al. Interaction of single nucleotide polymorphisms in ADRB2, ADRB3, TNF, IL6, IGF1R, LIPC, LEPR, and GHRL with physical activity on the risk of type 2 diabetes mellitus and changes in characteristics of the metabolic syndrome: The Finnish Diabetes Prevention Study. *Metabolism*, Mar., 2008, 57, 428-436.

[30] Flavell, D. M., Wootton, P. T., Myerson, S. G., World, M. J., Pennell, D. J., Humphries, S. E. et al. Variation in the lipoprotein lipase gene influences exercise-induced left ventricular growth. *J. Mol. Med*. (Berl.), Feb., 2006, 84, 126-131.

[31] Hagberg, J. M., Rankinen, T., Loos, R. J., Perusse, L., Roth, S. M., Wolfarth, B. et al. Advances in exercise, fitness, and performance genomics in 2010. *Med. Sci. Sports Exerc*., May, 2011, 43, 743-752.

[32] Bouchard, C. Overcoming barriers to progress in exercise genomics. *Exerc. Sport Sci. Rev*., Oct., 2011, 39, 212-217.

[33] Zhang, B., Sakai, T., Miura, S., Kiyonaga, A., Tanaka, H., Shindo, M. et al. Association of angiotensin-converting-enzyme gene polymorphism with the depressor response to mild exercise therapy in patients with mild to moderate essential hypertension. *Clin. Genet*., Oct., 2002, 62, 328-333.

[34] Jones, J. M., Park, J. J., Johnson, J., Vizcaino, D., Hand, B., Ferrell, R. et al. Renin-angiotensin system genes and exercise training-induced changes in sodium excretion in African American hypertensives. *Ethn. Dis*., Summer, 2006, 16, 666-674.

[35] Alioglu, E., Ercan, E., Tengiz, I., Turk, U. O., Ergun, M., Akgoz, S. et al. The influence of alpha-adducin gene polymorphism on response of blood pressure to exercise in patients with hypertension. *Anadolu. Kardiyol. Derg*., Oct., 2010, 10, 400-404.

[36] Klein, R. J., Zeiss, C., Chew, E. Y., Tsai, J. Y., Sackler, R. S., Haynes, C. et al. Complement factor H polymorphism in age-related macular degeneration. *Science*, Apr. 15, 2005, 308, 385-389.

[37] Kurtz, T. W. Genome-wide association studies will unlock the genetic basis of hypertension.: con side of the argument. *Hypertension*, Dec., 2010, 56, 1021-1025.

[38] Newton-Cheh, C., Johnson, T., Gateva, V., Tobin, M. D., Bochud, M., Coin, L. et al. Genome-wide association study identifies eight loci associated with blood pressure. *Nat. Genet*., Jun., 2009, 41, 666-676.

[39] Levy, D., Ehret, G. B., Rice, K., Verwoert, G. C., Launer, L. J., Dehghan, A. et al. Genome-wide association study of blood pressure and hypertension. *Nat. Genet*., Jun., 2009, 41, 677-687.

[40] International Consortium for Blood Pressure Genome-Wide Association Studies; Ehret, G. B., Munroe, P. B., Rice, K. M., Bochud, M., Johnson, A. D. et al. Genetic variants in novel pathways influence blood pressure and cardiovascular disease risk. *Nature*, Sep. 11, 2011, 478, 103-109.

[41] Keating, B. J., Tischfield, S., Murray, S. S., Bhangale, T., Price, T. S., Glessner, J. T. et al. Concept, design and implementation of a cardiovascular gene-centric 50 k SNP array for large-scale genomic association studies. *PLoS One*, 2008, 3, e3583.

[42] Sober, S., Org, E., Kepp, K., Juhanson, P., Eyheramendy, S., Gieger, C. et al. Targeting 160 candidate genes for blood pressure regulation with a genome-wide genotyping array. *PLoS One*, Jun. 29, 2009, 4, e6034.

[43] He, J., Gu, D., Kelly, T. N., Hixson, J. E., Rao, D. C., Jaquish, C. E. et al. Genetic variants in the renin-angiotensin-aldosterone system and blood pressure responses to potassium intake. *J. Hypertens.*, Sep., 2011, 29, 1719-1730.

[44] Tomaszewski, M., Debiec, R., Braund, P. S., Nelson, C. P., Hardwick, R., Christofidou, P. et al. Genetic architecture of ambulatory blood pressure in the general population: insights from cardiovascular gene-centric array. *Hypertension*, Dec., 2010, 56, 1069-1076.

[45] Bray, M. S., Hagberg, J. M., Perusse, L., Rankinen, T., Roth, S. M., Wolfarth, B. et al. The human gene map for performance and health-related fitness phenotypes: the 2006-2007 update. *Med. Sci. Sports Exerc*., Jan., 2009, 41, 35-73.

[46] Rankinen, T., Zuberi, A., Chagnon, Y. C., Weisnagel, S. J., Argyropoulos, G., Walts, B. et al. The human obesity gene map: the 2005 update. *Obesity* (Silver Spring), Apr., 2006, 14, 529-644.

[47] Ehret, G. B. Genome-wide association studies: contribution of genomics to understanding blood pressure and essential hypertension. *Curr. Hypertens. Rep.*, Feb., 2010, 12, 17-25.

[48] Hagberg, J. M. Do genetic variations alter the effects of exercise training on cardiovascular disease and can we identify the candidate variants now or in the future? *J. Appl. Physiol.*, Sep., 2011, 111, 916-928.

[49] Thompson, P. D., Moyna, N., Seip, R., Price, T., Clarkson, P., Angelopoulos, T. et al. Functional polymorphisms associated with human muscle size and strength. *Med. Sci. Sports Exerc*., Jul., 2004, 36, 1132-1139.

[50] Pescatello, L. S., Turner, D., Rodriguez, N., Blanchard, B. E., Tsongalis, G. J., Maresh, C. M. et al. Dietary calcium intake and renin angiotensin system polymorphisms alter the blood pressure response to aerobic exercise: A randomized control design. *Nutr. Metab*., 2007, 4,

[51] DiPetrillo, K., Wang, X., Stylianou, I. M., Paigen, B. Bioinformatics toolbox for narrowing rodent quantitative trait loci. *Trends Genet*., Dec., 2005, 21, 683-692.

[52] Bouchard, C. The biological predisposition to obesity: beyond the thrifty genotype scenario. *Int. J. Obes*. (Lond.), Sep., 2007, 31, 1337-1339.

[53] Sailors, M. H., Bray, M. S. The Interaction Between Genetic Variation and Exercise and Physical Activity in the Determnination of Body Composition and Obesity Status. In: Pescatello, L. S. and Roth, S. M., editors. Exercise Genomics. New York, NY: *Springer*; 2011; 101-128.

[54] De Bakker, P. I., Yelensky, R., Pe'er, I., Gabriel, S. B., Daly, M. J., Altshuler, D. Efficiency and power in genetic association studies. *Nat. Genet*., Nov., 2005, 37, 1217-1223.

[55] Clarke, R., Peden, J. F., Hopewell, J. C., Kyriakou, T., Goel, A., Heath, S. C. et al. Genetic variants associated with Lp(a) lipoprotein level and coronary disease. *N Engl. J. Med*., Dec 24, 2009, 361, 2518-2528.

[56] IBC 50K CAD Consortium. Large-scale gene-centric analysis identifies novel variants for coronary artery disease. *PLoS Genet*., Sep., 2011, 7, e1002260.

[57] Sayers, E. W., Barrett, T., Benson, D. A., Bolton, E., Bryant, S. H., Canese, K. et al. Database resources of the National Center for Biotechnology Information. *Nucleic Acids Res*., Jan., 2011, 39, D38-51.

[58] Safran, M., Solomon, I.,Shmueli, O., Lapidot, M., Shen-Orr, S., Adato, A. et al. GeneCards 2002: towards a complete, object-oriented, human gene compendium. *Bioinformatics*, Nov., 2002, 18, 1542-1543.

[59] Maglott, D., Ostell, J., Pruitt, K. D., Tatusova, T. Entrez Gene: gene-centered information at NCBI. *Nucleic Acids Res.*, Jan., 2011, 39, D52-7.

[60] Zacharova, J., Chiasson, J. L., Laakso, M. Leptin receptor gene variation predicts weight change in subjects with impaired glucose tolerance. *Obes. Res., Mar*., 2005, 13, 501-506.

[61] International HapMap Consortium; Frazer, K. A., Ballinger, D. G., Cox, D. R., Hinds, D. A., Stuve, L. L. et al. A second generation human haplotype map of over 3.1 million SNPs. *Nature*, Oct. 18, 2007, 449, 851-861.

[62] Flicek, P., Aken, B. L., Ballester, B., Beal, K., Bragin, E., Brent, S. et al. Ensembl's 10th year. *Nucleic Acids Res*., Jan., 2010, 38, D557-62.

[63] Roth, S. M. Genetics Primer for Exercise Science and Health. Champaign, IL: *Human Kinetics* 2007.

[64] Lewis, R. Human Genetics: Concepts and Applications. 9th ed. *McGraw-Hill Primis* 2009.

[65] Rice, T., Rankinen, T., Chagnon, Y. C., Province, M. A., Perusse, L., Leon, A. S. et al. Genomewide linkage scan of resting blood pressure: HERITAGE Family Study. Health, Risk Factors, Exercise Training, and Genetics. *Hypertension*, Jun., 2002, 39, 1037-1043.

[66] Nothnagel, M., Ellinghaus, D., Schreiber, S., Krawczak, M., Franke, A. A comprehensive evaluation of SNP genotype imputation. *Hum. Genet*., Mar., 2009, 125, 163-171.