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Supplemental Appendix 1. Details on the admixture mapping linear and logistic mixed models used for eGFR and CKD analyses.

The admixture mapping for eGFR and CKD were performed using a joint test implemented in the GENESIS R package[1], in which African, European , and Native American ancestries were tested simultaneously. Overall, the analysis consisted of two steps. We first fit a mixed model under the null hypothesis of no genetic association, including random and fixed effects as detailed in the Methods section. The fitted null models are then used to test the association between the local ancestry at each locus and the outcomes. The local ancestry calls were estimated on the phased genotype data as described elsewhere[2]. For Hispanic/Latino populations, it represents the African, European, and Native American allelic dosages (0, 1 or 2 copies of an ancestry-of-origin allele) at each locus.

For eGFR analysis, we used an admixture mapping linear mixed model. The full model is described by:

$$\boldsymbol{y} = \boldsymbol{X\alpha} + \boldsymbol{A_j\beta_j} + \boldsymbol{g} + \boldsymbol{\varepsilon},$$

where $\boldsymbol{y}$ is the vector of eGFR measures for the N individuals, $\boldsymbol{X}$ is the vector of covariates, and $\boldsymbol{\alpha}$ is the vector of fixed covariate effects including an intercept. Letting the third ancestral population be the reference population, $\boldsymbol{A_j}$ represents a $Nx(K-1)$ matrix of the local ancestry allelic dosages at the locus j for the $K-1$ parental populations, with the corresponding effect size vector $\boldsymbol{\beta_j}$ of length $K-1$. We assume that $\boldsymbol{g} \sim N(0, \sigma_a^2\Phi)$ is a vector $\boldsymbol{g} = (g_1, \ldots, g_N)$ of random effects for the N subjects, where σ_a^2 is the additive genetic variance and Φ is the genetic relatedness matrix, and that $\varepsilon \sim N(0, \sigma_e^2 I)$ is a vector $\varepsilon = (\varepsilon_1, \ldots, \varepsilon_N)$ of residual effects, where σ_e^2 represents the residual variance and I is an identity matrix. The average Information Restricted

Maximum Likelihood (AI-REML) approach was used to estimate the variance components σ_a^2 e σ_e^2 under the null model. The null hypothesis that $\boldsymbol{\beta_j} = \mathbf{0}$ was assessed via multivariate score test.

The admixture mapping linear mixed model was extended to analyze binary phenotypes, such as CKD, using an implementation that applies a penalized quasi-likelihood approximation to the generalized linear mixed model to fit the null model[3]. The full admixture logistic mixed model is described by:

$$logit(\pi) = \boldsymbol{X\alpha} + \boldsymbol{A_j\beta_j} + \boldsymbol{g},$$

where $\pi = P(y = 1|\boldsymbol{X}, \boldsymbol{A_j}, \boldsymbol{g})$ represents the $Nx1$ column vector of probabilities of being affected for the N individuals conditional to covariates, local ancestry calls and random effects. $\boldsymbol{X}$, $\boldsymbol{\alpha}$, $\boldsymbol{A_j}$, $\boldsymbol{\beta_j}$ and $\boldsymbol{g}$ are defined as above. As for the eGFR analysis, we used a multivariate score test to assess the null hypothesis that $\boldsymbol{\beta_j} = \mathbf{0}$.

We also conducted secondary single ancestry admixture mapping analyses to identify which ancestry population was driving the signal in each associated locus. Here, we tested each ancestry against the others to assess the effect of each ancestry separately. The local ancestry allelic dosages of the reference population (European, for example) is included as a predictor in the model and compared to the non-reference group (African + Native American in the example).

REFERENCES

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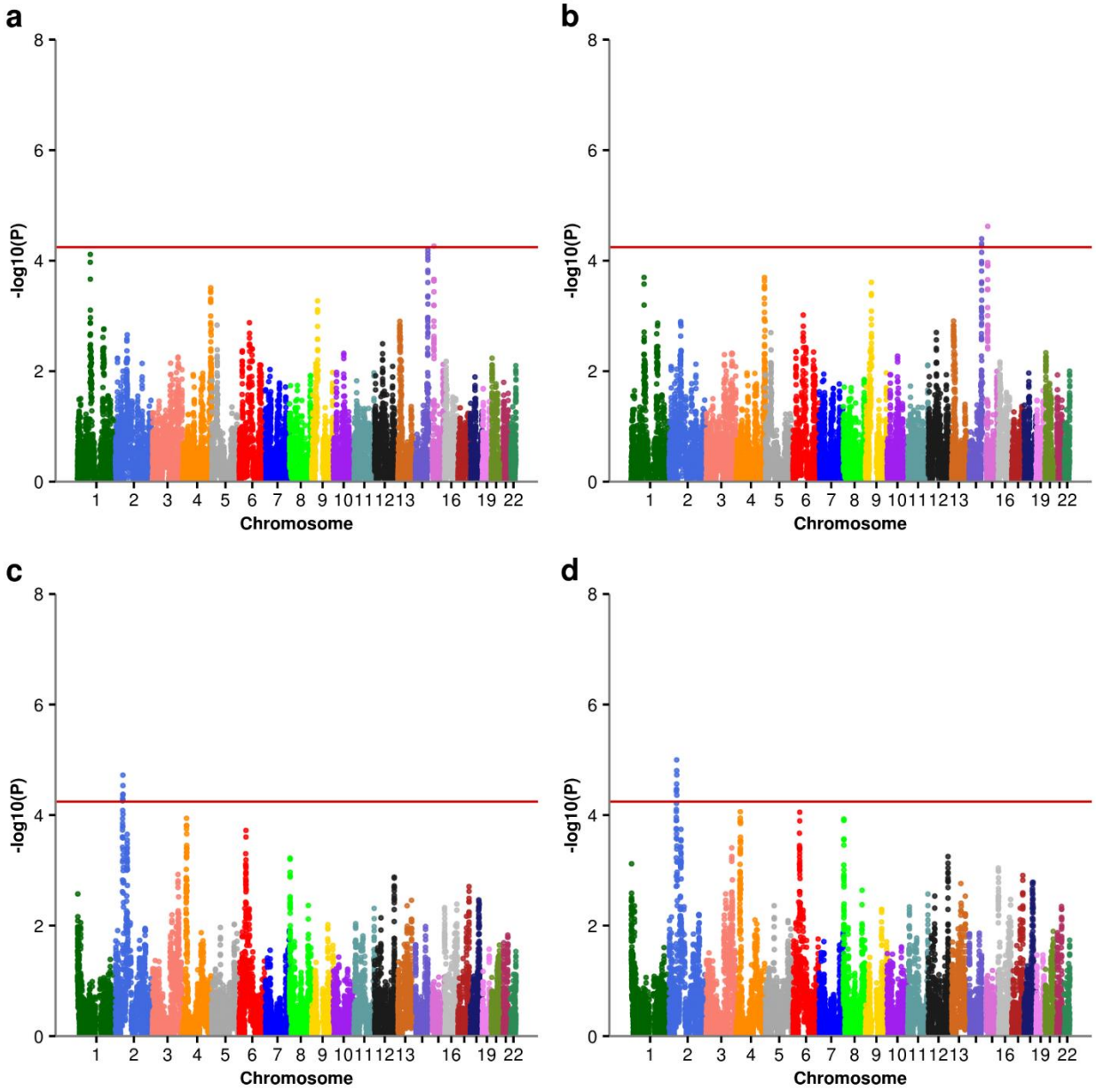
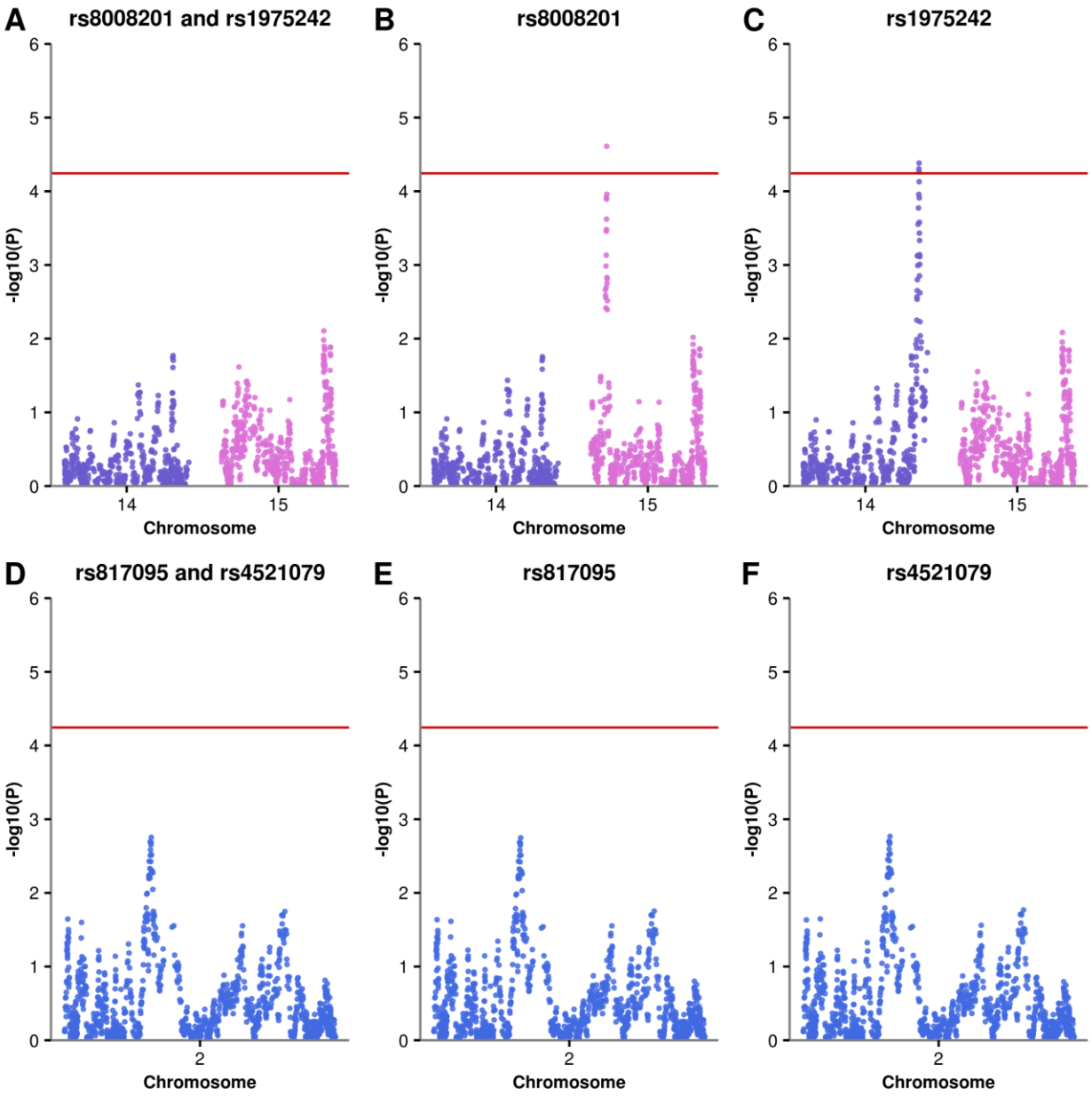
2. Browning SR, Grinde K, Plantinga A, Gogarten SM, Stilp AM, Kaplan RC, Avilés-Santa ML, Browning BL, Laurie CC: Local ancestry inference in a large US-based Hispanic/Latino study: Hispanic community health study/study of Latinos (HCHS/SOL). *G3 Genes, Genomes, Genet.* 6: 1525–1534, 2016
3. Chen H, Wang C, Conomos MP, Stilp AM, Li Z, Sofer T, Szpiro AA, Chen W, Brehm JM,

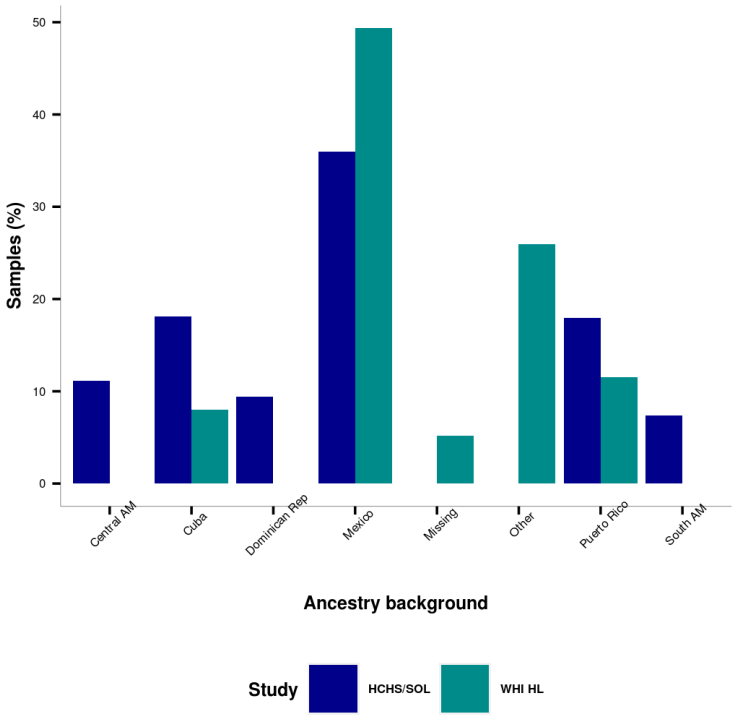
Celedón JC, Redline S, Papanicolaou GJ, Thornton TA, Laurie CC, Rice K, Lin X: Control for Population Structure and Relatedness for Binary Traits in Genetic Association Studies via Logistic Mixed Models. *Am. J. Hum. Genet.* [Internet] 98: 653–666, 2016 Available from: http://www.ncbi.nlm.nih.gov/pubmed/27018471 [cited 2020 Feb 13].



Supplemental Figure 1. Admixture mapping for eGFR and CKD including diabetes and hypertension as covariates. (a) eGFR analysis adjusted for diabetes; (b) eGFR analysis adjusted for hypertension; (c) CKD analysis adjusted for diabetes; (d) CKD analysis adjusted for hypertension.



Supplemental Figure 2. **Conditional admixture mapping analyses for eGFR and CKD including the lead SNP of each locus as covariate.** eGFR: (**A**) both SNPs from chromosomes 14 (rs8008201) and 15 (rs1975242) loci; (**B**) SNP from chromosome 14 locus (rs8008201); (**C**) SNP from chromosome 15 locus (rs1975242). CKD: (**D**) SNPs from both loci on chromosome 2 (rs817095 and rs4521079); (**E**) SNP rs817095 from the first locus; (**F**) SNP rs4521079 from the second locus. Note that adjusting for SNPs within chromosome 14 does not reduce the signal for chromosome 15, and vice-versa as seen in **B** and **C**.



Supplemental Figure 3. **Ancestry background of HCHS/SOL and WHI HL samples.** Central AM: Central America; Dominican Rep: Dominican Republic; South AM: South America. Other represents the ancestry backgrounds other than Cuban, Mexican or Puerto Rican.

Supplemental Table 1. Annotation of the SNPs within ancestry-of-origin loci associated with eGFR and CKD.

SNP	Chr	Phypos	Ref	Alt	AFR.f	EUR.f	NAM.f	Gene / Symbol	Feature type	Consequence	CADD	Epigenetic elements
rs817095	2	49571948	G	A	0.93	0.80	0.85	---	---	intergenic	0.55	Quies, H3K4me1, H3K9me3, H3K27me3
rs860133	2	49578937	T	G	0.50	0.18	0.33	---	---	intergenic	11.33	DHS, Quies
rs860994	2	49580566	G	A	0.05	0.09	0.04	---	---	intergenic	5.36	Quies
rs817081	2	49588657	T	G	0.37	0.12	0.12	---	---	intergenic	0.46	Quies
rs7583216	2	49599540	G	A	0.27	0.09	0.23	---	---	intergenic	0.74	Quies
rs2882306	2	49620211	C	T	0.64	0.80	0.88	---	---	intergenic	0.16	Quies
rs817035	2	49623006	C	T	0.29	0.17	0.27	---	---	intergenic	0.66	DHS, Quies, H3K9me3, H3K27me3
rs7580237	2	49623299	G	T	0.04	0.00	0.00	---	---	intergenic	0.17	Quies
rs817038	2	49626781	G	A	0.80	0.90	0.93	---	---	intergenic	0.57	Quies
rs17038697	2	49628461	G	A	0.06	0.00	0.04	---	---	intergenic	0.77	Quies, H3K27me3
rs1882345	2	49630281	T	C	0.56	0.73	0.66	---	---	intergenic	4.36	Quies, H3K4me3
rs817043	2	49630633	T	G	0.13	0.10	0.06	---	regulatory	regulatory	10.03	Quies
rs698840	2	49635681	A	G	0.66	0.83	0.72	---	---	intergenic	5.96	Quies
rs817060	2	49639121	A	G	0.04	0.09	0.04	---	---	intergenic	0.43	Quies
rs10170288	2	49640979	G	A	0.39	0.64	0.39	---	---	intergenic	0.47	Quies
rs1527898	2	49641262	T	G	0.31	0.19	0.19	---	---	intergenic	1.87	Quies
rs11125238	2	49643063	C	A	0.35	0.28	0.37	---	---	intergenic	1.23	Quies
rs11890365	2	49643222	G	A	0.06	0.00	0.01	---	---	intergenic	0.03	Quies

rs17038751	2	49644800	A	G	0.24	0.11	0.13	---	---	intergenic	0.23	Quies, H3K27me3
rs11892442	2	49646196	T	C	0.12	0.00	0.01	---	---	intergenic	6.97	Quies
rs10172488	2	49646785	G	A	0.21	0.22	0.13	---	---	intergenic	8.99	Quies
rs1405959	2	49647212	A	G	0.74	0.50	0.57	---	---	intergenic	15.33	Quies
rs843840	2	49650145	A	G	0.23	0.11	0.07	---	---	intergenic		Quies, H3K27me3
rs12105450	2	49653672	C	T	0.46	0.33	0.27	---	---	intergenic	14.52	Quies
rs1405969	2	49676328	A	G	0.55	0.61	0.57	---	---	intergenic	1.41	Quies
rs10495974	2	49678339	C	T	0.31	0.24	0.40	---	---	intergenic	0.36	Quies, H3K9me3
rs1405955	2	49684567	T	C	0.90	0.97	0.97	---	---	intergenic	0.30	Quies
rs10186177	2	49703199	A	C	0.21	0.46	0.37	---	---	intergenic	6.45	DHS, Quies
rs13427322	2	49707932	G	A	0.07	0.07	0.03	---	---	intergenic	0.25	Quies, H3K9me3
rs11888995	2	49714129	T	C	0.70	0.73	0.76	---	---	intergenic	13.97	Quies, H3K4me3
rs13382313	2	49714846	C	T	0.12	0.37	0.32	---	---	intergenic	1.11	Quies
rs12987465	2	49715021	G	A	0.58	0.36	0.44	---	---	intergenic	4.01	Quies
rs977134	2	49716202	C	T	0.21	0.08	0.22	---	---	intergenic	1.05	Quies, H3K9me3, H3K36me3
rs1405966	2	49716853	A	G	0.78	0.79	0.80	---	---	intergenic	12.65	Quies
rs12996690	2	49724966	T	C	0.19	0.28	0.21	---	---	intergenic	2.16	Quies
rs1405965	2	49737819	A	G	0.79	0.73	0.61	---	---	intergenic	4.72	Quies
rs6545119	2	49739361	C	T	0.77	0.83	0.72	---	---	intergenic	0.16	Quies
rs13422448	2	49743324	A	C	0.01	0.32	0.24	---	---	intergenic	9.60	Quies, H3K9me3
rs6709183	2	49749038	C	T	0.50	0.24	0.40	---	---	intergenic	4.23	Quies
rs4971621	2	49752589	T	C	0.15	0.53	0.48	---	---	intergenic	0.33	Quies
rs17038952	2	49788135	A	C	0.09	0.05	0.03	---	---	intergenic	19.30	Quies

rs1995172	2	49790063	C	T	0.19	0.57	0.46	---	---	intergenic	1.40	Quies
rs17038971	2	49795342	G	A	0.06	0.00	0.01	---	---	intergenic	0.34	Quies, H3K27me3
rs7595953	2	49796689	A	G	0.19	0.05	0.04	---	---	intergenic	2.90	DHS, Quies
rs13429217	2	49808562	C	T	0.21	0.09	0.21	---	---	intergenic	0.46	Quies
rs12469706	2	49811212	T	C	0.01	0.07	0.03	---	---	intergenic	9.88	Quies
rs1593705	2	49816534	G	A	0.29	0.73	0.61	---	---	intergenic	1.30	Quies
rs13399003	2	49819514	G	T	0.20	0.05	0.04	---	---	intergenic	0.29	Quies
rs13401858	2	49825768	G	A	0.01	0.24	0.22	---	regulatory	regulatory	1.91	Quies
rs1553129	2	49825824	C	T	0.09	0.00	0.01	---	---	intergenic	0.81	Quies
rs1498799	2	49829630	A	G	0.03	0.34	0.24	---	---	intergenic	1.66	DHS, Quies
rs2162518	2	49835794	A	C	0.25	0.11	0.23	---	---	intergenic	0.17	Quies
rs17039077	2	49847520	G	A	0.05	0.00	0.01	---	---	intergenic	0.38	DHS, Quies, H3K4me1
rs13423597	2	49849103	A	G	0.11	0.32	0.36	---	---	intergenic	3.07	Quies
rs7577053	2	49849708	T	C	0.62	0.74	0.74	---	---	intergenic	5.24	Quies
rs1391748	2	49850450	C	T	0.15	0.32	0.37	---	---	intergenic	2.83	Quies
rs4527244	2	49855331	T	C	0.92	0.83	0.86	---	---	intergenic	1.64	Quies, H3K9me3
rs976704	2	49856326	C	T	0.76	0.50	0.50	---	---	intergenic	1.83	DHS, Quies
rs13425236	2	49858261	T	C	0.08	0.31	0.35	---	---	intergenic	17.12	Quies
rs11125265	2	49861898	T	C	0.82	0.62	0.54	---	---	intergenic	3.15	Quies, H3K9me3
rs7564547	2	49862134	A	C	0.92	0.90	0.89	---	---	intergenic	1.77	Quies, H3K9me3
rs2350699	2	49871330	G	A	0.07	0.10	0.09	---	---	intergenic	0.19	Quies, H3K9me3
rs17794707	2	49876591	A	C	0.03	0.25	0.16	---	---	intergenic	10.04	Quies
rs12713068	2	49887106	A	G	0.17	0.40	0.44	---	---	intergenic	3.93	Quies
rs6545125	2	49888676	G	A	0.74	0.51	0.47	---	---	intergenic	4.86	Quies

rs10190188	2	49894154	T	C	0.11	0.34	0.24	---	---	intergenic	8.09	Quies
rs4521079	2	49909155	G	A	0.79	0.58	0.73	---	---	intergenic	0.17	Quies, H3K4me1
rs1568287	2	49909547	C	A	0.75	0.18	0.31	---	---	intergenic	1.03	Quies
rs2176603	2	49909670	A	C	0.23	0.07	0.08	---	---	intergenic	6.39	Quies
rs2350701	2	49913955	G	A	0.58	0.46	0.52	---	---	intergenic	9.31	Quies
rs10185615	2	49944565	A	C	0.08	0.40	0.26	---	---	intergenic	12.01	Quies
rs7593733	2	49963077	C	A	0.42	0.75	0.50	---	---	intergenic	11.27	Quies
rs17489439	2	49964349	G	A	0.04	0.34	0.21	---	---	intergenic	8.20	Quies
rs13386956	2	49967574	T	C	0.21	0.00	0.02	---	---	intergenic	3.87	Quies
rs2139156	2	49972394	T	C	0.04	0.44	0.27	---	---	intergenic	4.96	Quies
rs1914782	2	49975135	C	T	0.11	0.34	0.23	---	---	intergenic	11.89	Quies
rs10171772	2	49977093	G	A	0.37	0.44	0.45	---	---	intergenic	2.28	Quies
rs1914779	2	49986278	C	T	0.43	0.08	0.27	---	---	intergenic	1.53	Quies
rs7349353	2	49990017	A	G	0.12	0.32	0.22	---	---	intergenic	1.40	Quies
rs1518823	2	49990368	C	T	0.96	0.89	0.81	---	---	intergenic	0.06	Quies, H3K9me3
rs7595014	2	49992053	A	G	0.62	0.36	0.47	---	---	intergenic	5.38	Quies, H3K9me3
rs870168	2	49997218	G	A	0.88	0.45	0.66	---	---	intergenic	1.43	Quies
rs11903512	2	50005959	T	C	0.19	0.03	0.05	---	---	intergenic	0.71	Quies
rs17039294	2	50009220	A	G	0.04	0.01	0.01	---	---	intergenic	4.74	Quies, H3K4me1
rs17039309	2	50011821	G	A	0.14	0.00	0.01	---	---	intergenic	0.05	Quies
rs17039328	2	50022031	T	C	0.51	0.31	0.26	---	---	intergenic	3.09	Quies
rs7586200	2	50031813	G	A	0.32	0.02	0.04	---	---	intergenic	1.86	Quies
rs1518834	2	50048977	C	A	0.16	0.15	0.10	---	---	intergenic	0.59	Quies
rs885560	2	50055938	A	G	0.02	0.16	0.09	---	---	intergenic	4.68	DHS, Quies, H3K9me3

rs925931	2	50059808	T	C	0.07	0.16	0.10	---	---	intergenic	5.09	Quies
rs12466419	2	50061043	A	G	0.03	0.22	0.28	---	---	intergenic	2.39	Quies
rs1363047	2	50085965	A	G	0.08	0.19	0.12	---	---	intergenic	1.42	Quies
rs1156742	2	50125840	G	A	0.62	0.51	0.56	---	---	intergenic	0.74	Quies
rs1001943	2	50127552	T	C	0.23	0.01	0.04	---	---	intergenic	3.87	Quies, H3K9me3
rs7558063	2	50131767	A	C	0.46	0.12	0.14	---	---	intergenic	1.47	Quies
rs971732	2	50142117	A	C	0.41	0.37	0.42	NRXN1	transcript	downstream	1.54	DHS, Quies
rs1045881	2	50148972	C	T	0.12	0.16	0.10	NRXN1 NRXN1 NRXN1	transcript transcript transcript	3 prime UTR downstream non-coding exon	17.00	Quies
rs17039448	2	50149510	A	G	0.22	0.19	0.30	NRXN1 NRXN1	transcript transcript	intron non-coding	2.84	Quies
rs1421594	2	50176965	G	A	0.48	0.38	0.43	NRXN1 NRXN1	transcript transcript regulatory	intron non-coding regulatory	2.00	Quies, H3K9me3
rs2193870	2	50179975	C	T	0.01	0.24	0.20	NRXN1 NRXN1	transcript transcript	intron non-coding	11.285	Quies
rs17491881	2	50188135	T	C	0.10	0.19	0.12	NRXN1 NRXN1	transcript transcript	intron non-coding	3.90	Quies
rs17439140	2	50195048	C	T	0.13	0.34	0.38	NRXN1 NRXN1	transcript transcript	intron non-coding	4.49	Quies
rs11125280	2	50197075	C	T	0.52	0.28	0.40	NRXN1 NRXN1	transcript transcript	intron non-coding	1.30	DHS, Quies
rs8008201	14	101329926	G	A	0.09	0.23	0.12	MEG3	transcript	downstream	0.27	Quies, H3K36me3

								RP11-123M6.2	transcript	upstream		
rs8021312	14	101333646	T	C	0.32	0.25	0.20	MIR493	transcript	upstream	1.45	Quies
rs11851174	14	101345504	C	T	0.37	0.21	0.16	MIR337 RTL1 MIR665 MIR433 MIR127 MIR431	transcript transcript transcript transcript transcript transcript	downstream downstream downstream upstream upstream upstream	6.33	Quies
rs3825569	14	101350298	T	C	0.61	0.64	0.43	MIR433 MIR127 MIR431 MIR136 MIR432 RTL1	transcript transcript transcript transcript transcript transcript	downstream downstream downstream upstream upstream synonymous	1.40	Quies, H3K36me3
rs1975242	15	33801207	G	A	0.67	0.49	0.32	RYR3	transcript	intron	0.44	DHS, Quies, H3K27me3
rs7165389	15	33801946	T	C	0.21	0.13	0.09	RYR3	transcript	intron	4.62	DHS, Quies, H3K4me1, H3K27me3
rs2596211	15	33804910	T	G	0.98	0.66	0.55	RYR3	transcript	intron	5.28	Quies, H3K27me3
rs11632989	15	33806622	C	T	0.00	0.11	0.07	RYR3	transcript	intron	0.63	Quies
rs6495130	15	33810168	G	A	0.44	0.33	0.20	RYR3	transcript	intron	0.09	Quies
rs735545	15	33811083	T	G	0.57	0.46	0.29	RYR3	transcript regulatory	intron regulatory	3.07	DHS, Quies, H3K4me1
rs4281677	15	33816995	C	T	0.47	0.12	0.12	RYR3	transcript	intron	15.13	Quies

rs2596220	15	33818190	G	A	0.41	0.36	0.52	RYR3	transcript	intron	5.38	Quies
rs2572203	15	33818341	C	T	0.92	0.85	0.86	RYR3	transcript	intron	0.51	Quies
rs12909478	15	33829250	C	T	0.09	0.20	0.11	RYR3	transcript	intron	0.60	Quies, H3K27me3
rs957467	15	33830326	T	C	0.44	0.71	0.73	RYR3	transcript	intron	8.20	Quies, H3K27me3
rs6495164	15	33838470	C	T	0.11	0.17	0.33	RYR3	transcript	intron	4.10	Quies, H3K27me3
rs1435102	15	33839194	A	G	0.46	0.82	0.80	RYR3	transcript	intron	5.98	Quies
rs7163719	15	33841956	T	C	0.28	0.01	0.02	RYR3	transcript	intron	7.79	Quies, H3K4me3, H3K9me3
rs1865495	15	33847805	T	C	0.26	0.53	0.62	RYR3	transcript	intron	8.84	Quies
rs9744361	15	33857949	C	A	0.55	0.12	0.12	RYR3	transcript	intron	7.08	Quies, H3K9me3, H3K27me3
rs1435118	15	33865455	G	A	0.34	0.74	0.73	RYR3	transcript	intron	6.40	Quies
rs8041171	15	33866510	C	A	0.14	0.03	0.04	RYR3	transcript	intron	0.76	Quies
rs680851	15	33866632	T	C	0.34	0.74	0.73	RYR3	transcript	intron	4.18	Quies
rs674155	15	33872177	C	T	0.40	0.77	0.76	RYR3	transcript	missense splice synonymous	14.02	Quies
rs683484	15	33872692	G	A	0.40	0.77	0.76	RYR3	transcript regulatory	intron regulatory	4.17	Quies
rs581954	15	33873369	A	C	0.13	0.14	0.12	RYR3	transcript regulatory	intron regulatory	15.66	DHS, Quies
rs668570	15	33873657	C	T	0.87	0.81	0.61	RYR3	transcript regulatory	intron regulatory	1.69	Quies
rs2077268	15	33873751	G	A	0.36	0.11	0.07	RYR3	transcript	missense variant	16.97	Quies

									regulatory	regulatory		
rs748298	15	33873901	C	T	0.41	0.07	0.10	RYR3	transcript regulatory	intron regulatory	0.32	Quies
rs3794586	15	33875264	G	T	0.07	0.12	0.24	RYR3	transcript	intron	7.83	Quies
rs10431811	15	33876449	G	A	0.34	0.46	0.44	RYR3	transcript	intron	4.42	Quies
rs2643364	15	33876517	A	G	0.88	0.75	0.65	RYR3	transcript	intron	5.08	Quies
rs659517	15	33877066	G	T	0.31	0.10	0.25	RYR3	transcript regulatory	intron regulatory	1.42	Quies
rs2643363	15	33877938	A	G	0.21	0.23	0.13	RYR3	transcript	intron	1.28	Quies
rs16972835	15	33878846	C	A	0.12	0.10	0.08	RYR3	transcript	intron	2.49	Quies, H3K27me3
rs16972837	15	33879387	G	A	0.19	0.10	0.21	RYR3	transcript	intron	12.00	Quies, H3K27me3
rs10153042	15	33879608	A	G	0.53	0.38	0.28	RYR3	transcript	intron	2.26	Quies
rs671122	15	33879678	C	T	0.84	0.64	0.57	RYR3	transcript	intron	1.16	Quies
rs658750	15	33880181	G	A	0.65	0.54	0.36	RYR3	transcript	intron	1.89	Quies, H3K9me3
rs688939	15	33880493	A	G	0.04	0.13	0.06	RYR3	transcript	intron	6.36	Quies, H3K9me3
rs640152	15	33884488	A	G	0.84	0.64	0.58	RYR3	transcript regulatory	intron regulatory	3.70	Quies, H3K27me3

Chr: chromosome; Phypos: physical position in build GRCh37/hg19; Ref: reference allele (forward strand); Alt: alternative allele (forward strand); AFR.f: alternative allele frequency in African populations; EUR.f: alternative allele frequency in European populations; NAM.f: alternative allele frequency in Native American populations. Both reference allele and population-specific reference allele frequency were obtained from 1000 Genomes Project phase 3 using Ensembl (https://uswest.ensembl.org/index.html); Gene/Symbol, Feature type and Consequence were obtained using the Ensembl Variant Effect Predictor tool (https://uswest.ensembl.org/info/docs/tools/vep/index.html); CADD: scaled C-score for deleteriousness; Epigenetic elements: functional elements (DNase I hypersensitive sites [DHSs], histone mark chromatin immunoprecipitation [ChIP] broadpeaks, and hidden Markov model chromatin states) observed in fetal kidney tissue overlapping the SNPs were obtained using the Forge2 analysis tool (https://forge2.altiusinstitute.org/); Quies: quiescent state chromatin.