

Supplementary Information

| Index | | Page |
|--------------|---|-------------|
| Table S1. | Instrument for measuring corneal curvature. | S2 |
| Table S2. | Most strongly associated marker in each region in the GWAS meta-analysis of all Europeans aged >25 years. | S3 |
| Table S3. | Most strongly associated marker in each region in the GWAS meta-analysis of all Europeans aged <25 years. | S3 |
| Table S4. | Most strongly associated marker in each region in the GWAS meta-analysis of all Asians aged >25 years. | S4 |
| Table S5. | Most strongly associated marker in each region in the GWAS meta-analysis of all Asians aged <25 years. | S4 |
| Table S6. | Top 10 genes from VEGAS2 gene-based association test with ± 50 kb buffers for all Europeans. | S5 |
| Table S7. | Top 10 genes from MAGMA gene-based association test with ± 50 kb buffers for all Europeans. | S6 |
| Figure S1. | Manhattan plots for the separate ancestry/age strata fixed effects meta-analyses. | S7 |
| Figure S2. | Quantile-quantile plots for the separate ancestry/age strata fixed effects meta-analyses. | S8 |

Supplementary Table S1. Instrument for measuring corneal curvature.

| <i>Study</i> | <i>Instrument</i> |
|---------------|----------------------------------|
| ALSPAC | IOLmaster |
| BMES | IOLmaster |
| EPIC | IOLmaster V.4 |
| FITSA | IOLmaster |
| GenerationR | IOLmaster |
| GHS 1 | Lenstar LS 900 |
| GHS 2 | Lenstar LS 900 |
| RAINE | IOLmaster |
| Rotterdam-I | Javal Keratometer/Lenstar LS 900 |
| Rotterdam-II | Javal Keratometer/Lenstar LS 900 |
| Rotterdam-III | Javal Keratometer/Lenstar LS 900 |
| OGP-A | IOLmaster |
| OGP-B | IOLmaster |
| TwinsUK | Visionix VX-120 |
| BES-610K | Lenstar LS 900 |
| BES-OmniE | Lenstar LS 900 |
| SCES-610K | IOLmaster |
| SCES-OmniE | IOLmaster |
| SCORM | Canon RK-5 |
| SIMES | IOLmaster |
| SINDI | IOLmaster |
| STARS | IOLmaster |

Supplementary Table S2. Most strongly associated marker in each region in the GWAS meta-analysis of all Europeans aged >25 years.

EAf = effect allele frequency, OR = odds ratio.

| <i>SNP</i> | <i>Chr</i> | <i>Pos</i> | <i>Effect allele</i> | <i>Other allele</i> | <i>EAf</i> | <i>OR (95%CI)</i> | <i>P-value</i> | <i>Nearest gene</i> |
|-------------|------------|------------|----------------------|---------------------|------------|-------------------|-------------------------|---------------------|
| rs1620100 | 2 | 36179888 | T | C | 0.41 | 0.91 (0.87-0.94) | 1.14 x 10 ⁻⁶ | <i>MRPL50P1</i> |
| rs138222255 | 4 | 113801232 | A | T | 0.89 | 0.82 (0.76-0.89) | 2.52 x 10 ⁻⁶ | <i>ANK2</i> |
| rs73076614 | 12 | 22633729 | T | C | 0.95 | 1.24 (1.13-1.36) | 3.32 x 10 ⁻⁶ | <i>C2CD5</i> |
| rs10187347 | 2 | 227348324 | T | C | 0.47 | 0.91 (0.88-0.95) | 3.58 x 10 ⁻⁶ | <i>MIR5702</i> |
| rs11183146 | 12 | 46024937 | A | G | 0.54 | 0.84 (0.78-0.90) | 3.82 x 10 ⁻⁶ | <i>LINC00938</i> |
| rs4804959 | 19 | 31803331 | T | C | 0.61 | 1.12 (1.07-1.17) | 3.95 x 10 ⁻⁶ | <i>TSHZ3</i> |
| rs9393856 | 6 | 27767825 | T | G | 0.08 | 0.82 (0.75-0.89) | 4.37 x 10 ⁻⁶ | <i>TRNAQ10</i> |
| rs2184695 | 10 | 89890390 | A | C | 0.53 | 0.91 (0.87-0.95) | 4.66 x 10 ⁻⁶ | <i>MED6P1</i> |
| rs35587414 | 1 | 153174958 | T | C | 0.15 | 1.15 (1.08-1.23) | 4.84 x 10 ⁻⁶ | <i>LELP1</i> |
| rs5806282 | 13 | 102849565 | I | R | 0.75 | 1.12 (1.07-1.17) | 5.41 x 10 ⁻⁶ | <i>FGF14</i> |

Supplementary Table S3. Most strongly associated marker in each region in the GWAS meta-analysis of all Europeans aged <25 years.

EAf = effect allele frequency, OR = odds ratio.

| <i>SNP</i> | <i>Chr</i> | <i>Pos</i> | <i>Effect allele</i> | <i>Other allele</i> | <i>EAf</i> | <i>OR (95%CI)</i> | <i>P-value</i> | <i>Nearest gene</i> |
|-------------|------------|------------|----------------------|---------------------|------------|-------------------|-------------------------|---------------------|
| rs6005414 | 22 | 27783185 | A | G | 0.53 | 0.80 (0.74-0.87) | 5.83 x 10 ⁻⁸ | <i>LINC02554</i> |
| rs17056435 | 5 | 158453783 | A | G | 0.05 | 2.19 (1.64-2.92) | 1.14 x 10 ⁻⁷ | <i>EBF1</i> |
| rs2596618 | 3 | 24221506 | A | G | 0.11 | 1.38 (1.22-1.57) | 3.16 x 10 ⁻⁷ | <i>THR3</i> |
| rs12859952 | 13 | 26381179 | A | G | 0.77 | 0.77 (0.69-0.85) | 3.61 x 10 ⁻⁷ | <i>ATP8A2</i> |
| rs9652372 | 14 | 75377345 | T | C | 0.09 | 0.70 (0.61-0.81) | 7.43 x 10 ⁻⁷ | <i>RPS6KL1</i> |
| rs139812140 | 8 | 118821440 | D | R | 0.16 | 0.75 (0.67-0.85) | 1.34 x 10 ⁻⁶ | <i>EXT1</i> |
| rs7702605 | 5 | 2653180 | C | G | 0.88 | 0.75 (0.67-0.85) | 1.66 x 10 ⁻⁶ | <i>IRX2</i> |
| rs12130807 | 1 | 82036836 | A | C | 0.09 | 0.71 (0.61-0.82) | 3.43 x 10 ⁻⁶ | <i>ADGRL2</i> |
| rs202172201 | 4 | 40109940 | I | R | 0.09 | 1.41 (1.22-1.62) | 3.79 x 10 ⁻⁶ | <i>N4BP2</i> |
| rs9581136 | 13 | 19639265 | T | C | 0.06 | 0.65 (0.54-0.78) | 4.20 x 10 ⁻⁶ | <i>GTF2IP3</i> |

Supplementary Table S4. Most strongly associated marker in each region in the GWAS meta-analysis of all Asians aged >25 years. EAF = effect allele frequency, OR = odds ratio.

| SNP | Chr | Pos | Effect allele | Other allele | EAF | OR (95%CI) | P-value | Nearest gene |
|-------------|------------|------------|----------------------|---------------------|------------|-------------------|-------------------------|---------------------|
| rs16875983 | 8 | 108285287 | T | G | 0.25 | 1.22 (1.13-1.32) | 2.14 x 10 ⁻⁷ | ANGPT1 |
| rs67687099 | 3 | 152747454 | D | R | 0.20 | 1.37 (1.22-1.55) | 3.25 x 10 ⁻⁷ | HMG2P13 |
| rs35026266 | 15 | 48769044 | T | C | 0.31 | 0.84 (0.79-0.91) | 2.52 x 10 ⁻⁶ | FBN1 |
| rs10809667 | 9 | 1209532 | A | T | 0.23 | 1.20 (1.11-1.30) | 3.37 x 10 ⁻⁶ | RPS27AP14 |
| rs56738713 | 5 | 29586419 | A | G | 0.08 | 1.37 (1.20-1.57) | 5.17 x 10 ⁻⁶ | UBL5P1 |
| rs3924436 | 1 | 24908959 | A | G | 0.41 | 0.86 (0.81-0.92) | 5.42 x 10 ⁻⁶ | NCMAP |
| rs1687660 | 16 | 86416646 | C | G | 0.52 | 0.86 (0.81-0.92) | 6.11 x 10 ⁻⁶ | LINC00917 |
| rs58435984 | 4 | 55127990 | T | C | 0.78 | 0.84 (0.77-0.90) | 8.58 x 10 ⁻⁶ | PDGFRA |
| rs141310268 | 18 | 45633672 | D | R | 0.14 | 0.80 (0.72-0.88) | 9.87 x 10 ⁻⁶ | ZBTB7C |
| rs817755 | 7 | 98202672 | A | C | 0.91 | 1.42 (1.21-1.65) | 1.00 x 10 ⁻⁵ | NPTX2 |

Supplementary Table S5. Most strongly associated marker in each region in the GWAS meta-analysis of all Asians aged <25 years. EAF = effect allele frequency, OR = odds ratio.

| SNP | Chr | Pos | Effect allele | Other allele | EAF | OR (95%CI) | P-value | Nearest gene |
|-------------|------------|------------|----------------------|---------------------|------------|-------------------|-------------------------|---------------------|
| rs72971923 | 18 | 69822333 | A | G | 0.15 | 0.32 (0.21-0.50) | 2.68 x 10 ⁻⁷ | LOC101927537 |
| rs2069368 | 5 | 162870726 | C | G | 0.94 | 7.30 (3.28-16.26) | 1.14 x 10 ⁻⁶ | CCNG1 |
| rs7905017 | 10 | 92868457 | A | G | 0.62 | 1.98 (1.50-2.62) | 1.63 x 10 ⁻⁶ | LINC00502 |
| rs11079429 | 17 | 59472403 | A | G | 0.29 | 0.48 (0.35-0.65) | 2.23 x 10 ⁻⁶ | BCAS3 |
| rs9957 | 5 | 179290154 | C | G | 0.74 | 1.92 (1.47-2.53) | 2.48 x 10 ⁻⁶ | TBC1D9B |
| rs17072824 | 18 | 62003510 | A | G | 0.10 | 0.35 (0.23-0.54) | 2.80 x 10 ⁻⁶ | LINC01924 |
| rs779593 | 3 | 118029874 | T | C | 0.69 | 1.81 (1.41-2.32) | 2.95 x 10 ⁻⁶ | LOC101926968 |
| rs143004236 | 7 | 135420794 | A | G | 0.05 | 0.13 (0.06-0.31) | 3.00 x 10 ⁻⁶ | FAM180A |
| rs11085245 | 19 | 18859757 | A | G | 0.83 | 0.45 (0.32-0.63) | 3.31 x 10 ⁻⁶ | CRTC1 |
| rs12144639 | 1 | 213817311 | A | G | 0.22 | 0.53 (0.40-0.70) | 4.75 x 10 ⁻⁶ | PROX1-AS1 |

Supplementary Table S6. Top 10 genes from VEGAS2 gene-based association test with $\pm 50\text{kb}$ buffers for all Europeans. Start and stop positions listed include $\pm 50\text{kb}$ buffers.

nSNPs: number of variants included in gene region. Test Statistic: gene-based χ^2 test statistic to *nSNPs* degrees of freedom. P-value: obtained from Test Statistic and adjusting for LD between variants. FDR: false discovery rate (likelihood of gene association being a false positive result). Top SNP: variant within gene locus with strongest association signal from previous SNP-based association test. Genes shown in bold were also identified with MAGMA (Table S7).

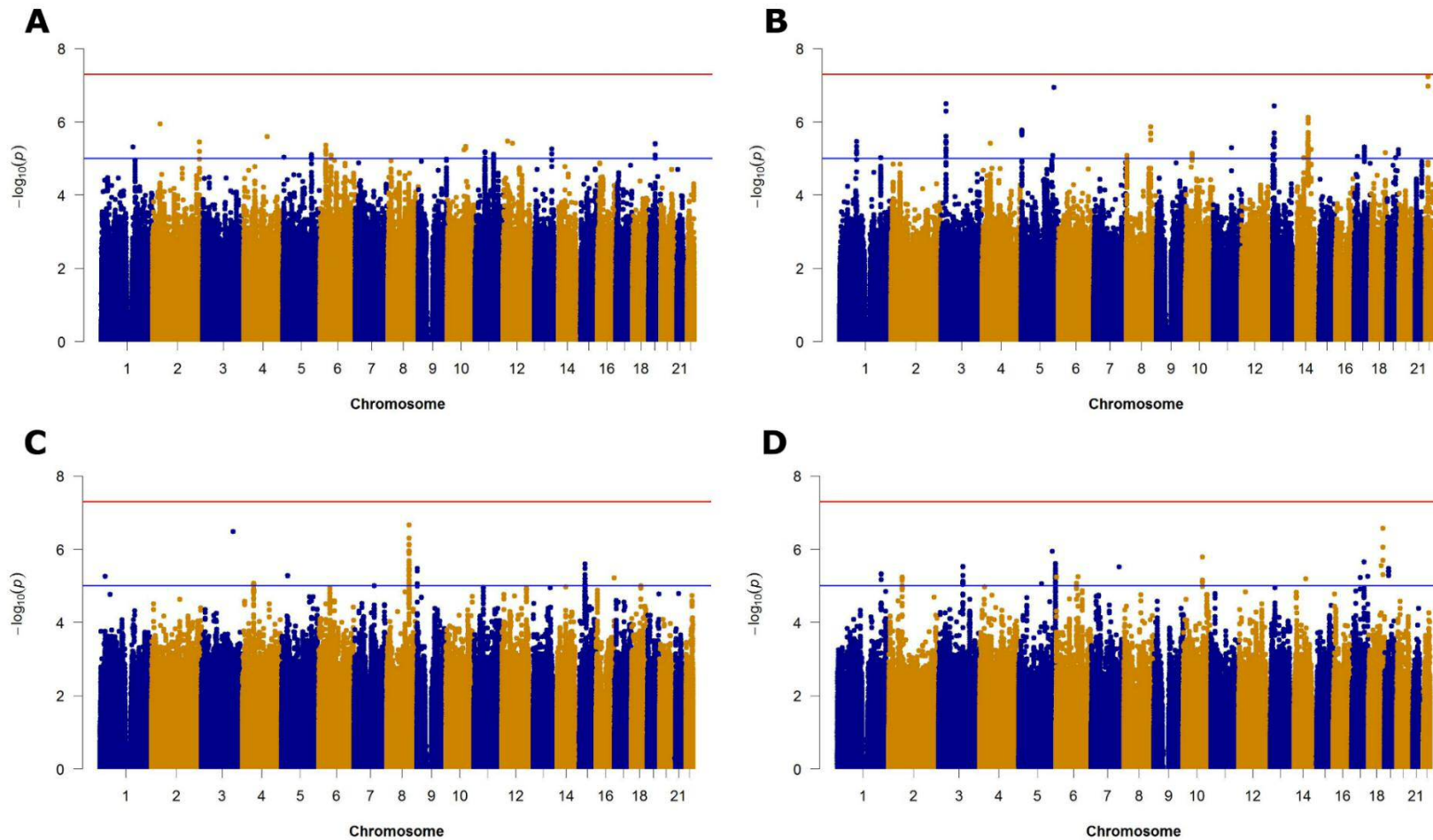
| Gene | Chr | Start | Stop | nSNPs | Test Statistic | P-value | FDR | Top SNP |
|----------------|-----|----------|----------|-------|----------------|-----------------------|-------|------------|
| ACP2 | 11 | 47210852 | 47320457 | 175 | 1680.63 | 1.00×10^{-5} | 0.097 | rs3758670 |
| MADD | 11 | 47240926 | 47401582 | 271 | 2472.89 | 1.10×10^{-5} | 0.097 | rs2697920 |
| NR1H3 | 11 | 47219850 | 47340584 | 191 | 1929.38 | 1.20×10^{-5} | 0.097 | rs3758670 |
| DDB2 | 11 | 47186492 | 47310769 | 193 | 1638.98 | 2.00×10^{-5} | 0.097 | rs3758670 |
| CLDN7 | 17 | 7113221 | 7216512 | 123 | 980.06 | 2.00×10^{-5} | 0.097 | rs222836 |
| CTDNEP1 | 17 | 7096905 | 7205259 | 114 | 1013.67 | 2.90×10^{-5} | 0.111 | rs222836 |
| ELP5 | 17 | 7105371 | 7213259 | 123 | 1012.32 | 3.20×10^{-5} | 0.111 | rs222836 |
| GABARAP | 17 | 7093737 | 7195753 | 96 | 952.50 | 4.10×10^{-5} | 0.118 | rs222836 |
| TYR | 11 | 88861039 | 89078927 | 402 | 3017.77 | 4.40×10^{-5} | 0.118 | rs12808354 |
| PHF23 | 17 | 7088346 | 7192825 | 104 | 903.47 | 7.90×10^{-5} | 0.174 | rs222836 |

Supplementary Table S7. Top 10 genes from MAGMA gene-based association test with $\pm 50\text{kb}$ buffers for all Europeans. Start and stop positions listed include $\pm 50\text{kb}$ buffers.

nSNPs: number of variants included in gene region. Z Statistic: gene-based test statistic. P-value: obtained from *Z Statistic* under the assumption of a normally distributed model. FDR: false discovery rate (likelihood of gene association being a false positive result). Genes shown in bold were also identified with VEGAS2 (Table S6).

| Gene | Chr | Start | Stop | nSNPs | Z Statistic | P-value | FDR | Bonferroni Adjusted P |
|------------------|-----|----------|----------|-------|-------------|-----------------------|-------|-----------------------|
| ELP5 | 17 | 7105372 | 7213259 | 123 | 4.71 | 1.23×10^{-6} | 0.009 | 0.023 |
| CLDN7 | 17 | 7113222 | 7216863 | 124 | 4.69 | 1.39×10^{-6} | 0.009 | 0.026 |
| CTDNEP1 | 17 | 7096906 | 7205259 | 114 | 4.67 | 1.50×10^{-6} | 0.009 | 0.028 |
| <i>TNFAIP8L3</i> | 15 | 51298798 | 51447473 | 212 | 4.59 | 2.26×10^{-6} | 0.009 | 0.042 |
| ACP2 | 11 | 47210853 | 47320457 | 175 | 4.56 | 2.52×10^{-6} | 0.009 | 0.046 |
| GABARAP | 17 | 7093738 | 7195753 | 96 | 4.45 | 4.23×10^{-6} | 0.013 | 0.078 |
| PHF23 | 17 | 7088347 | 7192825 | 104 | 4.36 | 6.59×10^{-6} | 0.017 | 0.121 |
| <i>DVL2</i> | 17 | 7078661 | 7187867 | 112 | 4.27 | 9.80×10^{-6} | 0.021 | 0.181 |
| <i>SLC2A4</i> | 17 | 7134986 | 7241367 | 155 | 4.22 | 1.21×10^{-5} | 0.021 | 0.223 |
| <i>ACADVL</i> | 17 | 7070444 | 7178586 | 104 | 4.22 | 1.22×10^{-5} | 0.021 | 0.224 |

Supplementary Figure S1. Manhattan plots for the separate ancestry/age strata fixed effects meta-analyses. Y-axes show negative \log_{10} p-values and X-axes show genomic position. Red line corresponds to $P = 5 \times 10^{-8}$, blue line corresponds to $P = 1 \times 10^{-5}$. Panel A, European ancestry, aged >25 years; B, European ancestry, aged <25 years; C, Asian ancestry, aged >25 years; D, Asian ancestry, aged <25 years.



Supplementary Figure S2. Quantile-quantile plots for the separate ancestry/age strata fixed effects meta-analyses. Y-axes show observed negative \log_{10} p-values and X-axes show expected negative \log_{10} p-values according to the null hypothesis of no genetic association. Red line is the line of unity ($y = x$). Panel **A**, European ancestry, aged >25 years; **B**, European ancestry, aged <25 years; **C**, Asian ancestry, aged >25 years; **D**, Asian ancestry, aged <25 years.

