

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.