

Supplementary Table 1. Forty-four AMPK variants associated with HbA1c in the MAGIC, restricted to participants of European descent

SNP	EA	NEA	Beta (%)	SE	P_{MAGIC}	$P_{\text{UK Biobank}}$
rs10230736	G	A	-0.0110	0.0038	4.44E-03	4.13E-04
rs10259821	A	G	-0.0037	0.0019	4.71E-02	1.20E-03
rs10492081	A	G	-0.0071	0.0024	2.87E-03	9.20E-21
rs1050187	C	T	-0.0042	0.0019	2.42E-02	1.71E-03
rs10783277	C	T	-0.0045	0.0019	1.58E-02	4.35E-05
rs10875764	C	T	-0.0077	0.0038	4.45E-02	1.32E-13
rs10875801	C	T	-0.0089	0.0023	9.35E-05	5.95E-30
rs10875814	G	A	-0.0051	0.0024	3.22E-02	1.34E-09
rs10875843	A	G	-0.0093	0.0045	3.67E-02	4.79E-08
rs11168355	G	A	-0.0055	0.0022	1.14E-02	2.63E-43
rs11168359	A	G	-0.0150	0.0032	1.61E-06	6.94E-91
rs11168547	T	C	-0.0079	0.0026	2.28E-03	1.06E-26
rs11168643	A	G	-0.0180	0.0061	2.89E-03	3.84E-08
rs11239944	A	G	-0.0180	0.0061	3.05E-03	1.88E-04
rs11884246	A	C	-0.0033	0.0017	4.64E-02	2.61E-02
rs12297820	A	G	-0.0170	0.0029	1.26E-08	1.09E-43
rs12322783	A	G	-0.0045	0.0023	4.82E-02	1.80E-08
rs12582586	T	C	-0.0050	0.0024	3.58E-02	1.92E-04
rs12582811	G	T	-0.0089	0.0033	7.23E-03	1.96E-06
rs12830014	G	A	-0.0074	0.0037	4.71E-02	8.62E-04
rs1365964	G	A	-0.0057	0.0029	4.93E-02	6.91E-03
rs1489107	A	G	-0.0140	0.0058	1.73E-02	2.16E-22
rs1563636	C	T	-0.0057	0.0025	2.18E-02	1.94E-03
rs1635527	C	G	-0.0038	0.0019	4.15E-02	4.35E-36
rs16858808	A	G	-0.0250	0.0120	3.22E-02	2.36E-03
rs17197593	T	C	-0.0140	0.0062	2.23E-02	5.50E-05
rs17572109	A	G	-0.0055	0.0020	5.18E-03	1.54E-05
rs17614932	A	C	-0.0120	0.0051	1.45E-02	2.70E-11
rs17834622	A	G	-0.0064	0.0019	5.95E-04	1.10E-17
rs1808593	T	G	-0.0049	0.0024	3.96E-02	3.83E-03
rs1859443	G	A	-0.0058	0.0025	1.96E-02	6.27E-13
rs1859444	C	T	-0.0048	0.0024	4.39E-02	1.42E-22
rs2059409	T	C	-0.0110	0.0047	2.17E-02	1.16E-02
rs2732480	A	C	-0.0120	0.0020	2.00E-09	1.07E-142
rs2932091	A	C	-0.0043	0.0021	3.79E-02	1.25E-03
rs3816560	C	T	-0.0040	0.0019	3.19E-02	2.07E-05
rs4760702	A	T	-0.0110	0.0048	1.98E-02	1.16E-09
rs6726126	A	G	-0.0038	0.0018	3.09E-02	3.38E-07
rs7134565	C	T	-0.0035	0.0018	4.68E-02	3.79E-37
rs7596500	G	T	-0.0160	0.0074	3.16E-02	8.87E-03
rs7780461	T	C	-0.0063	0.0032	4.97E-02	1.16E-02
rs7806203	C	T	-0.0039	0.0020	4.74E-02	6.75E-03
rs7959684	A	G	-0.0050	0.0021	1.58E-02	1.30E-50
rs7975821	A	G	-0.0041	0.0021	4.77E-02	2.81E-07

AMPK, AMP-activated protein kinase; MAGIC, Meta-Analyses of Glucose and Insulin-Related Traits Consortium; SNP, single nucleotide polymorphism; EA, effect allele; NEA, non-effect allele; SE, standard error.

Supplementary Table 2. Ninety-nine variants associated with HbA1c in the MAGIC, restricted to participants of European descent

SNP	EA	NEA	Beta (%)	SE	P
rs10151436	A	T	0.0130	0.0021	3.85E-11
rs10169706	T	C	0.0260	0.0046	1.48E-08
rs10231021	A	T	0.0089	0.0013	8.69E-14
rs10405535	A	G	0.0122	0.0016	6.47E-14
rs10419234	T	C	-0.0224	0.0038	1.47E-09
rs10774624	A	G	0.0093	0.0013	4.17E-14
rs10811661	T	C	0.0128	0.0017	1.74E-14
rs10830963	C	G	-0.0197	0.0015	1.54E-36
rs10998752	A	G	0.0125	0.0017	1.32E-14
rs11039154	T	C	-0.0087	0.0014	3.11E-09
rs11224314	A	G	-0.0152	0.0022	1.61E-13
rs11248914	T	C	0.0114	0.0014	1.42E-14
rs11257655	T	C	0.0110	0.0016	1.91E-13
rs112578089	A	G	-0.0360	0.0061	2.18E-11
rs112601576	T	C	0.0089	0.0016	2.85E-08
rs11558471	A	G	0.0151	0.0014	3.38E-25
rs11643024	A	G	0.0084	0.0015	7.98E-10
rs11656775	A	G	0.0070	0.0014	2.50E-08
rs11719201	T	C	-0.0129	0.0015	2.43E-18
rs117233107	A	G	-0.0470	0.0072	8.45E-11
rs1175549	A	C	0.0098	0.0015	7.13E-13
rs12491937	A	G	0.0090	0.0013	1.42E-13
rs12612492	T	C	0.0188	0.0019	1.88E-26
rs1278769	A	G	-0.0091	0.0015	5.52E-12
rs13089972	A	T	0.0111	0.0014	1.87E-15
rs13134327	A	G	0.0144	0.0014	2.81E-26
rs13234131	A	G	-0.0113	0.0020	2.06E-09
rs13389076	A	G	0.0332	0.0038	3.04E-18
rs13419763	T	C	0.0080	0.0014	5.48E-09
rs1367173	T	C	-0.0152	0.0020	1.66E-14
rs138374952	A	G	-0.0251	0.0045	3.32E-08
rs138917529	A	T	0.0377	0.0057	9.50E-11
rs145353824	A	C	-0.0381	0.0068	2.36E-09
rs1535464	A	G	-0.0086	0.0017	1.11E-08
rs16926246	T	C	-0.0727	0.0021	1.02E-268
rs17037289	A	G	-0.0089	0.0015	2.40E-09
rs174559	A	G	-0.0106	0.0014	3.31E-13
rs17533945	T	C	-0.0128	0.0014	1.62E-23
rs1799945	C	G	0.0245	0.0018	3.32E-47
rs1800562	A	G	-0.0383	0.0027	2.33E-50
rs192471087	C	G	0.0107	0.0019	1.37E-10
rs1948759	A	NEA	-0.0097	0.0017	2.44E-08
rs2273475	A	G	-0.0128	0.0023	1.99E-09
rs2375278	A	G	0.0112	0.0017	1.05E-11
rs247833	A	G	0.0085	0.0017	2.85E-08
rs267738	T	G	0.0109	0.0016	1.14E-11

Supplementary Table 2. Continued

SNP	EA	NEA	Beta (%)	SE	P
rs2748427	A	G	-0.0307	0.0022	9.82E-49
rs28671200	T	G	0.0086	0.0017	1.56E-08
rs2908277	A	G	0.0166	0.0020	1.29E-18
rs2954021	A	G	-0.0070	0.0012	1.92E-10
rs2971670	T	C	0.0316	0.0017	5.10E-88
rs340882	C	G	-0.0084	0.0013	1.48E-10
rs34664882	A	G	-0.0485	0.0040	4.82E-37
rs360140	A	C	-0.0084	0.0013	9.62E-13
rs3778321	A	G	-0.0106	0.0016	4.18E-11
rs3829109	A	G	-0.0086	0.0015	2.68E-08
rs3842753	T	G	0.0075	0.0016	3.93E-08
rs4076213	A	G	-0.0127	0.0016	3.54E-16
rs452306	T	C	-0.0098	0.0014	5.51E-13
rs453922	T	C	-0.0126	0.0021	1.36E-08
rs4727979	A	C	0.0121	0.0024	4.61E-08
rs4737009	A	G	0.0228	0.0015	8.29E-56
rs4760682	A	C	0.0164	0.0018	3.20E-20
rs4894769	A	T	-0.0073	0.0013	3.61E-09
rs4980325	T	G	0.0108	0.0014	4.70E-14
rs560887	T	C	-0.0307	0.0014	5.55E-122
rs608793	T	C	0.0065	0.0013	4.55E-08
rs61750929	T	C	-0.0284	0.0029	9.49E-24
rs62079722	A	C	0.0112	0.0018	1.91E-11
rs62175726	T	C	-0.0218	0.0036	1.29E-10
rs6445541	T	G	0.0077	0.0014	1.14E-08
rs651007	T	C	0.0108	0.0015	3.28E-15
rs6804915	A	C	-0.0108	0.0014	2.76E-16
rs6877043	T	C	0.0085	0.0014	1.99E-10
rs6931514	A	G	-0.0102	0.0014	1.18E-13
rs6980507	A	G	0.0109	0.0013	8.15E-20
rs7042939	A	G	0.0102	0.0013	1.50E-15
rs7190771	A	G	0.0085	0.0013	6.02E-11
rs7198799	T	C	0.0083	0.0014	4.76E-09
rs72864470	T	C	0.0105	0.0017	1.52E-09
rs7323938	T	C	-0.0098	0.0018	3.39E-10
rs737092	T	C	-0.0073	0.0013	7.57E-09
rs7534795	T	C	0.0100	0.0016	2.13E-09
rs7547793	A	C	-0.0118	0.0021	6.61E-09
rs76533333	A	G	-0.0265	0.0025	2.81E-29
rs76815645	A	G	-0.0131	0.0022	3.40E-09
rs7861647	T	C	0.0128	0.0016	4.50E-14
rs7903146	T	C	0.0133	0.0014	1.04E-22
rs7918272	C	G	-0.0147	0.0015	8.23E-23
rs8138197	A	G	-0.0073	0.0014	3.54E-08
rs837763	T	C	0.0176	0.0013	5.20E-38

Supplementary Table 2. Continued

SNP	EA	NEA	Beta (%)	SE	P
rs855791	A	G	0.0188	0.0013	1.34E-56
rs857725	T	G	-0.0208	0.0014	5.43E-55
rs9299503	A	G	0.0117	0.0023	1.27E-08
rs9376090	T	C	0.0247	0.0014	1.90E-62
rs9604472	C	G	0.0133	0.0023	1.79E-08
rs9818758	A	G	0.0131	0.0017	1.49E-13
rs9909940	T	C	0.0322	0.0014	1.43E-116
rs9914988	A	G	0.0125	0.0016	4.66E-17

MAGIC, Meta-Analyses of Glucose and Insulin-Related Traits Consortium; SNP, single nucleotide polymorphism; EA, effect allele; NEA, non-effect allele; SE, standard error.

Supplementary Table 3. Associations of genetically proxied AMPK activation with functional outcome after ischemic stroke based on the 3-month GWAS results with adjustment for NIHSS

Outcomes	OR (95% CI)	P
Sensitivity analysis (44 SNPs, $r^2 < 0.3$)		
mRS (3–6 vs. 0–2; adjusted NIHSS)		
IVW (P for Cochran's Q=0.92)	0.06 (0.01–0.76)	0.029
MR-RAPS	0.04 (0.00–0.93)	0.045
Weighted median	0.08 (0.00–3.61)	0.196
MR-Egger (P for intercept=0.80)	0.04 (0.00–5.29)	0.191
Ordinal mRS (adjusted NIHSS)		
IVW (P for Cochran's Q=0.29)	0.11 (0.02–0.69)	0.018
MR-RAPS	0.10 (0.01–0.91)	0.041
Weighted median	0.07 (0.00–1.08)	0.057
MR-Egger (P for intercept=0.73)	0.20 (0.00–9.62)	0.416
Sensitivity analysis (25 SNPs, $r^2 < 0.1$)		
mRS (3–6 vs. 0–2; adjusted NIHSS)		
IVW (P for Cochran's Q=0.76)	0.06 (0.00–1.14)	0.061
MR-RAPS	0.04 (0.00–1.42)	0.077
Weighted median	0.07 (0.00–6.81)	0.26
MR-Egger (P for intercept=0.61)	0.01 (0.00–5.92)	0.167
Ordinal mRS (adjusted NIHSS)		
IVW (P for Cochran's Q=0.40)	0.10 (0.01–0.91)	0.041
MR-RAPS	0.10 (0.01–1.43)	0.090
Weighted median	0.06 (0.00–1.48)	0.085
MR-Egger (P for intercept=0.67)	0.24 (0.00–23.08)	0.542

AMPK, AMP-activated protein kinase; GWAS, genome-wide association study; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; CI, confidence interval; SNPs, single nucleotide polymorphisms; mRS, modified Rankin Scale score; IVW, inverse-variance weighted; MR-RAPS, Mendelian randomization-robust adjusted profile score.