New Loci Associated with Kidney Function and Chronic Kidney Disease

Supplement

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Discovery Cohorts

Age Gene/Environment Susceptibility Reykjavik Study (AGES): The AGES-Reykjavik Study represents a sample drawn from the established prospective population-based cohort, the Reykjavik Study.[1] Between 2002 and 2006, the AGES-Reykjavik study re-examined 5764 survivors of the original cohort. Serum creatinine was measured at the Icelandic Heart Association using the Roche-Hitachi P-Module instrument with Roche Creatininase Plus assay. The coefficient of variation (CV) for the creatinine assay was 2.5%. Covariates were obtained at examination. Genotyping was performed at the Molecular Genetics Section and Laboratory of Neurogenetics, NIA, NIH, using using the Illumina 370CNV BeadChip array on 3664 participants. Standard protocols for working with Illumina data were followed, with clustering score greater than 0.4.

Amish Studies (Amish): Old Order Amish individuals included in this study were participants of several ongoing studies of cardiovascular health carried out at the University of Maryland. Participants were relatively healthy volunteers from the Old Order Amish community of Lancaster County, Pennsylvania and their family members.[2, 3] Study participants were enrolled within the 2000-2008 timeperiod. Serum creatinine was measured using a modified kinetic Jaffé reaction. Cystatin C measured using a particle-enhanced immunonephelometric method BNII, (Dade-Behring). Covariates were obtained at the index examination.

Atherosclerosis Risk in Communities Study (ARIC): The ARIC Study is an ongoing prospective population-based cohort study to investigate the etiology of atherosclerosis. The study started in 1987-89 with the enrollment of 15,792 adults aged 45-64 years in four US communities; participants mostly self-identified as black or white.[4] Participants for the current

study included those with measures of serum creatinine from visits 1, 2 (1990-92), or 4 (1996-98) for the analyses of eGFRcrea and CKD, and from visit 4 for the analyses of eGFRcys. Serum creatinine was measured using a modified kinetic Jaffé reaction. CKD was defined as cumulative CKD prevalence for individuals with eGFRcrea <60 ml/min/1.73m^2 at ARIC visits 1, 2, or 4. Individuals were not counted as CKD cases if CKD at an earlier study exam was not apparent at a later study exam, unless there was also a CKD related hospitalization from continuously collected hospitalization discharge records.[5] Serum cystatin C was measured by a particle enhanced immunonephelometric assay (N Latex Cystatin C, Dade Behring). Covariates were obtained at the visit from which eGFR was used in analyses.

Austrian Stroke Prevention study (ASPS): The Austrian Stroke Prevention study is a single center prospective follow-up study on the effects of vascular risk factors on brain structure and function in the normal elderly population of the city of Graz, Austria. The procedure of recruitment and diagnostic work-up of study participants has been described previously.[6, 7] A total of 2007 European Caucasian participants were randomly selected from the official community register stratified by gender and 5 year age groups. Individuals were excluded from the study if they had a history of neuropsychiatric disease, including previous stroke, transient ischemic attacks, and dementia, or an abnormal neurologic examination determined on the basis of a structured clinical interview and a physical and neurologic examination. Since 1992, blood was drawn from all study participants for DNA extraction; covariates were obtained at the index examination. Serum creatinine was measured.

Baltimore longitudinal study of Aging (BLSA): The Baltimore Longitudinal Study of Aging (BLSA) is an observational study that began in 1958 to investigate normative aging in community dwelling adults who were healthy at study entry.[8] Participants are examined every one to four years depending on their age. Currently there are approximately 1100 active participants enrolled in the study. Serum and urinary creatinine was measured by an enzymatic

method using the Vitros 750 analyzer (Johnson & Johnson Co., Rochester, NY). The Modification of Diet in Renal Disease (MDRD) Study equation was used to calculate eGFRcrea. The analysis was restricted to subjects with European ancestry. Each analysis was further adjusted for the top two principal components derived from an EIGENSTRAT analysis utilizing ~10,000 randomly selected SNPs from the 550K SNP panel.

Cardiovascular Health Study (CHS): The Cardiovascular Health Study (CHS) is a population-based longitudinal study of risk factors for cardiovascular disease and stroke in adults 65 years of age or older, recruited at four field centers (Forsyth County, NC; Sacramento County, CA; Washington County, MD; Pittsburgh, PA).[9] 5201 individuals of predominantly European ancestry were recruited in 1989-1990 from random samples of Medicare eligibility lists, followed by an additional 687 African-Americans recruited in 1992-1993 (total n=5888). A total of 1908 persons were excluded from the GWAS study sample due to the presence at study baseline of coronary heart disease, congestive heart failure, peripheral vascular disease, valvular heart disease, stroke or transient ischemic attack or lack of available DNA. African American participants were excluded from this analysis since the other cohorts were predominantly of European ancestry. Using a particle-enhanced immunonephelometric method, Cystatin C was measured (BNII, Dade-Behring). Covariates were obtained at baseline.

Erasmus Rucphen Family study (ERF): The Erasmus Rucphen Family (ERF) study is comprised of a family-based cohort embedded in the Genetic Research in Isolated Populations (GRIP) program in the Southwest of the Netherlands. Descriptions of ERF's design have been previously published.[10] Briefly, twenty-two families that had a minimum of five children baptized in the community church between 1850 and 1900 were identified with the help of detailed genealogical records. All living descendants of these couples, and their spouses, were invited to take part in the study. Participants included in the current study total 2079 individuals for whom

complete phenotypic and genotypic information was available. Covariates were obtained during the baseline examination.

Family Heart Study (FamHS): In 1992, the Family Heart Study began with the ascertainment of 1200 families, half due to excess of coronary heart disease (CHD) or abnormal risk factors as compared with sex- and age-specific population, the other half randomly selected.[11] These families, including about 6000 individuals, were sampled from four geographically diverse field centers: the Framingham Heart Study, the Utah Family Tree Study, and two ARIC centers (Minneapolis, and Forsyth County, NC). After about 8 years, a total of 2767 participants of European ancestry in 510 extended pedigrees were invited for a second clinical exam. A two-stage design was used for the GWAS conducted for this study. In the first stage, 1016 individuals chosen to be largely unrelated were selected, half from the highest quartile and half from the lowest quartile of sex- and age-adjusted coronary artery calcification values. The results presented here were derived using the first stage case-control sample. We did not observe association of eGFRcrea with the first ten principal components derived from the GWAS genotypes using Eigenstrat.[12]

Framingham Heart Study (FHS): In 1948, the Framingham Heart Study began when the Original Cohort was enrolled.[13] Beginning in 1971, the Offspring Cohort was enrolled (5124 participants); the methodology and design has been described.[14, 15] In 2002, the Third Generation cohort was enrolled (n=4095).[16] Participants for the current study include individuals from the original cohort who attended cohort exam 15 (1977 to 1979) or exam 24 (1995 to 1998) [n=2338], as well as participants from the offspring cohort who attended the second exam (1979 - 1983) or the seventh exam (1998-2001) [n=4182], and individuals from the Third Generation first examination (for eGFR only). CKD was defined as cumulative CKD prevalence for individuals with eGFR <60 ml/min/1.73m^2 at exam cycle 15 (original cohort) and exam cycle 2 (offspring cohort) for the earlier exams and exam 24 (original cohort) and exam 7 (offspring

cohort) for the later exam cycles. Using a particle-enhanced immunonephelometric method, Cystatin C was measured (BNII, Dade-Behring). Covariates were obtained at the index examination. We observed no association with CKD with the 10 principal components estimated using Eigenstrat.[12] Significant association between eGFR and the 10 principle components was observed, therefore principle components were included in the analysis for association between genotype and eGFR.

KORA Studies (KORA F3 and KORA F4): The KORA surveys for genetic research have been described in detail previously[17] and have been initiated as part of the MONICA (Monitoring of Trends of Cardiovascular Diseases) multi-center study. The third KORA survey (KORA S3) is a population-based sample from the general population of the South-German city of Augsburg and surrounding counties, recruited 1994/1995. A subsample consisting of 1644 individuals from this survey with 10-year follow-up (KORA F3) information available was successfully genotyped..The fourth KORA survey (KORA S4) is a sample recruited 1999-2002 independent from KORA S3 using the same platform with the same standard operating procedures and based on the same population. From the sample with a 10-year follow-up (KORA F4), 1814 subjects were available for the GWA analysis. All participants had a German passport and were of European origin. Serum creatinine in KORA F3 and F4 was measured using a modified kinetic Jaffé reaction. Using a particle-enhanced immunonephelometric method, serum cystatin C was measured (BNII, Dade-Behring).

Korcula Study (KORCULA): The Korcula Study (KORCULA) is a family-based, cross-sectional study on the Dalmatian island of Korcula.[18] Data for participants aged 18 years and over were used for this analysis. Fasting blood samples were collected and over 200 health-related phenotypes and environmental exposures were measured in each individual. Plasma creatinine was measured with the Jaffé rate method.

KORCULA, MICROS, NSPHS, ORCADES, and VIS used a polygenic linear model fitted to the residuals of log(eGFRcrea) on age for estimating the inverse of the variance/covariance matrix, which accounts for the inter-individual relatedness and is based upon a genomic kinship matrix[19] implemented in GenABEL. Genome-wide association between SNPs and the residuals was assessed by means of an approximate score test statistic[20]. For CKD, relatedness was accounted for by estimating the first three principal component of the genomic kinship matrix by multidimensional scaling. A genome-wide association scan was performed by means of a logistic regression model adjusted for age, sex, and the first three principal components.

Microisolates in South Tyrol Study (MICROS): The MICROS study is part of the genomic health care program 'GenNova' and was carried out in three villages of the Val Venosta, South Tyrol (Italy), in 2001-03. It comprised members of the populations of Stelvio, Vallelunga and Martello. A detailed description of the *MICROS* study is available elsewhere.[21] Information on the participant's health status was collected through a standardized questionnaire. Laboratory data were obtained from standard blood analyses. Serum creatinine was measured by an enzymatic photometric assay using an ADVIA1650 clinical chemistry analyzer (Siemens Healthcare Diagnostics GmbH, Eschborn, Germany) (PMID 3806017) and cystatin C was measured on a BN-ProSpec analyzer (Dade Behring, Marburg, Germany). Covariates were obtained during the interview phase. For study-specific statistical methods, see above page 8.

Northern Swedish Population Health Study (NSPHS): The Northern Swedish Population Health Study (*NSPHS*) is a family-based study including a comprehensive health investigation and the collection of data on family structure, lifestyle, diet, medical history and of samples for laboratory analyses.[22, 23] Participants came from the northern part of the Swedish mountain region (County of Norrbotten, Parish of Karesuando). Historic population accounts show that little migration or other dramatic population changes have occurred in this area over the last 200 years. Plasma creatinine was measured by an enzymatic photometric assay using an

ADVIA1650 clinical chemistry analyzer (Siemens Healthcare Diagnostics GmbH, Eschborn, Germany).[24] For study-specific statistical methods, see above page 8.

Orkney Complex Disease Study (ORCADES): The Orkney Complex Disease Study (*ORCADES*) is an ongoing family-based, cross-sectional study in the isolated Scottish archipelago of Orkney.[25] Genetic diversity in this population is decreased compared to Mainland Scotland, consistent with high levels of historical endogamy. Participants were aged 18-100 years and came from a subgroup of ten islands. Fasting blood samples were collected and over 200 health-related phenotypes and environmental exposures were measured in each individual. Plasma creatinine was measured by an enzymatic photometric assay using an ADVIA1650 clinical chemistry analyzer (Siemens Healthcare Diagnostics GmbH, Eschborn, Germany).[24] For study-specific statistical methods, see above page 8.

Rotterdam Study I (RSI) and Rotterdam Study II (RSII): The RS is a population-based cohort study aimed at assessing the occurrence of and risk factors for chronic diseases in the elderly. In brief, all inhabitants of Ommoord, a district of Rotterdam in the Netherlands, who were 55 years or older were invited and 7983 (RSI) agreed to participate (78% response rate).[26-28] The baseline visits took place between 1990-1993. In 1999, inhabitants who turned 55 years of age or moved into the study district since the start of the study were invited (RSII) of whom 3011 participated (67% response rate). Serum creatinine was assessed by a nonkinetic alkaline picrate (Jaffé) method (Kone Autoanalyzer; Kone Corp, Espoo, Finland, and Elan; Merck, Darmstadt, Germany). Covariates were obtained at baseline. Diabetes was defined as use of antidiabetes medication or abnormal nonfasting glucose or an abnormal oral glucose tolerance test. A nonfasting or post load glucose level ≥11.1 mmol/l was considered abnormal.

Study of Health in Pomerania (SHIP): The Study of Health in Pomerania (SHIP) is a longitudinal population-based cohort study conducted in West Pomerania, the north-east area of

Germany.[29] For the baseline examinations, a sample of 6267 eligible subjects aged 20 to 79 years was drawn from population registries. Only individuals with German citizenship and main residency in the study area were included. Baseline examinations were conducted between 1997 and 2001. Between 2002 and 2006 all participants were re-invited for an examination follow-up, in which 3300 subjects (83.5% of eligible persons) took part.[29] Serum creatinine levels were determined according to the Jaffè method. Serum cystatin C levels were measured using the Siemens N Latex Cystatin C assay, a particle-enhanced nephelometric immunoassay, on the BN ProSpec® System. The genetic data analysis workflow was created using the Software InforSense. Genetic data were stored using the database Caché (InterSystems).

Vis Study (VIS): The Vis Study (VIS) is a family-based, cross-sectional study on the Dalmatian island of Vis.[30, 31] Data for participants aged 18 years and over were used for this analysis. Fasting blood samples were collected and over 200 health-related phenotypes and environmental exposures were measured in each individual. Serum creatinine was measured by an enzymatic photometric assay using an ADVIA1650 clinical chemistry analyzer (Siemens Healthcare Diagnostics GmbH, Eschborn, Germany). For study-specific statistical methods, see above page 8.

Women's Genome Health Study (WGHS): The Women's Genome Health Study (WGHS) is a prospective cohort of female North American health care professionals representing participants in the Women's Health Study (WHS) who provided a blood sample at baseline and consent for blood-based analyses.[32] Participants in the WHS were 45 or older at enrollment and free of cardiovascular disease, cancer or other major chronic illness. Serum creatinine was measured in the baseline blood sample.[32] Covariates were assessed at the index examination. The current data are derived from 22,054 WGHS participants for whom whole genome genotype information was available at the time of analysis and self-reported European ancestry could be

confirmed by multidimensional scaling analysis of 1443 ancestry informative markers in PLINK v. 1.06.[33]

In silico Replication Cohorts

ARIC: Additional genotype data became available on 949 self-reported white ARIC participants over the course of this study. These individuals were not part of the discovery samples, did not have a first-degree relationship with any individual in the discovery sample, nor would they have been classified as an outlier based on allele sharing measures applied in data cleaning of the discovery sample.

Family Heart Study: In the replication stage, 1753 family members with self-reported white ancestry are used for replication; 1486 and 249 participants were genotyped. We used field centers in regression models to account for potential population stratification.

GENOA: The GENOA study of the Family Blood Pressure Program (FBPP) was initiated between 1995-2000 to identify genetic determinants of hypertension in multiple ethnic groups.[34, 35] In Rochester, MN, the Mayo Clinic diagnostic index and medical record linkage system of the Rochester Epidemiology Project were used to identify non-Hispanic white (NHW) residents of Olmsted County with a diagnosis of essential hypertension made before age 60.[36] Sibships in which either index hypertensive sibling was known to have impaired kidney function (e.g., serum creatinine ≥2.0 mg/dL) were not recruited, as impaired kidney function may cause secondary hypertension. A second stage of the FBPP was undertaken between 2000-2005 to identify genetic determinants of susceptibility to cardiac and renal complications of hypertension, consisting of 1239 whites in Rochester (76.6%), and 28 siblings of Rochester participants underwent an examination. Serum creatinine was measured using a modified kinetic Jaffé reaction. Covariates were obtained at the second stage examination.

Gutenberg Heart Study: The Gutenberg Heart Study began in 2007 as a community-based prospective study with participants ranging in age from 35 to 74 years. All participants have been drawn randomly from the local registry offices in the city of Mainz and the district of Mainz-Bingen. The present analysis was based on an initial sample of 3,500 subjects successively enrolled into the GHS from April 2007 to April 2008. Genomic DNA was isolated from all participants. Serum creatinine was measured in Heparin-Plasma using the Jaffe reaction method (Abbott Diagnostics; Delkenheim, Germany). Genotyping, imputation, and the statistical analysis were performed as indicated in Supplemental Table 1.

Health ABC: The Health ABC Study is a community-based prospective cohort study that began in 1997, consisting of 3075 men and women in the original cohort. Participants of the cohort were recruited from Medicare listings in Pittsburgh, Pennsylvania and Memphis, Tennessee. Eligibility criteria included age 70–79 years, self-report of no difficulty walking one-quarter mile or climbing 10 steps, or with activities of daily living, no history of active treatment for cancer in the prior 3 years, and no plan to move out of the area. These analyses included only those Health ABC participants who reported their race/ethnicity as European-American. Serum creatinine was measured using a modified kinetic Jaffé reaction; serum cystatin C was measured using particle-enhanced immunonephelometric method (BNII, Dade-Behring). Covariates were obtained at baseline. Genomic DNA was extracted from buffy coat collected using PUREGENE® DNA Purification Kit during the baseline exam. In 2009, genotyping was performed by the Center for Inherited Disease Research (CIDR).

Nurses Health Study/Health Professionals Follow-up Study (NHS/HPFS): The NHS was established in 1976 when 121,700 female registered nurses aged 30-55 years and residing in 11 large U.S. states completed a mailed questionnaire on their medical history and lifestyle characteristics.[37] Every two years, follow-up questionnaires have been sent to update information on exposures and newly diagnosed illnesses. The HPFS was initiated in 1986 when

51,529 male U.S. health professionals aged 40-75 and residing in 50 U.S. states answered a detailed questionnaire that included a comprehensive diet survey, and items on lifestyle practice and medical history.[38] The cohort is followed through biennial mailed questionnaire. Blood was collected from 32,826 NHS members between 1989 and 1990 and from 18,159 HPFS members between 1993 and 1999. Creatinine measures were performed on the samples from 1194 women and 1000 men with diabetes. Diabetes was defined as initially self-reported diabetes subsequently confirmed by a validated supplementary questionnaire.[39, 40] Between 2008 and 2009, a subset of these men and women were genotyped as part of a GWAS of type 2 diabetes. Plasma creatinine was measured by a modified kinetic Jaffé reaction. Covariates were obtained from the questionnaire administered closest to the time creatinine was measured (1990 for NHS and 1994 for HPFS). Standardized protocols for the NHS and HPFS genome-wide scans were developed as part of the GENEVA consortium. In the initial GWAS, NHS (N=3529) and HPFS (N=2668) samples were genotyped approximately two months apart and underwent independent QC.

POPGen: Using the POPGen biobank, data on healthy control individuals from Germany were obtained.[41] As part of the GWAS initiative of the German National Genome Research Network (NGFN), genotyping was performed. Serum creatinine was measured with an enzymatic *in vitro* assay (CREAplus, Cobas®, Roche Diagnostics, Indianapolis, IN).

SORBS: All participants are part of a sample from an extensively phenotyped self-contained population from Eastern Germany, the Sorbs.[42] Sampling comprised unrelated subjects as well as families; 888 participants were available for the present study. Serum creatinine was measured using a kinetic enzymatic method (Roche Inc). Covariates were obtained at the index examination. Adjustment for genomic control was used to control for increased genetic sharing due to long term isolation of this population.

SPLIT: The Split Study (SPLIT) is a population-based, cross-sectional study in the Dalmatian city of Split. Data for participants aged 18 years and over were used for this analysis. Fasting blood samples were collected and over 200 health-related phenotypes and environmental exposures were measured in each individual. Serum creatinine was measured using the photometric Jaffé method.

De novo genotyped replication cohorts

Genotyping methods of these four cohorts are described above (Replication Analysis).

KORA F3/F4: The subjects of KORA F3 and KORA F4 who had not been genotyped genome wide as described under "discovery cohorts" were used as replication samples including 1498 and 1202 subjects from KORA F3 and F4, respectively. Covariates were obtained at the index examination. In KORA F3, the mean call rate was 99.4%, the concordance among samples genotyped in duplicate across SNPs was 99.1%. In KORA F4, the mean call rate was 99.1%, the concordance among samples genotyped in duplicate across SNPs was 100%.

SAPALDIA: The SAPALDIA study was originally designed to investigate the effects of air pollutants on respiratory health in a random sample of the adult population of Switzerland.[43, 44] The original study consisted of 9651 adults as described elsewhere.[43] Of the surviving 9368 participants, 93% (*n* = 8715) could be traced between 2001 and 2003, and were re-contacted for SAPALDIA 2.[44] In the second survey, there was additionally a collection of blood specimens for analysis of blood and DNA markers.[44] Included in this study are subjects with blood and DNA samples available (n=6031) who had consented to the general blood marker and DNA analyses. Blood samples were processed and stored in a standardized fashion according to the SAPALDIA protocol.[44] Serum creatinine was measured using the Jaffé reaction (Roche) and calibrated to the Roche enzymatic gold standard reference. DNA was extracted as previously

described.[44] The mean call rate was 98.0%, the concordance among samples genotyped in duplicate across SNPs was 98.1%.

SAPHIR Study: The "Salzburg Atherosclerosis Prevention Program in subjects at High Individual Risk" (SAPHIR) is an observational study conducted in the years 1999-2002 involving healthy unrelated subjects: 641 females from 39 to 67 years of age and 1092 males from 39 to 66 years of age. Study participants were recruited by health screening programs in large companies in and around the city of Salzburg as described recently.[45] All individuals were of West-European origin. Participants with established coronary artery, cerebrovascular or peripheral arterial disease, congestive heart failure, valvular heart disease, chronic alcohol (more than three drinks a day) or drug abuse, severe obesity (BMI>40 kg/m²) and pregnant women were excluded. Serum creatinine (mg/dl) was measured using a modified kinetic Jaffé reaction (CREA®, Roche Diagnostics GmbH, Mannheim, Germany). Among the total of 1733 phenotyped participants, a total of 1733 had eGFR and genotype information, and 1733 had CKD status and genotype data. However, there were too few cases with CKD (n=19) to warrant analysis of this trait. Covariates were obtained at the index examination. The mean call rate was 98.7%, the concordance among samples genotyped in duplicate across SNPs was 99.1%.

Supplementary Note – Full Acknowledgements

Discovery Cohorts

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Replication Cohorts

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Supplementary Table 1a- Study Design and Sample sizes

	Study design	Overall sample size	Analyzed sample size eGFRcrea / CKD/ eGFRcys
Stage 1 discovery			
AGES	Population-based prospective	5764	3,219 / 3,219/NA
Amish	Amish founder "healthy"population	1611	1211 / NA/ 783
ARIC	Population-based	15792	8069/8069/6430
ASPS	Community-based prospective longitudinal	2007	850/850/NA
BLSA	Prospective population-based cohort	848	723 / 723 / NA
CHS	Population-based	5888	3259 / 3259 / 2820
ERF	Cross-sectional population-based study with pedigree information	2313	2079 / 2079 / NA
Family Heart Study	Case-Control	2756	883 / 883 / NA
Framingham Heart Study	Community-based family multi-generation	6520	7782 / 4140 / 2992
KORA F3	General population, unrelated, age-range 35-84yrs	3006	1641 / 1641 / 1642
KORA F4	General population, unrelated, age 32-81 yrs	3080	1814 / 1814 / 1811
Korcula Croatia	Cross-sectional population-based study with pedigree information	909	888 / 888 / NA
MICROS	Cross-sectional population-based study with pedigree information	1287	1201 / 1201/ 1248
NSPHS	Cross-sectional population-based study with pedigree information	720	565 / 565 / NA
ORCADES	Cross-sectional population-based study with pedigree information	1019	704 / 704 / NA
RS 1	Population-based	6239	4390/4390/NA
RS2	Population-based	2020	1863 / 1863 / NA
SHIP	Population-based	3300	3231 / 3228/ 3231
Vis Croatia	Cross-sectional population-based study with pedigree information	795	768 / 768 / NA
WGHS	Population-based, women only	22054	21953 / 21953 / NA
Stage 2 replication, in silico			
ARIC*	Population-based	15792	944/944/751
Family Heart Study*	Family-based cohort	2756	1537/1537/NA
GENOA	Community-based sibships	1605	1056/1056/NA
Gutenberg Heart Study	Community-based Prospective Cohort	5000	3180/3180/NA
Health ABC	Population-based elderly cohort	1663	1663/1663/1663

HPFS	Health Professional –based cohort study	51,529	818/818/X
Nurses Health Study	Health Professional –based cohort study	121,700	786/786/NA
Popgen	Population-based biobank	1241	1163/1163/NA
Sorbs	Self-contained population	1047	888/888/NA
SPLIT	Community-based cohort	499	479/NA/NA
Stage 2 replication, de novo genotyped			
KORA F3*	General population, unrelated, age-range 35-84yrs	3006	1498/1498/1498
KORA F4*	General population, unrelated, age 32-81 yrs	3080	1202/1202/1202
SAPALDIA	Random Sample, Switzerland	9651	6031/6031/NA
SAPHIR	Health Working Cohort	1733	1733/1733/NA

* subjects independent from subjects contributing to discovery analyses

Supplementary Table 1b - Genotyping and Imputation Platforms

	Array type	Genotype calling	QC filters for genotyped SNPs used for imputation	# SNPs used for imputation	Imputation	Imputation Backbone for phased CEU haplotypes (NCBI build)	Filtering of imputed genotypes	Data management and statistical analysis
Stage 1: Discovery								
AGES	Illumina 370CNV	BeadStudio	call rate <97%, MAF <1%, pHWE <1e-6, Mishap p <1e-9, A/T and G/C SNPs, Mismatches between Illumina, dbSNP and/or HapMap position	308,340	MACH v1.0.16	HapMap release 22 (build 36)	none	PLINK, R
Amish	Affymetrix 500K	BRLMM	call rate <95%, MAF <1%, pHWE <1e-6, SNPs not in HapMap	338,598	MACH v1.0.15	HapMap release 22 (build 36)		MAPP, mixed model to account for relatedness
ARIC	Affymetrix 6.0	Birdseed	call rate <95%, MAF<1%, pHWE<10E-5	602,642	MACH v1.0.16	HapMap release 21 (build 35)	none	ProbABEL, PLINK, R
ASPS	Illumina Human610-Quad BeadChip®	BeadStudio	call rate <98%, pHWE<10E-6	550,635	MACH v1.0.15	HapMap release 22 (build 36)	none	ProbABEL
BLSA	Illumina HumanHap 550K	Beadstudio	call rate <99%, MAF <1%, pHWE <10E-4	501,764	MACH v1.0.15	HapMap release 21 (build 35)	MAF<1%, r^2<0.3	SAS,MERLIN (fastAssoc option),R
CHS	Illumina 370CNV	BeadStudio	call rate <97%, heterozygotes=0, pHWE<10E-5, SNP not in HapMap	306,655	BimBam	HapMap release 21A (build 36)	dosage variance <0.01	R, robust variance option
ERF	Illumina, 300K	Illumina	MAF≤1% , pHWE ≤1e-6 , call rate ≤98%	460,584	MACH v1.0.15	HapMap release 22 (build 36)	none	R, GenABEL , ProbABEL, GC correction to account for relatedness
Family Heart Study	Illumina550K	BeadStudio-Gencall v3.0	call rate <98%, MAF <1%, pHWE<10E-6	456,293	MACH v1.0.15	HapMap release 22 (build 36)	none	SAS, linear mixed effect and logistic models
Framingham Heart Study	Affymetrix 500K Affymetrix 50K supplemental	Affymetrix	pHWE<1e-6, call rate<97%, mishap p<1e-9, MAF<0.01, Mendelian errors>100, SNPs not in Hapmap or strandedness issues merging with Hapmap	378,163	MACH v1.0.15	HapMap release 22 (build 36)	none	R, linear mixed effect models and GEE models, robust variance option to account for relatedness

KORA F3	Affymetrix 500K	BRLMM	per-chip call rate <93%, MAF <5%, discrepancy for one of the 50 SNPs common on both chips, gender checks	380,407	MACH	HapMap release 22, (build 35)	none	MACH2QTL, ProbABEL, R, Visual basic
KORA F4	Affymetrix 6.0	BRLMM	per-chip call rate <93%, per-SNP call rate <93%, MAF<1%, gender checks	629,893	MACH	HapMap release 22, (build 36)	none	ProbABEL, R, Visual basic
Korcula	Illumina, 370K	Beadstudio	call rate <98%, MAF < 1%, pHWE<10E-6	317,896	MACH v1.0.16	HapMap release 22 (build 36)	none	R , ProbABLE
MICROS	Illumina, 300K	Beadstudio	call rate <98%, MAF < 1%, pHWE<10E-6	292,917	MACH v1.0.16	HapMap release 22 (build 36)	none	R, GenABEL, ProbABEL; details in Study-Specific Methods
NSPHS	Illumina, 300K	Beadstudio	MAF≤1%, pHWE ≤ 1e-6 , call rate ≤98%	318,049	MACH v1.0.15	HapMap release 22 (build 36)	none	R, GenABEL, ProbABEL; details in Study-Specific Methods
ORCADES	Illumina, 300K	Beadstudio	MAF≤1%, pHWE ≤1e-6 , call rate ≤98%	306,207	MACH v1.0.15	HapMap release 22 (build 36)	none	R, GenABEL, ProbABEL; details in Study-Specific Methods
RS-I, RS-II	Illumina 550K	Beadstudio	call rate <90%, MAF<1%, pHWE<10E-5	530,683	MACH v1.0.15	HapMap release 22 (build 36)	none	Linear and logistic regression using ProbABEL, R
SHIP	Affymetrix 6.0	Birdseed V2	per-chip call rate <92%	869,224	IMPUTE v0.5.0	HapMap release 22 (build 36)	none	SNPTEST v1.1.5, QUICKTEST v0.94
Vis	Illumina, 300K	Beadstudio	MAF≤1% , pHWE ≤1e-6 , call rate≤98%	305,068	MACH v1.0.15	HapMap release 22 (build 36)	none	R, GenABEL, ProbABEL; details in Study-Specific Methods
WGHS	Illumina HumanHap 300 Duo "+"	BeadStudio 3.3	call rate < 98% on SNPs; pHWE < 10-6	317,186	MACH	HapMap release 21 (build 35), SNP positions updated to build 36	none	R, ProbABEL, bash scripting
	Array type	**Genotype calling**	**QC filters for genotyped SNPs used for imputation**	**# SNPs used for imputation**	**Imputation**	**Imputation Backbone (NCBI build)**	**Filtering of imputed genotypes**	**Data management and statistical analysis**
Stage 2: in silico replication								
ARIC*	Affymetrix 6.0	Birdseed	call rate <95%, MAF<1%, pHWE <10E-5	669,450	MACH v1.0.16	HapMap release 22 (build 36)	none	ProbABEL, PLINK, R

Family Heart Study*	Illumina Human 1M	GenomeStudio	call rate <97%, MAF< 1%, pHWE <10E-6	682,874	MACH v1.0.16	HapMap release 22 (build 36)	none	SAS, linear mixed effect models
GENOA	Affymetrix 6.0	Birdseed v2	call rate < 95%, pHWE <10E-6		MACH v1.0.16	HapMap release 22 (build 36)	none	PLINK; linear mixed models (R multic); GEE models (R gee glm); robust variance option to account for relatedness
Gutenberg Heart Study	Affymetrix 6.0	Birdseed v2	call rate <98%, maf <1%, pHWE <10E-4	608,203	IMPUTE v1.0.0	HapMap release 22 (build 36)	none	R
Health ABC	Illumina Human1M-Duo	Illumina BeadStudio	call rate < 97%, HWE p<10E-06, MAF<1%	914,263	MACH v1.0.16	Hapmap release 22 build 36	none	R
HPFS	Affymetrix 6.0	Birdseed	call rate <97%, pHWE<10E-4, MAF<2%, >1 discordance/29 replicates, significant plate associations	607,569	MACH v1.0.15	HapMap release 22 (build 36)	none	ProbABEL (R), SAS 9.0
Nurses Health Study	Affymetrix 6.0	Birdseed	call rate <97%, pHWE <10E-4, MAF <2%, >1 discordance/12 replicates, significant plate associations	606,626	MACH v1.0.15	HapMap release 22 (build 36)	none	ProbABEL (R), SAS 9.0
popgen	Affymetrix 6.0	Birdseed v2	per-person-call rate <0.90, per-SNP call rate <0.95, pHWE<10E-4, MAF <1%	709,003	MACH v1.0.16	HapMap release 22 (build 36)	none	PLINK, R
Sorbs	500K Affymetrix, Affymetrix 6.0	BRLMM; Birdseed	call rate <95%, pHWE<10E-4, MAF≤1%	378,513	IMPUTE	HapMap release 21 (build 35)	Proper-info>0.4, MAF>1%, HWE<10-4	SNPTEST, GC correction to account for relatedness
SPLIT	Illumina 370CNV	Illumina GenTrain Algorithm	call rate <98%, pHWE<1E-10	NA	NA	NA	NA	R, GenAbel
	Genotyping platform		**Quality control of genotyped SNPs**	**# SNPs genotyped**				**Data management and statistical analysis**
Stage 2: De novo genotyping replication								
KORA F3*	Sequenom, TaqMan		mean call rate 99.4%, concordance of duplicates 99.1%, pHWE > 0.05	22	NA	NA	NA	ProbABEL (R)

KORA F4*	Sequenom, TaqMan		mean call rate 99.1%, concordance of duplicates 100%, pHWE > 0.05	22	NA	NA	NA	ProbABEL (R)
SAPALDIA	Sequenom, TaqMan		mean call rate 98.0%, concordance of duplicates 98.1%, pHWE > 0.001	22	NA	NA	NA	ProbABEL (R)
SAPHIR	Sequenom, TaqMan		mean call rate 98.7%, concordance of duplicates 99.1%, pHWE > 0.05	22	NA	NA	NA	SAS 9.1.3.

* subjects independent from subjects contributing to discovery analyses

Supplementary Table 2- Genome-wide Significant Loci: SNP Imputation Quality in Stage 1 Discovery Cohorts.

Study	rs16864170 (CKD)	rs1933182	rs267734	rs1260326	rs13538	rs7422339	rs347685	rs17319721	rs11959928	rs6420094	rs881858
AGES	0.99	0.96	0.99	1.00	0.94	0.79	1.00	0.99	0.97	1.00	0.87
Amish	1.00	0.98	1.00	0.96	0.95	0.50	1.00	0.99	0.81	0.37	0.66
ARIC	0.99	0.99	1.00	0.98	1.00	0.66	1.00	1.00	0.98	0.61	0.95
ASPS	0.99	0.98	0.97	1.00	1.00	0.80	1.00	0.98	0.98	1.00	0.75
BLSA	0.96	0.98	0.99	0.96	0.98	0.60	1.00	0.99	0.97	0.99	0.89
CHS	0.51	0.80	0.95	1.01	0.45	0.23	1.02	0.74	0.87	0.99	0.83
ERF	0.94	0.97	0.98	0.98	0.94	0.81	1.00	0.99	0.95	0.95	0.77
FamHS	0.99	0.96	0.49	0.98	0.91	0.80	0.95	1.07	1.00	1.03	0.92
FHS	0.92	1.00	0.98	0.99	0.99	0.99	1.03	1.01	0.99	0.48	0.69
KORA F3	0.88	1.00	1.00	0.96	0.95	0.54	1.00	0.96	0.89	0.51	0.73
KORA F4	0.98	0.97	1.00	0.96	0.98	0.60	1.00	1.00	0.93	0.62	0.93
Korcula	0.97	0.94	0.99	0.99	0.99	0.82	1.00	0.95	0.93	1.00	0.69
Micros	0.83	0.94	0.99	0.95	0.91	0.74	1.00	0.97	0.95	0.99	0.85
Orcades	0.98	0.98	1.00	0.96	0.89	0.78	0.99	0.97	0.96	1.00	0.80
RS-1	0.98	0.98	0.99	0.96	0.99	0.82	1.00	0.99	0.98	1.00	0.88
RS-11	0.99	0.99	1.04	1.00	1.00	0.78	0.98	0.98	0.99	0.98	0.91
NHSPH	0.77	0.97	1.00	0.99	0.88	0.82	1.00	0.94	0.95	1.00	0.89
SHIP	0.98	0.99	1.00	0.99	0.99	0.88	1.00	1.00	0.99	0.70	0.95
Vis	0.98	0.96	0.94	0.96	0.91	0.76	0.99	0.96	0.95	0.99	0.84
WGHS	0.90	0.94	0.97	0.97	0.72	0.99	1.00	0.91	0.92	1.00	0.86
median imputation quality	0.98	0.97	0.99	0.98	0.95	0.78	1.00	0.98	0.96	0.99	0.86

Study	rs2279463	rs6465825	rs7805747	rs10109414	rs4744712	rs10794720	rs4014195	rs10774021	rs626277	rs2453533
AGES	0.99	1.00	0.53	0.99	1.00	0.99	1.00	1.00	0.99	1.00
Amish	0.98	0.92	0.44	0.88	0.95	0.98	0.93	0.83	0.46	0.98
ARIC	0.99	0.99	0.57	0.99	1.00	1.00	0.99	0.98	0.99	1.00
ASPS	1.00	1.00	0.94	0.99	1.00	1.00	0.99	1.00	1.00	1.00
BLSA	0.99	1.00	0.93	0.99	1.00	1.00	0.99	1.00	1.00	1.00
CHS	0.95	0.96	0.43	0.85	0.96	1.01	0.96	1.01	0.98	0.95
ERF	0.96	1.00	0.56	0.99	1.00	1.00	1.00	0.98	0.99	1.00
FamHS	1.00	0.95	0.94	0.97	0.94	1.04	0.42	1.00	0.98	1.00
FHS	1.01	1.00	0.50	0.99	1.00	0.99	0.99	0.94	0.78	0.98
KORA F3	0.95	0.98	0.54	1.00	1.00	1.00	0.99	0.84	0.58	1.00
KORA F4	0.98	0.97	0.52	0.98	0.98	1.00	1.00	0.92	1.00	0.99
Korcula	0.97	1.00	0.52	0.97	0.99	1.00	0.98	1.00	1.00	1.00
Micros	0.98	1.00	0.56	0.99	1.00	0.99	0.99	1.00	0.99	1.00
Orcades	0.97	1.00	0.60	1.00	1.00	1.00	0.97	1.00	1.00	1.00
RS-1	0.99	1.00	0.92	0.99	1.00	1.00	1.00	1.00	1.00	1.00
RS-11	1.02	1.04	0.95	0.99	1.00	1.01	1.02	1.00	1.01	0.98
NHSPH	0.97	1.00	0.43	0.98	0.99	0.99	0.98	1.00	0.99	1.00
SHIP	0.97	0.99	0.51	1.00	0.99	1.00	1.00	0.96	1.00	1.00
Vis	0.96	1.00	0.51	0.99	1.00	0.97	0.96	1.00	1.00	1.00
WGHS	0.99	1.00	0.99	0.91	0.99	1.00	0.98	1.00	1.00	0.97
median imputation quality	0.98	1.00	0.55	0.99	1.00	1.00	0.99	1.00	1.00	1.00

Study	rs491567	rs1394125	rs12917707	rs9895661	rs12460876	eGFRcys: rs653178
AGES	1.00	0.97	0.98	0.79	1.00	1.00
Amish	0.91	0.56	0.90	0.65	0.81	0.50
ARIC	0.99	0.68	0.94	1.00	0.99	0.99
ASPS	0.99	0.96	0.96	0.86	1.00	1.00
BLSA	1.00	0.94	0.96	0.99	0.99	1.00
CHS	0.92	1.01	0.96	0.68	0.87	1.05
ERF	0.99	0.91	0.89	0.72	0.98	1.00
FamHS	0.93	0.95	1.03	0.97	0.96	1.00
FHS	1.00	0.71	0.96	0.70	0.98	0.99
KORA F3	1.00	0.54	0.86	0.70	0.93	0.79
KORA F4	0.99	0.67	0.87	1.00	0.94	1.00
Korcula	0.99	0.96	0.96	0.84	0.98	1.00
Micros	0.98	0.95	0.95	0.72	0.98	1.00
Orcades	0.98	0.95	0.98	0.72	0.99	1.00
RS-1	1.00	0.94	0.98	1.00	1.00	1.00
RS-11	1.01	0.96	0.94	1.00	1.02	1.00
NHSPH	0.99	0.98	0.91	0.81	0.93	1.00
SHIP	0.99	0.79	0.99	1.00	0.98	1.00
Vis	0.99	0.96	0.92	0.75	0.97	1.00
WGHS	0.98	0.99	0.95	0.80	0.95	1.00
median imputation quality	0.99	0.95	0.95	0.81	0.98	1.00

Supplementary Table 3 - Genome-Wide Significant Loci: SNP Association Across Renal Traits in Stage 1 Discovery and Stage 2 Replication Meta-Analyses. eGFRcrea (n=67093), CKD (n=62237) or eGFRcys (n=20907)

	Chr	position (b36)	Genes Nearby	modeled allele#	eGFRcrea beta	eGFRcrea SE	p-value	eGFRcrea beta	eGFRcrea SE	1-sided p-value
Renal Function Loci, Association with eGFRcrea					**Discovery**			**Replication**		
rs1933182	1	109801361	SYPL2;ATXN7L2,CYB561D1,PSMA5,AMIGO1,SORT1	a	-0.008	0.001	1.3E-08	-0.002	0.002	1.9E-01
rs267734	1	149218101	ANXA9;FAM63A,PRUNE,BNIPL,LASS2,SETDB1	c	0.010	0.002	5.2E-09	0.008	0.002	1.1E-04
rs16864170 (CKD)	2	5825331	SOX11	c	-0.011	0.003	6.9E-04	0.000	0.004	4.8E-01
rs1260326	2	27584444	**GCKR**;IFT172,FNDC4	t	0.009	0.001	1.3E-10	0.007	0.002	1.1E-04
rs13538	2	73721836	**NAT8**;NAT8B,ALMS1	g	0.009	0.002	2.6E-08	0.010	0.002	7.2E-07
rs347685	3	143289827	TFDP2	c	0.009	0.001	7.0E-09	0.006	0.002	1.4E-03
rs11959928	5	39432889	**DAB2**;C9	a	-0.009	0.001	1.8E-11	-0.009	0.002	5.6E-07
rs6420094	5	176750242	**SLC34A1**;GRK6,RGS14,LMAN2,PRR7,F12,PFN3	g	-0.011	0.002	3.8E-12	-0.006	0.002	6.6E-04
rs881858	6	43914587	VEGFA	g	0.011	0.002	2.2E-11	0.006	0.002	7.7E-04
rs7805747	7	151038734	**PRKAG2**	a	-0.012	0.002	5.1E-11	-0.012	0.002	1.8E-08
rs4744712	9	70624527	**PIP5K1B**;FAM122A	a	-0.008	0.001	7.2E-10	-0.007	0.002	6.6E-05
rs4014195	11	65263398	RNASEH2C;DKFZp761E198,HTATIP,OVOL1	g	-0.008	0.001	3.3E-08	-0.002	0.002	1.4E-01
rs653178	12	110492139	**ATXN2**	t	0.003	0.001	3.0E-02	0.005	0.002	2.9E-03
rs626277	13	71245697	**DACH1**	c	0.009	0.001	2.9E-10	0.004	0.002	1.0E-02
rs1394125	15	73946038	**UBE2Q2**;FBXO22	a	-0.009	0.001	3.7E-10	-0.010	0.002	4.7E-08
rs12460876	19	38048731	**SLC7A9**;CCDC123,ECAT8	c	0.008	0.001	5.5E-09	0.009	0.002	2.5E-07
Creatinine Production Loci, Association with eGFRcrea										
rs7422339	2	211248752	**CPS1**	a	-0.009	0.002	2.4E-09	-0.010	0.002	2.6E-07
rs2279463	6	160588379	**SLC22A2**	g	-0.013	0.002	8.7E-10	-0.008	0.003	1.7E-03
rs6465825	7	77254375	TMEM60;RSBN1L,PHTF2	c	-0.008	0.001	3.5E-09	-0.003	0.002	3.5E-02
rs10794720	10	1146165	**WDR37**	t	-0.014	0.002	2.1E-08	-0.006	0.003	4.7E-02

rs10774021	12	219559	**SLC6A13**;JARID1A,SLC6A12	c	0.008	0.001	6.7E-09	0.004	0.003	7.1E-02
rs491567	15	51733885	**WDR72**	c	0.009	0.002	1.3E-08	0.009	0.002	1.0E-05
rs9895661	17	56811371	**BCAS3**;TBX2,C17orf82	c	-0.011	0.002	1.4E-08	-0.012	0.002	3.0E-08

	Chr	**position (b36)**	**Genes Nearby**	**modeled allele#**	**OR CKD**	**95% CI**	**p-value**	**OR CKD**	**95% CI**	**1-sided p-value**
Renal Function Loci, Association with CKD					**Discovery**			**Replication**		
rs1933182	1	109801361	SYPL2;ATXN7L2,CYB561D1,PSMA5,AMIGO1,SORT1	a	1.06	1.01 - 1.10	2.3E-02	1.00	0.91-1.10	4.9E-01
rs267734	1	149218101	ANXA9;FAM63A,PRUNE,BNIPL,LASS2,SETDB1	c	0.93	0.88 - 0.98	5.3E-03	0.94	0.85-1.05	1.5E-01
rs16864170 (CKD)	2	5825331	SOX11	c	1.30	1.18 - 1.43	4.5E-08	1.04	0.84-1.28	3.5E-01
rs1260326	2	27584444	**GCKR**;IFT172,FNDC4	t	0.97	0.93 - 1.01	1.8E-01	0.95	0.87-1.04	1.3E-01
rs13538	2	73721836	**NAT8**;NAT8B,ALMS1	g	0.95	0.91 - 1.01	8.4E-02	0.87	0.78-0.97	5.0E-03
rs347685	3	143289827	TFDP2	c	0.92	0.88 - 0.96	3.3E-04	1.01	0.91-1.11	4.6E-01
rs11959928	5	39432889	**DAB2**;C9	a	1.11	1.06 - 1.15	4.6E-06	0.99	0.90-1.07	3.7E-01
rs6420094	5	176750242	**SLC34A1**;GRK6,RGS14,LMAN2,PRR7,F12,PFN3	g	1.09	1.05 - 1.15	1.6E-04	1.03	0.93-1.14	3.0E-01
rs881858	6	43914587	VEGFA	g	0.93	0.88 - 0.98	4.4E-03	0.97	0.88-1.06	2.4E-01
rs7805747	7	151038734	**PRKAG2**	a	1.18	1.12 - 1.25	8.6E-09	1.24	1.11-1.38	7.7E-05
rs4744712	9	70624527	**PIP5K1B**;FAM122A	a	1.06	1.02 - 1.11	6.6E-03	1.10	1.01-1.20	1.9E-02
rs4014195	11	65263398	RNASEH2C;DKFZp761E198,HTATIP,OVOL1	g	1.10	1.05 - 1.14	4.1E-05	1.07	0.98-1.17	7.7E-02
rs653178	12	110492139	**ATXN2**	t	0.97	0.93 - 1.01	1.2E-01	0.95	0.87-1.04	1.3E-01
rs626277	13	71245697	**DACH1**	c	0.93	0.89 - 0.97	1.4E-03	1.01	0.93-1.10	4.1E-01
rs1394125	15	73946038	**UBE2Q2**;FBXO22	a	1.07	1.02 - 1.12	3.2E-03	1.15	1.05-1.27	1.8E-03
rs12460876	19	38048731	**SLC7A9**;CCDC123,ECAT8	c	0.94	0.90 - 0.98	7.9E-03	0.88	0.81-0.96	2.6E-03
Creatinine Production Loci, Association with CKD										
rs7422339	2	211248752	**CPS1**	a	1.12	1.07 - 1.18	8.0E-06	1.15	1.04-1.27	2.5E-03
rs2279463	6	160588379	**SLC22A2**	g	1.11	1.04 - 1.18	1.1E-03	1.07	0.94-1.23	1.5E-01

rs6465825	7	77254375	TMEM60;RSBN1L,PHTF2	c	1.04	1.00 - 1.09	4.7E-02	1.04	0.95-1.13	2.0E-01
rs10794720	10	1146165	**WDR37**	t	1.16	1.08 - 1.26	1.5E-04	1.09	0.93-1.27	1.5E-01
rs10774021	12	219559	**SLC6A13**;JARID1A,SLC6A12	c	0.95	0.91 - 0.99	2.4E-02	1.00	0.90-1.10	4.7E-01
rs491567	15	51733885	**WDR72**	c	0.94	0.89 - 0.98	1.1E-02	0.84	0.75-0.93	6.3E-04
rs9895661	17	56811371	**BCAS3**;TBX2,C17orf82	c	1.07	1.01 - 1.13	2.6E-02	1.17	1.05-1.31	2.0E-03

	Chr	**position (b36)**	**Genes Nearby**	**modeled allele#**	**eGFRcys beta**	**eGFRcys SE**	**p-value**	**eGFRcys beta**	**eGFRcys SE**	**1-sided p-value**
Renal Function Loci, Association with eGFRcys					**Discovery**			**Replication**		
rs1933182	1	109801361	SYPL2;ATXN7L2,CYB561D1, PSMA5,AMIGO1,SORT1	a	-0.006	0.003	1.6E-02	0.002	0.005	3.4E-01
rs267734	1	149218101	ANXA9;FAM63A,PRUNE, BNIPL,LASS2,SETDB1	c	0.004	0.003	1.5E-01	0.016	0.006	2.3E-03
rs16864170 (CKD)	2	5825331	SOX11	c	-0.010	0.005	6.8E-02	-0.013	0.011	1.2E-01
rs1260326	2	27584444	**GCKR**;IFT172,FNDC4	t	0.006	0.002	6.4E-03	0.004	0.004	1.6E-01
rs13538	2	73721836	**NAT8**;NAT8B,ALMS1	g	0.010	0.003	5.0E-04	0.007	0.005	7.9E-02
rs347685	3	143289827	TFDP2	c	0.008	0.003	1.5E-03	-0.001	0.005	4.3E-01
rs11959928	5	39432889	**DAB2**;C9	a	-0.007	0.002	2.6E-03	-0.010	0.004	1.0E-02
rs6420094	5	176750242	**SLC34A1**;GRK6,RGS14, LMAN2,PRR7,F12,PFN3	g	-0.009	0.003	1.6E-03	-0.014	0.005	8.7E-04
rs881858	6	43914587	VEGFA	g	0.011	0.003	6.4E-05	0.018	0.005	9.0E-05
rs7805747	7	151038734	**PRKAG2**	a	-0.014	0.004	4.5E-04	-0.018	0.005	2.7E-04
rs4744712	9	70624527	**PIP5K1B**;FAM122A	a	-0.006	0.002	1.8E-02	-0.006	0.004	1.1E-01
rs4014195	11	65263398	RNASEH2C;DKFZp761E198, HTATIP,OVOL1	g	-0.005	0.002	4.3E-02	-0.004	0.005	1.9E-01
rs653178	12	110492139	**ATXN2**	t	0.013	0.002	3.8E-08	0.016	0.004	1.4E-04
rs626277	13	71245697	**DACH1**	c	0.006	0.002	2.4E-02	0.013	0.004	1.7E-03
rs1394125	15	73946038	**UBE2Q2**;FBXO22	a	-0.009	0.003	8.3E-04	-0.004	0.005	1.7E-01
rs12460876	19	38048731	**SLC7A9**;CCDC123,ECAT8	c	0.006	0.002	8.2E-03	0.001	0.004	3.9E-01
Creatinine Production Loci, Association with eGFRcys										

rs7422339	2	211248752	**CPS1**	a	0.003	0.003	3.9E-01	0.005	0.005	1.3E-01
rs2279463	6	160588379	**SLC22A2**	g	-0.001	0.004	7.7E-01	-0.007	0.007	1.6E-01
rs6465825	7	77254375	TMEM60;RSBN1L,PHTF2	c	0.000	0.002	9.5E-01	0.004	0.004	1.9E-01
rs10794720	10	1146165	**WDR37**	t	-0.006	0.004	1.1E-01	-0.005	0.008	2.8E-01
rs10774021	12	219559	**SLC6A13**;JARID1A,SLC6A12	c	0.000	0.002	9.3E-01	0.005	0.008	2.8E-01
rs491567	15	51733885	**WDR72**	c	0.003	0.003	2.3E-01	0.008	0.005	7.3E-02
rs9895661	17	56811371	**BCAS3**;TBX2,C17orf82	c	-0.004	0.003	1.8E-01	0.001	0.006	4.1E-01

#The minor allele based on sample size weighted mean allele frequency in the discovery cohorts is modeled. Genes within 60 kb were based on RefSeq genes (b36). The gene closest to the SNP is listed first and bold if the SNP is located within the gene. Other genes in the region are listed after ";". Betas for eGFR refer to age-adjusted sex-specific residuals of natural log transformed eGFR. P-values in discovery analyses are corrected for genomic control before and after meta-analysis.

Supplementary Table 4 - Additional Gene Biology. This table lists additional genes in associated regions containing a gene highlighted in Box 1, as well as genes in other associated regions. For novel regions associated with both eGFRcrea and eGFRcys, the gene(s) in closest physical proximity and/or in strong LD (r^2>0.8) with the lead SNP is presented. For novel regions association with eGFRcrea only, the gene in closest physical proximity is presented.

Location	Gene	Function
1q21	*LASS2*	LAG1 homolog, ceramide synthase 2 (*LASS2*) is highly expressed in the kidney and may be involved in cell growth.[46] A non-synonymous coding SNP in *LASS2*, rs267738 (E115A), was in perfect LD with the lead SNP in the region and of predicted damaging function.[47] *LASS2* has been implicated in the synthesis of specific ceramides.[48] Ceramides and their product sphingolipids are important in genetic diseases of the kidney,[49] and have a role in aging mechanisms.
1q21, *LASS2* region	*ANXA9*	Annexin A9 (*ANXA9*) is expressed in kidney and functions as a calcium-sensitive protein.[50]
1q21, *LASS2* region	*SETDB1*	SET domain, bifurcated 1 (*SETDB1*) is a key histone methyltransferase important in chromatin homeostasis and thus epigenetic regulation of gene expression.[51] It is expressed in numerous tissues including the kidney (UniGene).
2p23.3, *GCKR* region	*FNDC4*	Encodes fibronectin type III domain containing 4 gene. This gene shows low expression in the kidney,[52] and is involved in cell adhesion activity.
2q35	*CPS1*	Encodes carbamoyl-phosphate synthetase 1. Has 3 isoforms and is involved in the hepatic urea cycle and in production of arginine, a precursor to creatine production that could potentially affect serum creatinine levels. Moreover, *CPS1* is associated with hyperammonemia, which has been shown to decrease creatine synthesis.[53] The associated SNP causes a nonsynonymous amino acid change.
3q23	*TFDP2*	*TFDP2* encodes E2F dimerization partner (DP) 2. Dimerization of DP proteins with E2F proteins increases the transcription activity of E2F. The role of TFDP2 has mainly been studied in the context of tumorigenesis via its known interaction with E2F[54] and with the TGFβ signaling pathway,[55] and not in the context of renal disease.

3q23, *TFDP2* region	*ATP1B3*	Encodes ATPase, Na+/K+ transporting, beta 3 polypeptide. eSNP data points to this gene (Table 4). It contains a highly conserved actin nucleation and is involved in membrane growth and polarity. It is expressed in numerous tissues, including kidney (UniGene).
6q26	*SLC22A2*	*SLC22A2* encodes solute carrier family 22, member 2 which functions as an organic cation transporter and mediates the uptake of a variety of organic cations, including creatinine in the basolateral membrane of renal tubular epithelial cells.[56] Neighboring genes are *SLC22A1* and *SLC22A3*, which have similar function.
7q11.23	*TMEM60*	Encodes transmembrane protein 60. It is expressed in many tissues including the kidney and muscle. Its biological function in unknown.
9q13	*PIP5K1B*	*PIP5K1B* encodes phosphatidylinositol-4-phosphate 5-kinase, type 1 with a possible role in cell polarization.[57] The lead SNP we identified is an intronic SNP in a region with high conservation across species. Expression is complex, with multiple transcripts detected in a wide variety of tissues, including the kidney. No publications connecting this gene and kidney function.
9q21.11, *PIP5K1B* region	*FAM122A*	Encodes the protein family with sequence similarity 122A. No known association with kidney disease.
10p15.3	*WDR37*	Encodes WD repeat domain 37. Members of this protein family are involved in a variety of cellular processes, including cell cycle progression, signal transduction, apoptosis, and gene regulation. Specific biological function is unknown.
12p13.3	*SLC6A13*	Encodes solute carrier family 6 (neurotransmitter transporter, betaine/GABA), member 13, which is expressed in the kidney. It is induced by hypertonicity and mediates chloride- and sodium-dependent transport of both betaine and the neurotransmitter GABA, and shows high homology to a known creatinine transporter encoded by *SLC8A13*.[58]
12q24, *ATXN2* region	*BRAP*	In a monocyte differentiation model, BRAP (BRCA-associated protein) interacts directly with CDKN1A.[59] Knockout of *CDKN1A* ameliorates the development of chronic renal failure in a mouse model.[60]
15q21.3	*WDR72*	WD repeat-containing protein 7 (*WDR72*) is a protein of unknown function. The SNP rs17730281 is a coding SNP in *WDR72* with predicted damaging function (SIFT) and in LD with the lead SNP we identified (r^2=0.75). It is highly expressed in the kidney.
15q24.2	*UBE2Q2*	Ubiquitin-conjugating enzyme E2Q family member 2 is reported to catalyze the covalent attachment of ubiquitin to other proteins. UBE2Q2 has a role in the cell cycle.[61] It is expressed in

		the kidney.
15q24.2, *UBE2Q2* region	*FBXO22*	Encodes F-box protein 22, which contains an F box motif (OMIM). It constitutes one of four parts of the ubiquitin protein ligase complex with a role in ubiquitination (www.genecards.org) It is expressed in kidney.
17q23	*BCAS3*	Encodes breast carcinoma amplified sequence 3. Involves a functional estrogen response element. It is ubiquitously expressed, and has been associated with human height, which could secondarily be associated with muscle mass.[62] Our identified SNP was also in strong LD with the *TBX2* gene.
19q13.11, *SLC7A9* region	*CCDC123*	Coiled-coil domain containing 123 (CCDC123) encodes a mitochondrial protein. It is expressed in the kidney (www.genecards.org).

Supplementary Table 5: Effect sizes of association with eGFRcrea across strata of diabetes and hypertension. Results are presented for the lead SNP at known and novel loci related to renal function.

							Diabetes			No Diabetes			
SNPID	**locus**	**chr**	**pos**	**A1**	**A2**	**Freq1**	**Beta**	**SE**	**pval**	**Beta**	**SE**	**pval**	**pval diff**
rs267734	ANXA9	1	149218101	t	c	0.79	-0.011	0.007	1.2E-01	-0.009	0.002	7.9E-08	8.0E-01
rs1260326	GCKR	2	27584444	t	c	0.41	0.015	0.006	1.2E-02	0.009	0.001	3.8E-10	3.2E-01
rs13538	ALMS1	2	73721836	a	g	0.77	0.001	0.007	9.4E-01	-0.010	0.002	6.7E-09	1.5E-01
rs347685	TFDP2	3	143289827	a	c	0.72	-0.010	0.006	1.1E-01	-0.009	0.001	2.4E-09	8.5E-01
rs17319721	SHROOM3	4	77587871	a	g	0.43	-0.025	0.006	1.3E-05	-0.012	0.001	2.8E-17	2.3E-02
rs11959928	DAB2	5	39432889	a	t	0.44	-0.012	0.006	4.6E-02	-0.009	0.001	4.1E-10	6.3E-01
rs6420094	SLC34A1	5	176750242	a	g	0.66	0.020	0.007	3.1E-03	0.010	0.002	3.9E-11	1.7E-01
rs881858	VEGFA	6	43914587	a	g	0.72	-0.018	0.007	8.3E-03	-0.010	0.002	2.1E-10	2.8E-01
rs7805747	PRKAG2	7	151038734	a	g	0.25	0.004	0.008	6.6E-01	-0.013	0.002	9.2E-13	4.8E-02
rs10109414	STC1	8	23807096	t	c	0.42	-0.005	0.006	3.6E-01	-0.008	0.001	1.3E-09	6.0E-01
rs4744712	PIP5K1B	9	70624527	a	c	0.39	-0.008	0.006	1.9E-01	-0.009	0.001	2.4E-10	8.4E-01
rs10794720	WDR37	10	1146165	t	c	0.08	-0.015	0.011	1.6E-01	-0.014	0.002	5.7E-08	9.1E-01
rs653178	ATXN2	12	110492139	t	c	0.51	0.012	0.006	4.1E-02	0.003	0.001	4.8E-02	1.3E-01
rs626277	DACH1	13	71245697	a	c	0.60	-0.012	0.006	3.9E-02	-0.008	0.001	9.1E-09	5.1E-01
rs491567	WDR72	15	51733885	a	c	0.78	-0.012	0.007	6.9E-02	-0.009	0.002	3.4E-08	6.3E-01
rs1394125	UBE2Q2	15	73946038	a	g	0.35	-0.016	0.006	1.2E-02	-0.009	0.002	5.0E-09	2.8E-01
rs12917707	UMOD	16	20275191	t	g	0.18	0.033	0.007	1.4E-05	0.015	0.002	1.3E-17	2.3E-02
rs12460876	SLC7A9	19	38048731	t	c	0.60	0.000	0.006	1.0E+00	-0.009	0.001	6.4E-10	1.5E-01
							Hypertension			No Hypertension			
SNPID	**locus**	**chr**	**pos**	**A1**	**A2**	**Freq1**	**Beta**	**SE**	**pval**	**Beta**	**SE**	**pval**	**pval diff**
rs267734	ANXA9	1	149218101	t	c	0.79	-0.008	0.003	6.1E-03	-0.010	0.002	6.1E-07	6.0E-01
rs1260326	GCKR	2	27584444	t	c	0.41	0.009	0.002	2.4E-04	0.009	0.002	6.2E-09	7.7E-01
rs13538	ALMS1	2	73721836	a	g	0.77	-0.007	0.003	1.0E-02	-0.010	0.002	4.5E-07	4.2E-01
rs347685	TFDP2	3	143289827	a	c	0.72	-0.011	0.003	2.4E-05	-0.007	0.002	2.3E-05	2.8E-01
rs17319721	SHROOM3	4	77587871	a	g	0.43	-0.010	0.002	6.8E-06	-0.014	0.002	2.7E-18	2.0E-01
rs11959928	DAB2	5	39432889	a	t	0.44	-0.010	0.002	2.1E-05	-0.009	0.002	1.2E-07	6.4E-01
rs6420094	SLC34A1	5	176750242	a	g	0.66	0.012	0.003	7.4E-06	0.010	0.002	6.9E-08	5.8E-01
rs881858	VEGFA	6	43914587	a	g	0.72	-0.012	0.003	1.8E-05	-0.011	0.002	1.2E-08	8.0E-01
rs7805747	PRKAG2	7	151038734	a	g	0.25	-0.016	0.003	2.6E-07	-0.010	0.002	4.6E-06	8.1E-02
rs10109414	STC1	8	23807096	t	c	0.42	-0.010	0.002	1.5E-05	-0.007	0.002	3.4E-06	3.7E-01

rs4744712	PIP5K1B	9	70624527	a	c	0.39	-0.008	0.002	5.8E-04	-0.009	0.002	7.8E-08	8.0E-01
rs10794720	WDR37	10	1146165	t	c	0.08	-0.010	0.004	1.8E-02	-0.016	0.003	2.6E-08	2.1E-01
rs653178	ATXN2	12	110492139	t	c	0.51	0.004	0.002	7.7E-02	0.001	0.002	3.8E-01	3.3E-01
rs626277	DACH1	13	71245697	a	c	0.60	-0.007	0.002	2.0E-03	-0.009	0.002	3.9E-08	5.4E-01
rs491567	WDR72	15	51733885	a	c	0.78	-0.010	0.003	2.4E-04	-0.009	0.002	5.5E-06	6.8E-01
rs1394125	UBE2Q2	15	73946038	a	g	0.35	-0.010	0.003	5.5E-05	-0.009	0.002	2.5E-07	7.2E-01
rs12917707	UMOD	16	20275191	t	g	0.18	0.023	0.003	4.7E-15	0.012	0.002	1.6E-09	**1.8E-03**
rs12460876	SLC7A9	19	38048731	t	c	0.60	-0.007	0.002	4.0E-03	-0.009	0.002	5.6E-09	3.2E-01

P-value for difference are from a t-test for independent samples (b1hat -b2hat ~ N(b1-b2,SE1^2+SE2^2)): under the null hypothesis, the difference between the effects in the two groups follows a normal distribution N(0, σ2), with σ2 estimated as the sum of the squares of the standard errors. Differences were considered significant if p<5.6*10E-03 (0.1/18) and are indicated in bold font. All discovery studies contributed to the meta-analyses of eGFR among those without diabetes and without hypertension. The BLSA Study did not contribute to the meta-analysis among those with hypertension, and theAmish, the BLSA, and the Family Heart Study did not contribute to the meta-analysis among those with diabetes. Sample sizes for hypertension and diabetes are presented in Table 1.

Supplementary Table 6: Expression Associated SNP Analysis. SNPs significantly associated with eGFRcrea, CKD or eGFRcys in Stage 1 discovery analyses that are associated with gene expression in liver, lymphoblastoid cell lines (LCL) or lymphocytes. Starred loci (*) were also detected in association with eGFRcrea using the FDR method.

Tissue: LIVER															
SNP	p-value				inGene	Genes within 60kb	Closest gene		Second closest gene		Expressed Gene	Expressed Probe	r2 to top SNP	top SNP	notes
	eGFRcys	CKD	eGFRcrea	eSNP			Name	Distance (bp)	Name	Distance (bp)					
rs10857787	2.4E-02	4.5E-02	**6.2E-08**	2.8E-35	SYPL2	ATXN7L2; CYB561D1; SYPL2; PSMA5; AMIGO1	SYPL2	1190	ATXN7L2	16271	SYPL2		0.92	rs1933182	
rs8076494	3.8E-01	2.5E-02	**4.2E-07**	7.9E-07	FBXL20	MED1; FBXL20	FBXL20	41154	MED1	43815	PERLD1				*
rs2268755	2.2E-01	1.6E-02	**2.9E-06**	5.5E-08	ACVR2B	ACVR2B; XYLB; ENDOGL1	ACVR2B	6127	ENDOGL1	35916	HSS00051291				*
rs7374458	2.4E-01	7.2E-03	**4.4E-06**	2.4E-06	ACVR2B	SCN5A; ACVR2B; ENDOGL1	ACVR2B	3420	ENDOGL1	6621	XYLB				*
rs4256249	2.7E-01	8.0E-02	**1.0E-05**	4.3E-06	SHROOM3	SHROOM3	SHROOM3	102327	FLJ25770	130121	SHROOM3		0.06	rs17319721	
rs11070327	5.5E-03	1.6E-03	**1.9E-05**	5.3E-06	OIP5	NUSAP1; OIP5; CHP	OIP5	1399	NUSAP1	22202	Contig53488				*
rs1589576	**6.5E-05**	4.0E-02	**1.9E-05**	5.0E-11	ALMS1	ALMS1	ALMS1	98242	NAT8	129045	ALMS1		0.85	rs13538	
rs11078895	7.6E-01	1.0E-02	**2.3E-05**	2.0E-11		FBXL20; RPL19; CACNB1; STAC2	FBXL20	15789	STAC2	19077	CRKRS				*
rs3372	3.0E-01	4.9E-03	**3.9E-05**	2.2E-08	HTATIP; RNASEH2C	DKFZp761E198; HTATIP; RELA; RNASEH2C	RNASEH2C	73	HTATIP	1856	RNASEH2C		0.26	rs4014195	
rs7035163	8.0E-01	2.4E-02	**4.0E-05**	2.4E-11	PIP5K1B	FAM122A; PIP5K1B	FAM122A	8922	PIP5K1B	65426	FAM122A		0.19	rs4744712	
rs12113119	1.1E-02	2.5E-01	**4.6E-05**	6.0E-08		RSBN1L; PTPN12	RSBN1L	10941	PTPN12	45432	BC037783		0.21	rs6465825	
rs2593280	2.9E-01	3.4E-03	**6.1E-05**	2.1E-07	UBE2Q2	UBE2Q2; FBXO22	UBE2Q2	15166	FBXO22	45234	UBE2Q2		0.00	rs1394125	
rs6762208	3.1E-01	7.6E-01	**6.9E-05**	5.2E-09	SENP2	IGF2BP2; SENP2	SENP2	17718	IGF2BP2	30362	HSS00090370				

rs17350188	**2.5E-04**	8.2E-02	**7.0E-05**	4.4E-06		TPRKB; FLJ43987; DUSP11; NAT8B	TPRKB	329	DUSP11	24488	TPRKB		0.39	rs13538	
rs16967572	5.3E-02	1.9E-01	**7.2E-05**	9.6E-13	CCDC123	RHPN2; SLC7A9; C19orf40; CCDC123	CCDC123	42608	C19orf40	50664	SLC7A9		0.58	rs12460876	
rs2927743	3.2E-01	3.0E-01	**7.6E-05**	7.3E-11	ZFP30	ZNF571; ZFP30; ZNF781; ZNF607; ZNF540	ZFP30	8946	ZNF781	26315	ZFP30				
rs10838738	1.7E-01	2.9E-03	**8.7E-05**	1.8E-11	MTCH2	C1QTNF4; MTCH2; AGBL2; NDUFS3	MTCH2	1015	AGBL2	18095	CUGBP1				
rs3887266	7.9E-01	4.0E-02	**1.0E-04**	2.3E-06		SLC17A1; SLC17A3	SLC17A3	1581	SLC17A1	11459	SLC17A1				
rs164749	1.8E-01	9.0E-01	**1.3E-04**	2.5E-09		C16orf55; CHMP1A; CDK10; DPEP1; SPATA2L; CPNE7	CHMP1A	2619	DPEP1	3387	C16orf55				
rs1103851	8.0E-03	2.4E-02	**1.9E-04**	1.3E-06	ANKRD27	ANKRD27; RGS9BP; NUDT19	ANKRD27	19688	RGS9BP	19898	SNORA68				
rs409783	1.3E-02	4.2E-01	**3.1E-04**	5.5E-07		STC1	STC1	3530	NKX3-1	155453	C2orf29		0.29	rs10109414	
rs2734974	2.9E-01	**1.9E-04**	4.1E-03	2.5E-10		HLA-G	HLA-G	34902	HLA-A	76551	HLA-A				
rs3768439	**2.2E-04**	1.8E-01	2.3E-01	3.6E-06	C1orf164	C1orf164; TMEM53	C1orf164	4070	TMEM53	6175	C1orf164				

Tissue: Lymphoblastoid Cell Lines (LCL)

SNP	p-value				inGene	Genes within 60kb	Closest gene		Second closest gene		Expressed Gene	Expressed Probe	r2 to top SNP	top SNP	notes
	eGFRcys	CKD	eGFRcrea	eSNP			Name	Distance (bp)	Name	Distance (bp)					
rs6955503	2.9E-01	9.2E-02	**1.5E-07**	5.3E-09	PTPN12	PTPN12	PTPN12	42145	RSBN1L	98518	PTPN12	244356_at	0.35	rs6465825	
rs4390625	3.5E-01	2.0E-02	**3.6E-07**	6.2E-10	CRKRS	MED1; CRKRS	CRKRS	2056	MED1	12820		225697_at			*
rs867282	6.6E-02	1.2E-01	**4.4E-07**	1.1E-07		MRPL33; SLC4A1AP; RBKS	SLC4A1AP	33811	MRPL33	42925		209313_at			
rs1544457	2.9E-01	1.8E-01	**4.4E-07**	2.9E-08		TMEM60; RSBN1L; PHTF2	TMEM60	3755	RSBN1L	10287	PTPN12	244356_at	0.72	rs6465825	
rs12450559	3.7E-01	2.1E-02	**4.4E-07**	3.3E-10		CRKRS	CRKRS	6191	NEUROD2	65312		225697_at			*

rs6685648	1.4E-03	1.6E-01	**4.5E-07**	7.4E-12	CASP9	ELA2B; ELA2A; CTRC; CASP9; DNAJC16	CASP9	6399	ELA2B	7301		221648_s_at			*
rs7503705	3.6E-01	2.0E-02	**4.7E-07**	2.8E-10	CRKRS	CRKRS	CRKRS	18814	MED1	62177		225697_at			*
rs2338800	3.9E-01	2.4E-02	**5.2E-07**	4.8E-10	FBXL20	FBXL20	FBXL20	59727	MED1	62388		225697_at			*
rs2338755	4.1E-01	2.9E-02	**6.0E-07**	4.8E-10	FBXL20	FBXL20; RPL19; STAC2	FBXL20	2477	STAC2	37343		225697_at			*
rs588193	4.1E-01	3.1E-02	**6.5E-07**	4.8E-10	FBXL20	FBXL20; STAC2	FBXL20	23599	STAC2	58465		225697_at			*
rs2061342	4.6E-01	2.6E-02	**6.9E-07**	4.6E-10		FBXL20; RPL19; CACNB1; STAC2	FBXL20	11183	STAC2	23683		225697_at			*
rs2868813	1.8E-01	1.8E-01	**9.8E-07**	1.1E-08	RSBN1L	TMEM60; RSBN1L	RSBN1L	3262	TMEM60	17304	PTPN12	244356_at	0.69	rs6465825	
rs711309	3.3E-01	2.1E-01	**1.3E-06**	4.3E-09	PHTF2	PHTF2	PHTF2	46795	MAGI2	106629	PTPN12	244356_at	0.69	rs6465825	
rs1619021	2.4E-01	4.8E-02	**1.5E-06**	3.2E-10		PPP1R1B; NEUROD2; STARD3; CRKRS	NEUROD2	20747	PPP1R1B	43904		225697_at			*
rs848493	2.8E-01	2.3E-01	**1.6E-06**	4.9E-08	PHTF2	PHTF2	PHTF2	54018	TMEM60	104774	PTPN12	244356_at	0.66	rs6465825	
rs4795369	3.9E-01	2.2E-02	**4.9E-06**	1.1E-09		MED1; FBXL20; CRKRS	MED1	1593	CRKRS	9171		225697_at			*
rs522063	1.7E-01	4.2E-03	**5.6E-06**	3.5E-08	EXDL1	EXDL1; CHP	EXDL1	1278	CHP	47227		204125_at			*
rs535211	6.7E-01	1.8E-01	**5.7E-06**	1.9E-15		RBM14; CCDC87; RBM4; SPTBN2; RBM4B; CCS	RBM4	5657	RBM14	5669		203522_at			
rs6956726	2.1E-01	2.8E-01	**6.1E-06**	2.7E-09	RSBN1L	TMEM60; RSBN1L	RSBN1L	34157	TMEM60	48199	PTPN12	244356_at	0.67	rs6465825	
rs10441228	2.3E-01	2.9E-01	**6.5E-06**	2.1E-10	RSBN1L	TMEM60; RSBN1L	RSBN1L	38341	TMEM60	52383	PTPN12	244356_at	0.67	rs6465825	
rs521890	1.9E-01	5.2E-03	**6.7E-06**	1.4E-07		EXDL1; CHP	EXDL1	1788	CHP	50293		204125_at			*
rs3811644	2.1E-02	2.4E-01	**1.3E-05**	6.5E-09	C2orf16	GCKR; XAB1; CCDC121; ZNF512; C2orf16	C2orf16	2784	ZNF512	3087	GPN1	209313_at	0.03	rs1260326	
rs6503513	6.6E-01	3.3E-02	**1.4E-05**	7.6E-08	MED1	MED1; FBXL20; CRKRS	MED1	1076	FBXL20	3737		225697_at			*
rs6734059	2.1E-02	2.4E-01	**2.0E-05**	2.1E-10	ZNF512	XAB1; CCDC121; ZNF512; C2orf16	ZNF512	2262	C2orf16	2565	GPN1	209313_at	0.04	rs1260326	
rs618838	6.2E-01	2.3E-02	**2.0E-05**	1.4E-12	ACTN3	RBM14; CCDC87; BBS1; ZDHHC24; CCS; CTSF; ACTN3; DPP3	ACTN3	2078	CTSF	2216		203522_at			

rs1815739	6.5E-01	2.6E-02	**2.2E-05**	3.2E-13	ACTN3	RBM14; CCDC87; BBS1; ZDHHC24; CCS; CTSF; ACTN3; DPP3	ACTN3	2702	CTSF	2840		203522_at			
rs1324087	1.9E-01	4.7E-03	**2.4E-05**	3.5E-13		SLC17A1; SLC17A3	SLC17A3	3919	SLC17A1	9121		209846_s_at			
rs1881396	2.2E-02	2.3E-01	**2.6E-05**	4.7E-09	ZNF512	XAB1; SLC4A1AP; CCDC121; SUPT7L; ZNF512; C2orf16	ZNF512	1357	CCDC121	3904	GPN1	209313_at	0.03	rs1260326	
rs2295626	9.6E-04	3.3E-01	**3.1E-05**	9.5E-13	DNAJC16	ELA2B; AGMAT; CASP9; DNAJC16	DNAJC16	21610	CASP9	24171		221648_s_at			*
rs2290999	1.8E-01	2.0E-01	**3.4E-05**	5.1E-08	ZFP30	ZNF571; ZFP30; ZNF781; ZNF607; ZNF540	ZFP30	7426	ZNF781	19762		235373_at			
rs241935	1.6E-01	2.7E-01	**3.5E-05**	7.9E-08		ZNF573	ZNF573	23763	ZNF607	83272		235373_at			
rs316611	3.4E-02	8.9E-04	**4.1E-05**	1.0E-15	RTF1	LTK; NDUFAF1; RTF1; RPAP1; ITPKA	RTF1	24076	ITPKA	34443		204125_at			*
rs7810273	1.2E-02	2.4E-01	**4.7E-05**	1.4E-10		RSBN1L; PTPN12	RSBN1L	11115	PTPN12	45258	PTPN12	244356_at	0.21	rs6465825	
rs4727461	1.5E-02	2.5E-01	**4.8E-05**	1.4E-10		RSBN1L; PTPN12	RSBN1L	5371	PTPN12	51002	PTPN12	244356_at	0.19	rs6465825	
rs7254809	1.8E-01	2.8E-01	**4.9E-05**	9.2E-08		SIPA1L3	SIPA1L3	32172	ZNF573	95495		235373_at			
rs1725745	3.4E-01	1.8E-01	**5.7E-05**	2.5E-08		MAGI2; PHTF2	PHTF2	11999	MAGI2	47835	PTPN12	244356_at	0.45	rs6465825	
rs1377416	7.6E-02	**1.0E-05**	**5.8E-05**	2.5E-08		RAPSN; PSMC3; MYBPC3; SLC39A13; SPI1	SLC39A13	13435	SPI1	16619		229272_at			
rs4752801	2.8E-01	1.1E-03	**6.0E-05**	2.4E-12		NUP160	NUP160	37584	PTPRJ	94468		229272_at			
rs3766160	9.4E-03	4.7E-01	**6.8E-05**	3.0E-08	ELA2B	ELA2B; ELA2A; CTRC; CASP9; EFHD2; DNAJC16	ELA2B	6277	CASP9	9924		221648_s_at			*
rs3820071	1.0E-02	4.7E-01	**6.9E-05**	1.4E-08	ELA2B	ELA2B; ELA2A; CTRC; CASP9; EFHD2; DNAJC16	ELA2B	6172	CASP9	10029		221648_s_at			*
rs896817	1.3E-01	**3.0E-05**	**7.1E-05**	4.6E-09	SPI1	PSMC3; MYBPC3; SLC39A13; MADD; SPI1	SPI1	5822	MYBPC3	20052		229272_at			

rs10769258	1.4E-01	1.6E-03	**8.1E-05**	3.2E-10	SPI1	PSMC3; SLC39A13; MADD; MYBPC3; SPI1	SPI1	9088	MYBPC3	16786		229272_at			
rs1757468	1.1E-01	6.9E-04	**8.4E-05**	8.7E-15	RTF1	LTK; NDUFAF1; RTF1; ITPKA	RTF1	32180	ITPKA	42547		204125_at			*
rs10838738	1.7E-01	2.9E-03	**8.7E-05**	9.0E-11	MTCH2	C1QTNF4; MTCH2; AGBL2; NDUFS3	MTCH2	1015	AGBL2	18095		229272_at			
rs1768808	**6.4E-05**	9.3E-02	1.2E-02	8.5E-28		MAST2; PIK3R3	MAST2	1421	PIK3R3	2596		1560263_at			
rs11211152	**6.8E-05**	1.9E-01	2.7E-02	1.3E-44	GPBP1L1	GPBP1L1; NASP; IPP; TMEM69; CCDC17	GPBP1L1	12654	CCDC17	24484		1560263_at			
rs3811436	**7.2E-05**	1.9E-01	2.8E-02	8.4E-52	GPBP1L1	GPBP1L1; NASP; IPP; TMEM69; CCDC17	GPBP1L1	931	TMEM69	27966		1560263_at			
rs10430105	**7.3E-05**	1.9E-01	2.8E-02	1.3E-44		GPBP1L1; NASP; IPP; TMEM69; CCDC17	GPBP1L1	12065	TMEM69	14970		1560263_at			

Tissue: LYMPHOCYTE

SNP	p-value				inGene	Genes within 60kb	Closest gene		Second closest gene		Expressed Gene	Expressed Probe	r2 to top SNP	top SNP	notes
	eGFRcys	CKD	eGFRcrea	eSNP			Name	Distance (bp)	Name	Distance (bp)					
rs1346268	8.3E-01	**2.8E-06**	**2.1E-19**	8.4E-24		C15orf48; SPATA5L1; GATM	GATM	2049	SPATA5L1	21556	SPATA5L1	GI_13129039-S	0.44	rs2453533	
rs9806699	8.4E-01	1.8E-04	**2.6E-13**	5.6E-19		SPATA5L1; C15orf48; SLC30A4	C15orf48	14747	SPATA5L1	26781	SPATA5L1	GI_13129039-S	0.35	rs2453533	
rs1260326	6.4E-03	1.8E-01	**1.3E-10**	7.0E-12	GCKR	GCKR; IFT172; FNDC4	GCKR	11235	FNDC4	12854	IFT172	GI_37546863-S	top SNP		
rs835223	5.5E-03	**2.2E-05**	**1.7E-10**	4.7E-04	DAB2	C9; DAB2	DAB2	9578	C9	16702	DAB2	GI_4503250-S	0.93	rs11959928	
rs700221	1.1E-03	**3.1E-05**	**1.8E-10**	7.0E-05	C9	C9; DAB2	C9	7480	DAB2	14604	DAB2	GI_4503250-S	0.84	rs11959928	
rs700233	1.2E-03	3.7E-05	**2.5E-10**	1.0E-03	C9	C9; DAB2	C9	101	DAB2	7225	DAB2	GI_4503250-S	0.84	rs11959928	

rs950027	8.0E-01	4.5E-03	**4.1E-10**	2.7E-10	SLC30A4	C15orf21; SLC30A4	C15orf21	2298	SLC30A4	13967	SPATA5L1	GI_13129039-S	0.62	rs2453533	
rs1421095	2.1E-03	2.6E-04	**6.8E-10**	8.8E-04	C9	C9; DAB2	C9	9007	DAB2	16131	DAB2	GI_4503250-S	0.81	rs11959928	
rs10512696	5.9E-03	**6.4E-06**	**1.4E-09**	9.3E-04	DAB2	C9; DAB2	DAB2	1428	C9	59252	DAB2	GI_4503250-S	0.72	rs11959928	
rs3737267	3.2E-01	4.8E-04	**3.2E-09**	5.9E-05	SPATA5L1	C15orf48; SPATA5L1; GATM	SPATA5L1	8214	C15orf48	19963	SPATA5L1	GI_13129039-S	0.13	rs2453533	
rs335675	2.0E-04	4.3E-01	**9.4E-08**	2.1E-03	FBXO22	NRG4; UBE2Q2; FBXO22	FBXO22	3028	NRG4	15558	FBXO22	GI_22547148-I	0.01	rs1394125	
rs6546838	4.0E-05	1.9E-01	**1.1E-07**	1.8E-04	ALMS1	ALMS1	ALMS1	66395	EGR4	158607	ALMS1	GI_27436958-S	0.95	rs13538	
rs2901438	6.5E-05	1.8E-01	**1.2E-07**	7.0E-05	ALMS1	ALMS1	ALMS1	52771	EGR4	144983	ALMS1	GI_27436958-S	0.95	rs13538	
rs6546835	6.6E-05	1.8E-01	**1.3E-07**	4.8E-05	ALMS1	ALMS1	ALMS1	51830	EGR4	144042	ALMS1	GI_27436958-S	0.95	rs13538	
rs10496191	6.0E-05	1.8E-01	**1.3E-07**	6.7E-05	ALMS1	ALMS1	ALMS1	60913	EGR4	153125	ALMS1	GI_27436958-S	0.95	rs13538	
rs13384952	**2.6E-05**	1.1E-01	**1.3E-07**	5.8E-08	ALMS1	ALMS1	ALMS1	111074	NAT8	143890	ALMS1	GI_27436958-S	0.95	rs13538	
rs3813227	9.2E-05	1.8E-01	**1.5E-07**	8.6E-05	ALMS1	ALMS1	ALMS1	39082	EGR4	131294	ALMS1	GI_27436958-S	0.95	rs13538	
rs10193972	7.4E-05	1.7E-01	**1.5E-07**	2.8E-04	ALMS1	ALMS1	ALMS1	104771	NAT8	150193	ALMS1	GI_27436958-S	0.95	rs13538	
rs2056486	8.5E-05	1.9E-01	**1.6E-07**	7.5E-05	ALMS1	ALMS1	ALMS1	104682	NAT8	150282	ALMS1	GI_27436958-S	0.95	rs13538	
rs335684	2.4E-04	4.3E-01	**2.2E-07**	2.1E-03		NRG4; UBE2Q2; FBXO22	UBE2Q2	924	FBXO22	1895	FBXO22	GI_22547148-I		rs13538	
rs10198549	9.1E-04	1.4E-01	**3.8E-07**	4.8E-09	ALMS1	ALMS1	ALMS1	42642	NAT8	73445	ALMS1	GI_27436958-S	1.00	rs13538	
rs4645989	1.3E-03	1.5E-01	**4.2E-07**	1.5E-14	CASP9	ELA2B; AGMAT; ELA2A; CASP9; DNAJC16	CASP9	447	DNAJC16	3008		GI_14790127-A			*
rs12450559	3.7E-01	2.1E-02	**4.4E-07**	6.0E-06		CRKRS	CRKRS	6191	NEUROD2	65312		GI_7706548-S			*
rs6685648	1.4E-03	1.6E-01	**4.5E-07**	9.5E-15	CASP9	ELA2B; ELA2A; CTRC; CASP9; DNAJC16	CASP9	6399	ELA2B	7301		GI_14790127-A			*
rs6440052	1.5E-02	3.0E-04	**5.0E-07**	5.2E-22		ATP1B3; TFDP2	TFDP2	12086	ATP1B3	13859		GI_4502280-S			
rs8025019	1.7E-01	2.2E-03	**5.4E-07**	1.4E-04		SPATA5L1; C15orf48; SLC30A4	C15orf48	10220	SPATA5L1	22254	SPATA5L1	GI_13129039-S	0.21	rs2453533	
rs12439639	7.7E-02	3.7E-02	**9.2E-07**	3.1E-10	C15orf21	C15orf21; SLC30A4; PLDN	C15orf21	1848	SLC30A4	32078	SPATA5L1	GI_13129039-S	0.10	rs2453533	
rs7216086	4.0E-01	3.2E-02	**9.4E-07**	3.8E-06		NEUROD2; CRKRS	CRKRS	20904	NEUROD2	50599		GI_7706548-S			*

rs7116712	9.9E-02	9.9E-03	**2.1E-06**	1.2E-05	MAP3K11	LTBP3; MAP3K11; RELA; SIPA1; SSSCA1; FAM89B; KCNK7; EHBP1L1	MAP3K11	7292	KCNK7	9051		GI_21735553-S			
rs11062357	5.3E-01	1.9E-01	**2.4E-06**	5.5E-07	JARID1A	JARID1A; SLC6A13	JARID1A	32172	SLC6A13	49392	JARID1A	GI_4826967-S	0.37	rs10774021	
rs1678750	2.3E-01	6.9E-04	**2.9E-06**	9.4E-04		INOC1	INOC1	2365	EXDL1	64226		GI_38570147-A			*
rs4407366	2.4E-01	7.2E-03	**2.9E-06**	7.8E-04	ACVR2B	ACVR2B; ENDOGL1	ACVR2B	13206	ENDOGL1	16407		GI_10862697-S			*
rs3812042	1.7E-01	2.5E-03	**3.0E-06**	1.2E-08		C9; DAB2	DAB2	872	C9	6252	DAB2	GI_4503250-S	0.72	rs11959928	
rs9838614	1.9E-01	8.1E-03	**4.2E-06**	8.2E-04		SCN5A; ACVR2B; ENDOGL1	ENDOGL1	161	ACVR2B	3040		GI_10862697-S			*
rs2297797	1.1E-01	1.2E-01	**4.2E-06**	2.7E-05	CYB561D1	ATXN7L2; CYB561D1; SYPL2; GNAI3; GPR61; AMIGO1	CYB561D1	797	ATXN7L2	5326	CYB561D	GI_32698981-S	0.32	rs1933182	
rs1132064	2.4E-01	9.3E-03	**4.3E-06**	4.4E-06		SCN5A; ACVR2B; ENDOGL1	ENDOGL1	340	SCN5A	23033		GI_4826713-S			*
rs7374458	2.4E-01	7.2E-03	**4.4E-06**	1.8E-05	ACVR2B	SCN5A; ACVR2B; ENDOGL1	ACVR2B	3420	ENDOGL1	6621		GI_4826713-S			*
rs2300669	2.4E-01	7.5E-03	**4.5E-06**	7.3E-05	ENDOGL1	SCN5A; ACVR2B; ENDOGL1	ENDOGL1	3486	ACVR2B	6687		GI_4826713-S			*
rs4795369	3.9E-01	2.2E-02	**4.9E-06**	5.3E-07		MED1; FBXL20; CRKRS	MED1	1593	CRKRS	9171		GI_7706548-S			*
rs3741414	2.7E-02	1.5E-01	**5.2E-06**	2.5E-06	INHBC	INHBE; GLI1; ARHGAP9; MARS; INHBC	INHBC	560	INHBE	5046		GI_14210509-S			*
rs4311394	9.6E-01	2.5E-02	**5.5E-06**	2.5E-03	ARL15	ARL15	ARL15	120049	NDUFS4	321495		Hs.306852-S			*
rs6546862	3.7E-03	1.2E-01	**5.7E-06**	5.7E-06		NAT8; ALMS1	NAT8	7501	ALMS1	23302	ALMS1	GI_27436958-S	0.57	rs13538	

rs12472502	3.4E-03	1.2E-01	**5.8E-06**	8.3E-06		NAT8; ALMS1	NAT8	8665	ALMS1	22138	ALMS1	GI_27436958-S	0.57	rs13538	
rs931127	1.8E-02	3.7E-04	**8.6E-06**	1.8E-03		MAP3K11; RELA; SIPA1; KCNK7; EHBP1L1	SIPA1	294	RELA	16516		hmm1261-S			
rs7736354	8.7E-01	3.5E-02	**1.0E-05**	3.0E-03	ARL15	ARL15	ARL15	116978	NDUFS4	318424		Hs.306852-S			*
rs2163294	7.1E-02	4.7E-02	**1.0E-05**	4.9E-08		ATP1B3; TFDP2	TFDP2	2874	ATP1B3	23071		GI_4502280-S			
rs11126414	3.7E-04	1.8E-01	**1.0E-05**	1.5E-05		TPRKB; DUSP11; NAT8B	NAT8B	3577	TPRKB	24959	TPRKB	GI_7705589-S	0.35	rs13538	
rs4852976	4.3E-04	9.5E-02	**1.5E-05**	5.6E-06		TPRKB; DUSP11; NAT8B	NAT8B	7855	TPRKB	20681	TPRKB	GI_7705589-S	0.39	rs13538	
rs12620091	2.9E-03	1.4E-01	**1.8E-05**	4.6E-06		TPRKB; NAT8; NAT8B	NAT8B	20818	NAT8	37282	NAT8	GI_7705327-S	0.42	rs13538	
rs7210	1.4E-04	5.3E-02	**1.8E-05**	9.8E-06	TPRKB	TPRKB; FLJ43987; DUSP11; NAT8B	TPRKB	121	NAT8B	28657	TPRKB	GI_7705589-S	0.39	rs13538	
rs1589576	6.5E-05	4.0E-02	**1.9E-05**	1.5E-12	ALMS1	ALMS1	ALMS1	98242	NAT8	129045	ALMS1	GI_27436958-S	0.85	rs13538	
rs2141372	2.0E-02	2.5E-01	**2.0E-05**	9.4E-05	ZNF512	XAB1; SLC4A1AP; CCDC121; SUPT7L; ZNF512; C2orf16	ZNF512	18762	CCDC121	21309	GPN1	GI_14149628-S	0.04	rs1260326	
rs618838	6.2E-01	2.3E-02	**2.0E-05**	6.0E-10	ACTN3	RBM14; CCDC87; BBS1; ZDHHC24; CCS; CTSF; ACTN3; DPP3	ACTN3	2078	CTSF	2216		GI_6042195-S			
rs1815739	6.5E-01	2.6E-02	**2.2E-05**	8.0E-10	ACTN3	RBM14; CCDC87; BBS1; ZDHHC24; CCS; CTSF; ACTN3; DPP3	ACTN3	2702	CTSF	2840		GI_6042195-S			
rs1881396	2.2E-02	2.3E-01	**2.6E-05**	4.1E-04	ZNF512	XAB1; SLC4A1AP; CCDC121; SUPT7L; ZNF512; C2orf16	ZNF512	1357	CCDC121	3904		GI_14149628-S			
rs12101934	2.0E-01	4.4E-03	**2.8E-05**	2.1E-03	INOC1	INOC1	INOC1	55261	CHAC1	104370		GI_38570147-A			*

rs2051216	1.4E-01	7.7E-03	**2.9E-05**	2.4E-05	ENDOGL1	SCN5A; ACVR2B; ENDOGL1	ENDOGL1	3891	SCN5A	27264		GI_4826713-S			*
rs9933029	8.5E-01	2.2E-01	**3.0E-05**	2.1E-04	SLC7A6	SLC7A6; NFATC3; RBM35B; SLC7A6OS; LYPLA3; PRMT7	SLC7A6	4988	LYPLA3	8451		GI_4507052-S			*
rs816828	1.9E-01	2.8E-01	**3.1E-05**	2.6E-22	KCNMA1	KCNMA1	KCNMA1	105709	DLG5	258682		GI_26638649-S			
rs1065212	1.0E+00	**1.2E-05**	3.9E-01	6.8E-16	HSPC111	C5orf25; HIGD2A; KIAA1191; CLTB; HSPC111; ARL10	HSPC111	192	HIGD2A	4650		GI_20270388-S			*
rs10838702	7.6E-02	**1.4E-05**	4.6E-05	4.6E-04		RAPSN; PSMC3; MYBPC3; SLC39A13; MADD; SPI1	SPI1	10761	SLC39A13	19293		GI_4507174-S			
rs17751897	**0.0E+00**	4.4E-02	7.7E-02	3.1E-07		CST3; CST9L; CST9	CST9	6201	CST3	21579		GI_19882253-S			
rs13043610	**0.0E+00**	4.7E-02	1.0E-01	8.0E-08		CST3; CST9L; CST9	CST9	428	CST3	27352		GI_19882253-S			
rs6036478	**0.0E+00**	6.4E-02	6.1E-02	1.3E-07		CST3; CST4; CST9	CST3	2934	CST9	24846		GI_19882253-S			

Supplementary Table 7 - Additional SNPs associated with eGFRcrea and CKD at an FDR of 0.05. Shown are SNPs with p-value >5x10E-08 in stage 1 discovery analyses that are associated with eGFRcrea and CKD at an FDR of 0.05 (p<4.8x10E-06)

trait	SNP^	chr	pos	beta	se	pval	qval	coded allele	coded allele freq.	eSNP**, (r2 to FDR SNP)	beta cys	pval eGFRcys	genes
eGFRcrea	rs4233535	1	15717784	-0.008	0.001	1.9E-07	0.024	c	0.30	rs4645989 (1)	-0.008	1.3E-03	*CASP9; AGMAT, CTRC, DDI2, DNAJC16, EFHD2, ELA2A, ELA2B*
eGFRcrea	rs6431731	2	15780453	-0.018	0.003	3.2E-07	0.024	t	0.94		-0.006	4.0E-01	*DDX1;*
eGFRcrea	rs7593901	2	205598761	0.012	0.002	1.6E-06	0.047	t	0.08		0.008	8.4E-02	*PARD3B;*
eGFRcrea	rs6893522	5	53335192	-0.015	0.003	1.5E-06	0.046	t	0.95	rs7736354 (0.18)	-0.003	5.3E-01	*ARL15;*
eGFRcrea	rs963837	11	30705666	-0.007	0.001	5.3E-08	0.024	t	0.54		-0.006	1.1E-02	
eGFRcrea	rs2193172	12	15223609	0.008	0.002	1.7E-06	0.049	c	0.19		0.011	2.2E-04	*RERG;*
eGFRcrea	rs11845823	14	92623469	-0.008	0.002	1.6E-06	0.047	a	0.78		-0.006	1.9E-02	*ITPK1; C14orf109, C14orf85, MOAP1*
eGFRcrea	rs2453583	17	19382628	0.007	0.001	5.8E-07	0.024	a	0.59		0.005	7.3E-02	*SLC47A1; SNORA59A, SNORA59B*
eGFRcrea	rs12936996	17	34919080	-0.008	0.002	2.8E-07	0.024	a	0.74	rs4390625 (1)	-0.003	3.2E-01	*CRKRS; MED1, NEUROD2*

All SNPs within 10^6 bp of genomewide associations excluded from FDR analysis. ^Best (smallest p-value) SNP from each locus with at least one SNP reaching FDR < 0.05. **eSNPs were selected among those significant for the same trait listed in this table as the one with the highest r2 to the SNP presented in this table. For CKD, the known GATM locus was additionally identified. q-value corresponds to the FDR value of for each locus.

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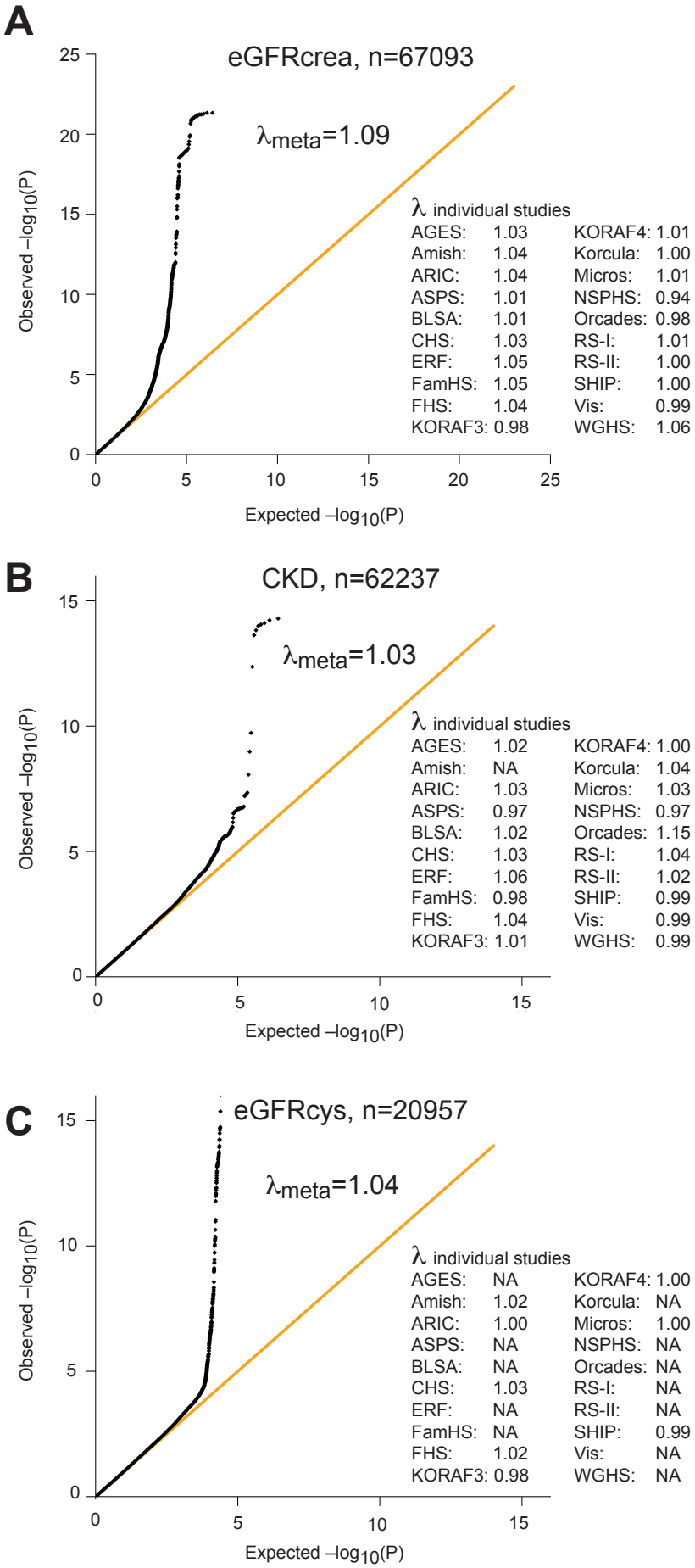
Suppl. Figure 1: Quantile-quantile plots of observed vs. expected -log10(p-values) from discovery analyses of eGFRcrea (A), CKD (B), and eGFRcys (C).

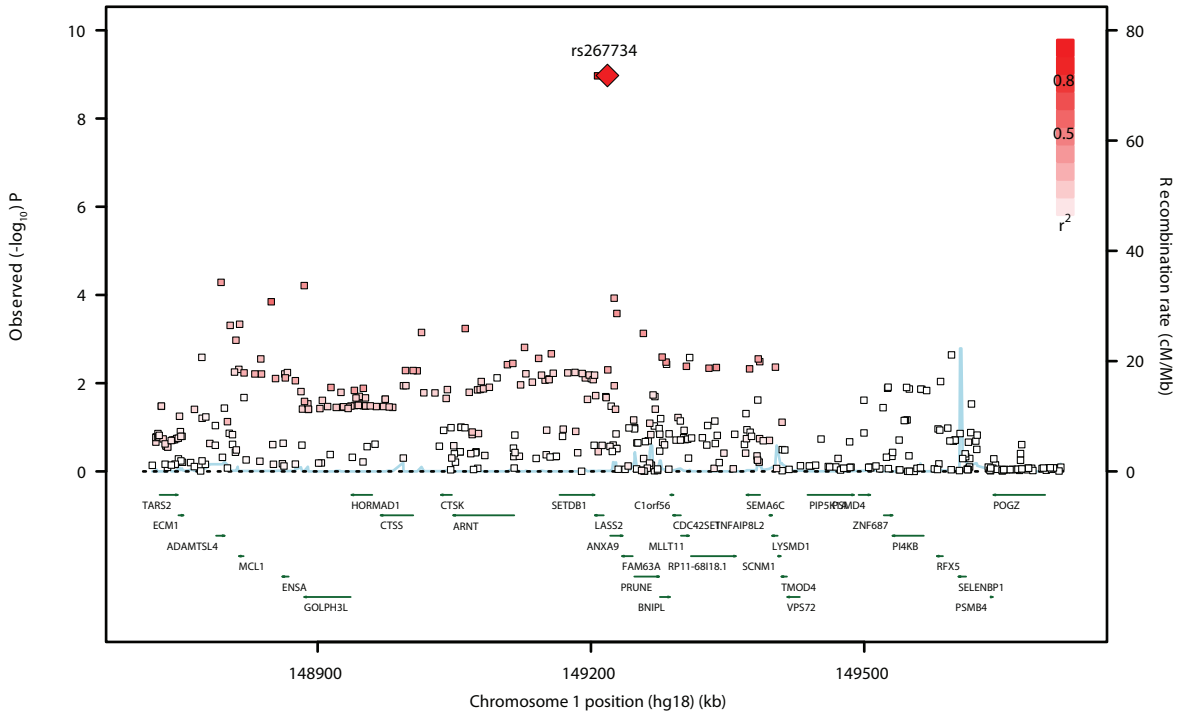


λ_{meta} represents the genomic control parameters after discovery meta-analysis, and the λ for the individuals studies is reported next to each trait. The graphs present p-values corrected for inflation at the study-specific level before meta-analysis as well as after meta-analysis for the meta-analysis genomic control parameter. No correction was applied to data from studies with λ<1.The graph for eGFRcys is cut off; all SNPs with lower p-values are located at the *CST* locus on chromosome 20. NA denotes phenotype unavailability. Black: results from meta-analysis, orange: null hypothesis.

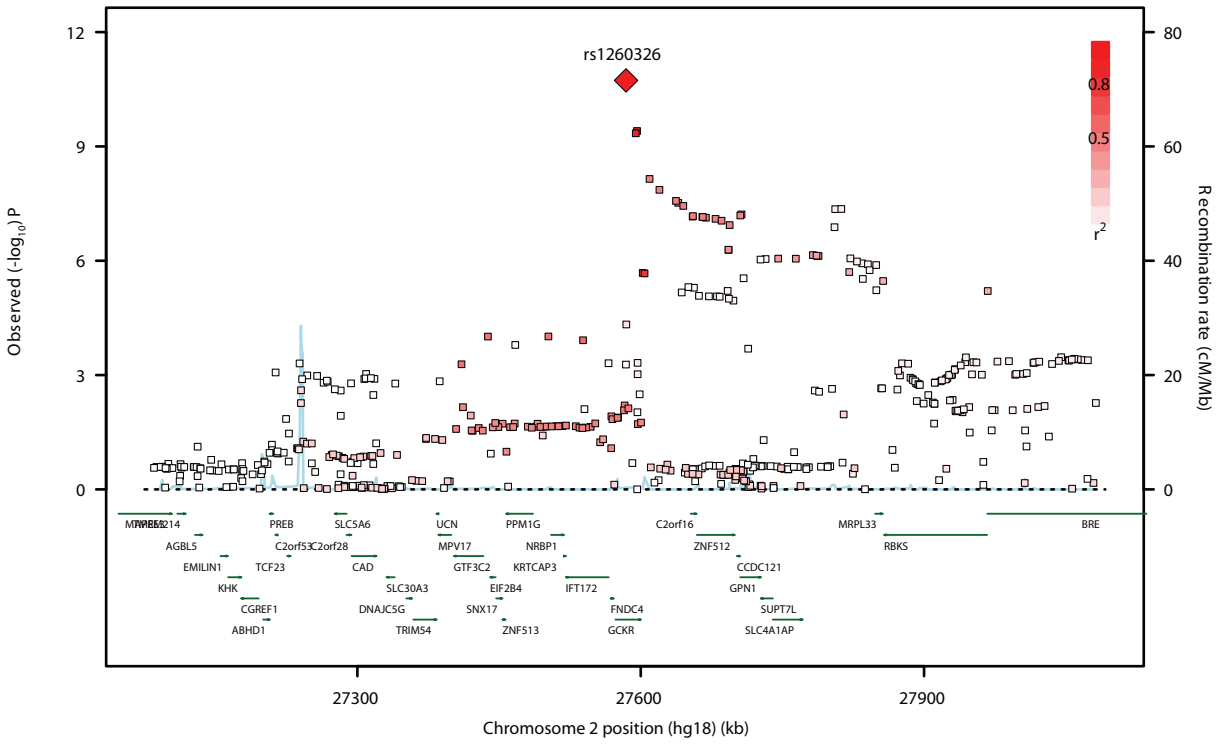
Supplementary Figure 2

Regional Association Plots - Susceptibility Loci for Reduced Renal Function and Chronic Kidney Disease

chromosome 1, rs267734, *LASS2* region

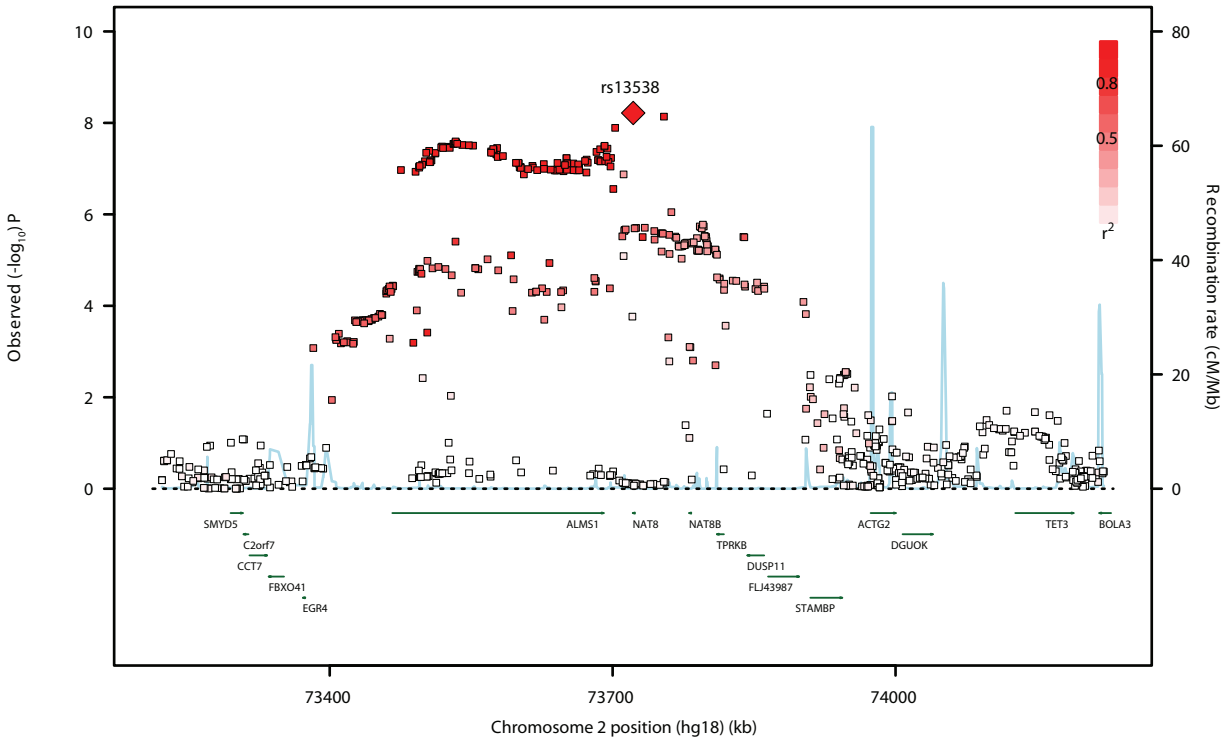


chromosome 2, rs1260326, *GCKR* region

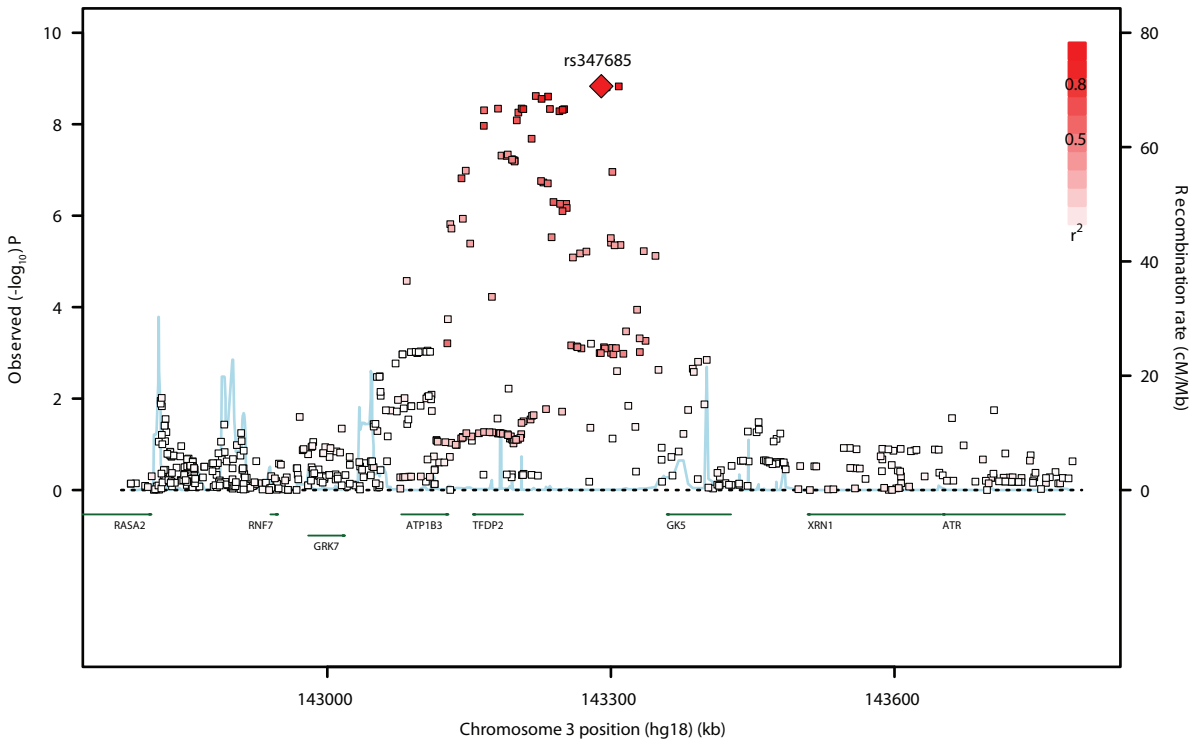


-$\log_{10}$ p-values are plotted versus genomic position (build 36). The lead SNP in each region is labeled. Other SNPs in each region are color-coded based on their LD to the lead SNP (LD based on the HapMap CEU, see color legend). Gene annotations are based on UCSC Genome Browser (RefSeq Genes, b36) and arrows indicate direction of transcription. Graphs were generated using the software SNAP (http://www.broadinstitute.org/mpg/snap/index.php).

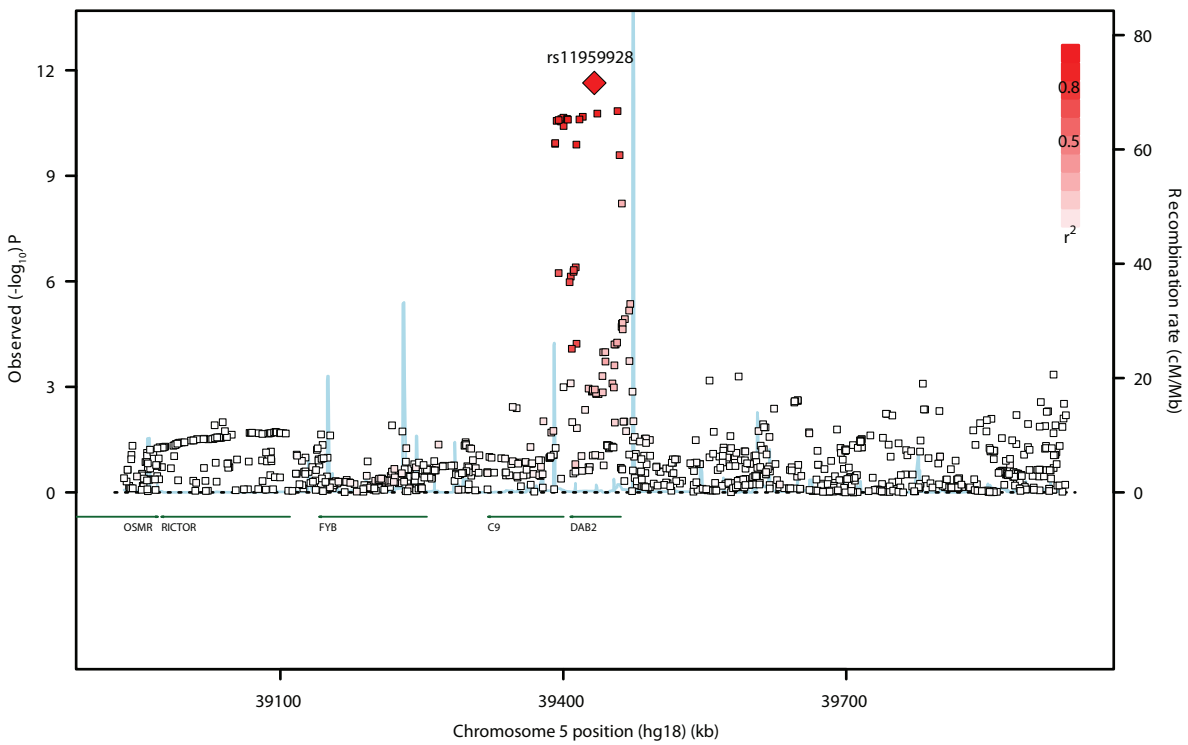
chromosome 2, rs13538, *ALMS1* region



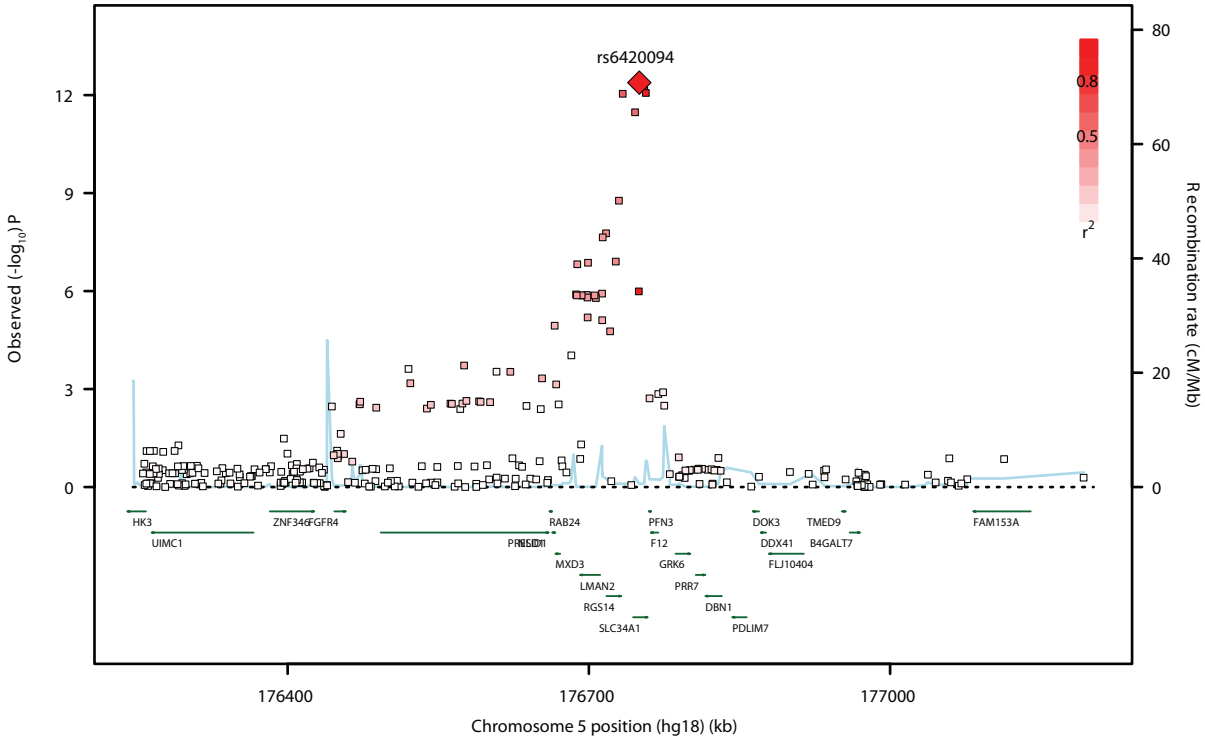
chromosome 3, rs347685, *TFDP2* region



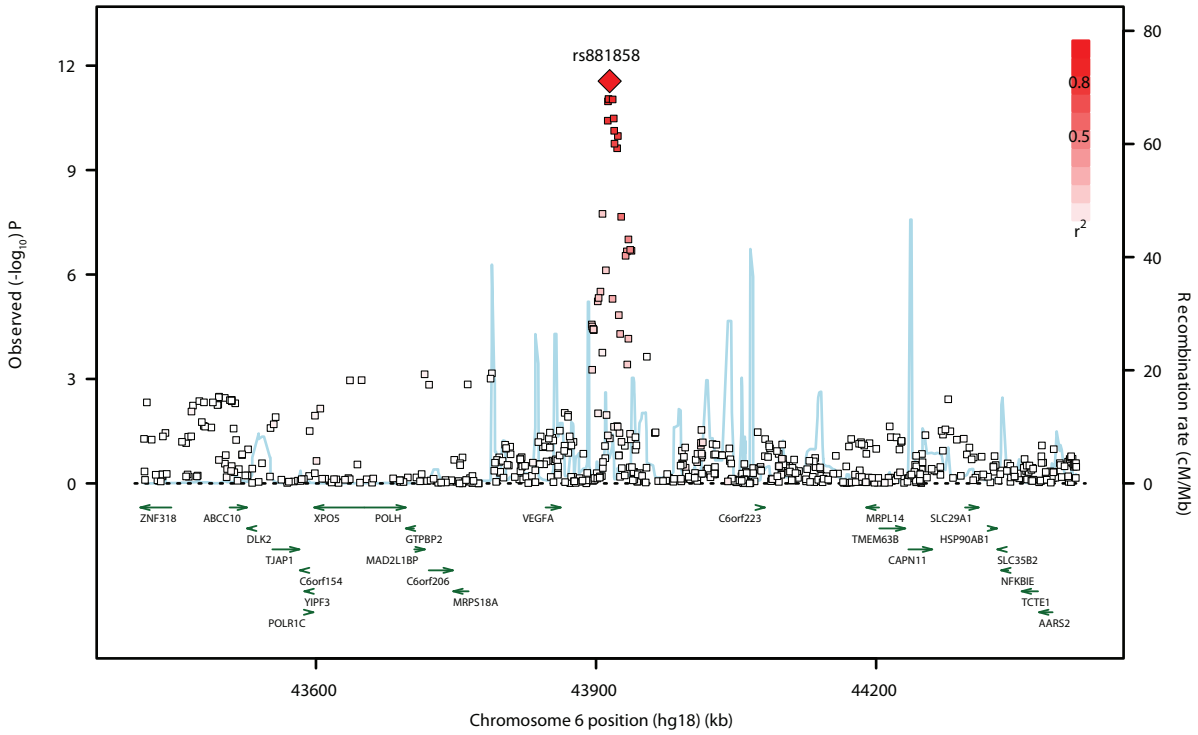
chromosome 5, rs11959928, *DAB2* region



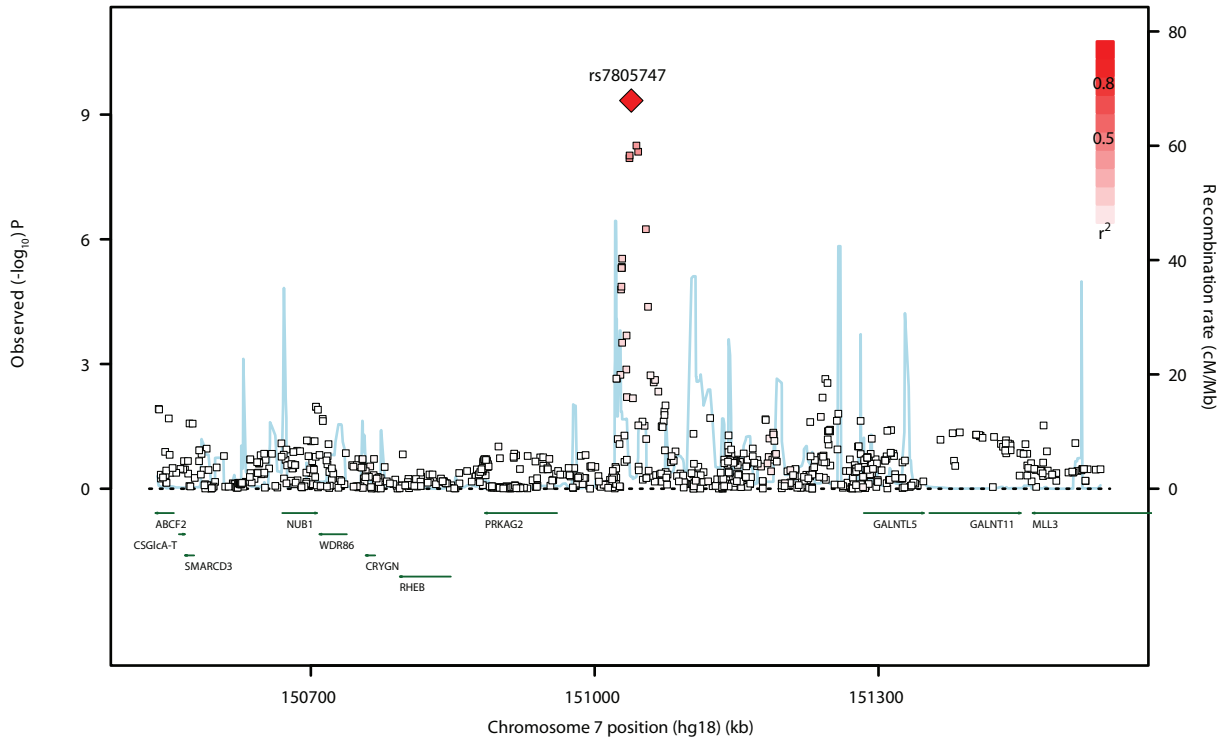
chromosome 5, rs6420094, *SLC34A1* region



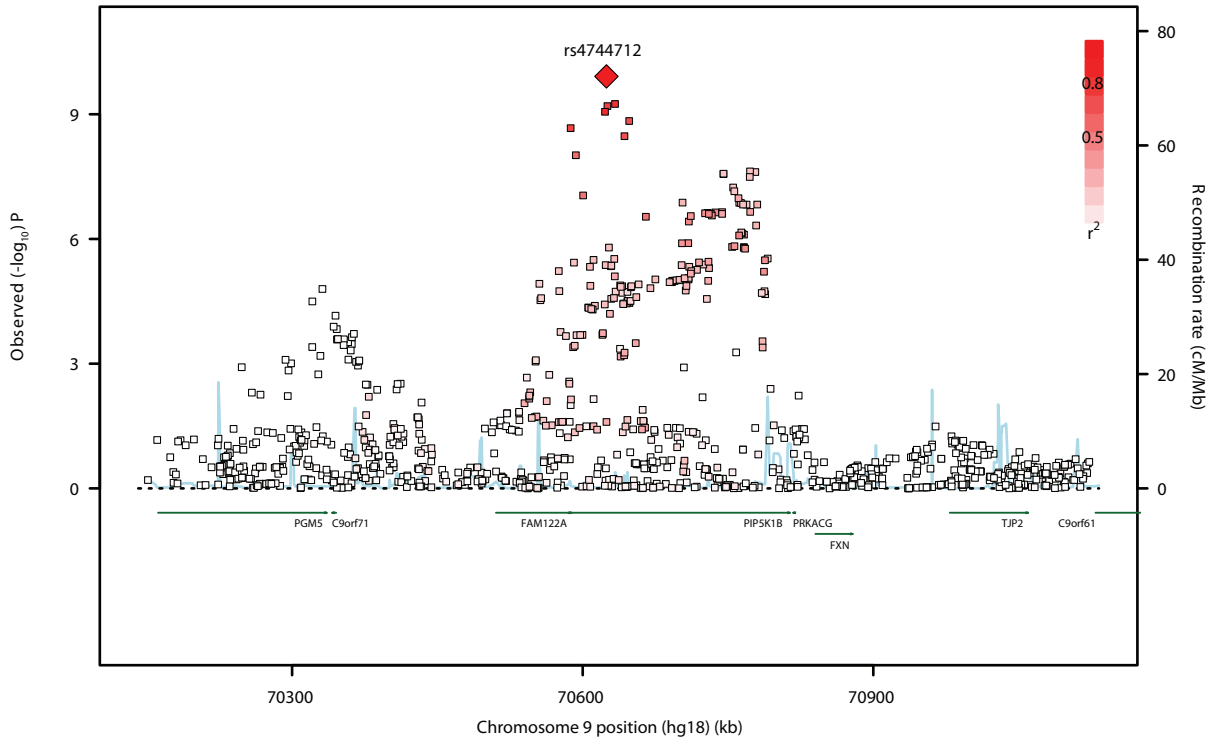
chromosome 6, rs881858, *VEGFA* region



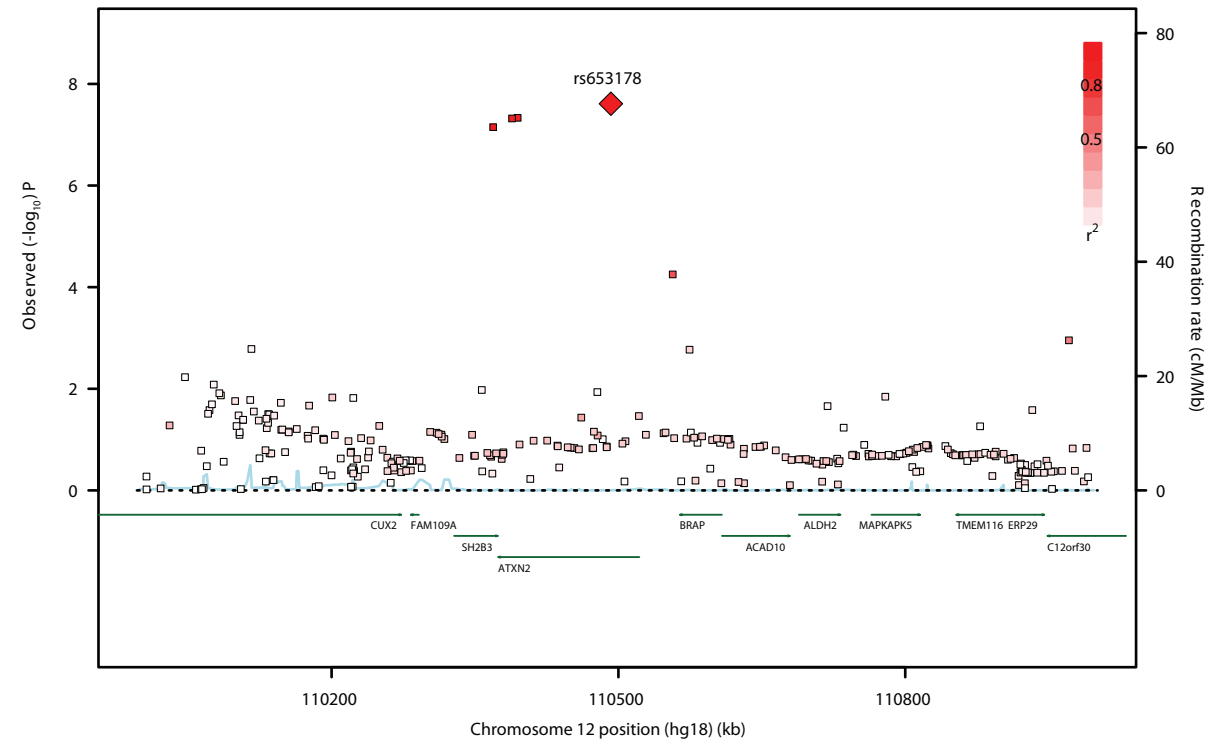
chromosome 7, rs7805747, *PRKAG2* region



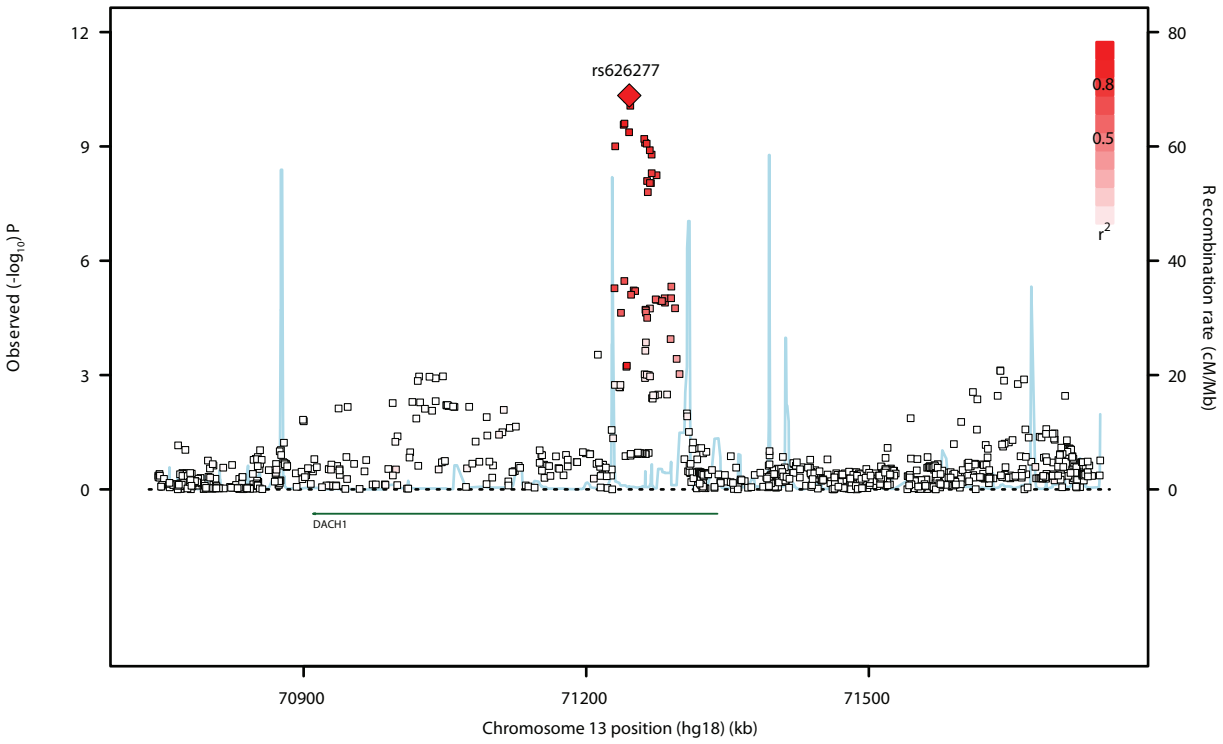
chromosome 9, rs4744712, *PIP5K1B* region



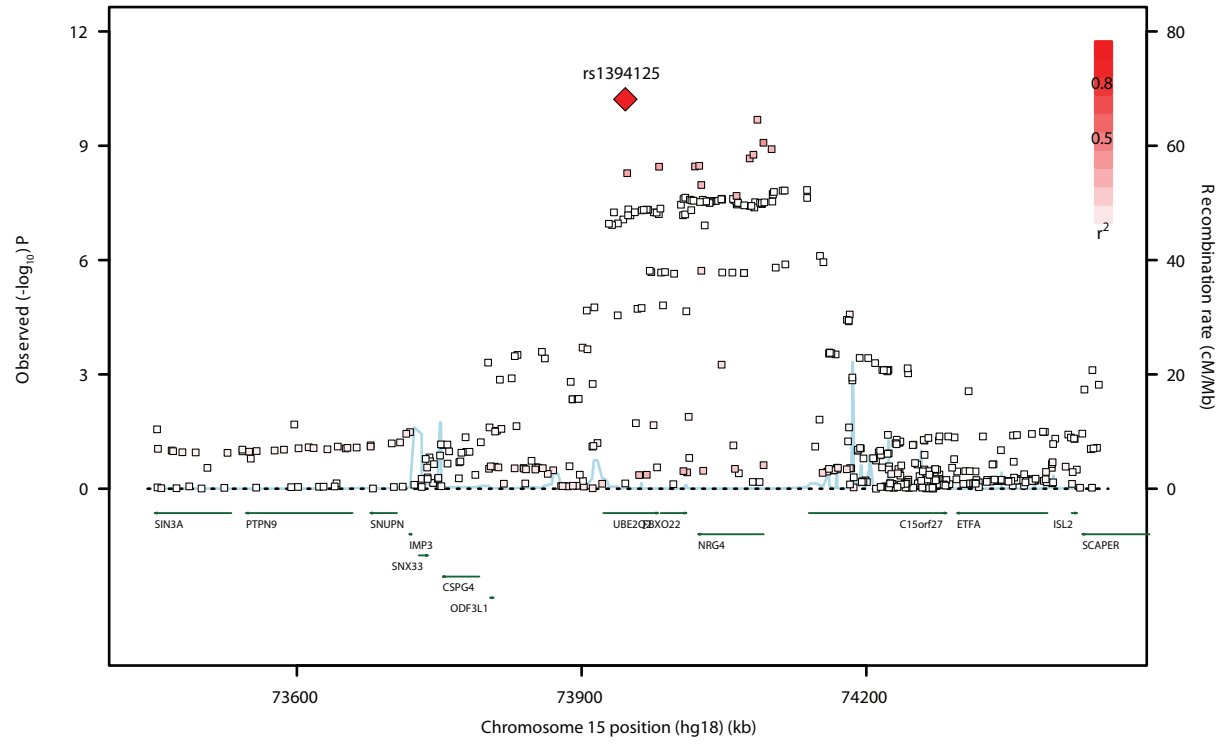
chromosome 12, rs653178, *ATXN2* region



chromosome 13, rs626277, *DACH1* region



chromosome 15, rs1394125, *UBE2Q2* region



chromosome 19, rs12460876, *SLC7A9* region