**Appendix 5.** Summary of rare (≤1% minor allele frequency in the wider European population) or novel, damaging missense/nonsense variants in our sample of 75 sequenced cases and controls that were located in any of the 35 gene regions associated with risk of advanced AMD from 2 meta-analyses[1,2].

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Chr** | **Bp position** | **RS ID** | **Minor** | **Major** | **MAF cases** | **MAF controls** | **Gene** | **IAMDGC exome chip p-value** |
| 1 | 196709816 | rs149474608 | T | G | 0.01 | 0 | CFH1,2 | 0.003 |
| 2 | 228172594 | rs200302125 | C | T | 0 | 0.01 | COL4A32 | 0.62 |
| 4 | 110662230 | \* | C | T | 0.01 | 0 | CFI1,2 | NA |
| 4 | 110681450 | rs182078921 | T | C | 0.01 | 0 | CFI1,2 | 0.01 |
| 4 | 110685820 | rs141853578 | T | C | 0.01 | 0 | CFI1,2 | 6.27x10-10 |
| 5 | 35070325 | rs370907111 | C | G | 0 | 0.01 | PRLR2 | NA |
| 5 | 39331894 | rs34882957 | A | G | 0.03 | 0 | C92 | 1.62x10-14 |
| 5 | 35646784 | rs80010329 | G | A | 0.03 | 0 | SPEF22 | 0.97 |
| 5 | 35646853 |  | T | C | 0.01 | 0 | SPEF22 | NA |
| 5 | 35691247 | rs185000070 | T | C | 0.03 | 0 | SPEF22 | 0.30 |
| 5 | 35779447 | rs2277044 | C | A | 0 | 0.01 | SPEF22 | 0.94 |
| 6 | 31917333 | rs201798809 | G | C | 0.01 | 0 | CFB1,2 | NA |
| 6 | 31929786 | rs200093212 | C | T | 0.01 | 0 | SKIV2L2 | NA |
| 6 | 116442654 | rs146114911 | T | C | 0.01 | 0 | COL10A11 | 0.64 |
| 6 | 116443023 | rs145214720 | T | C | 0.01 | 0 | COL10A11 | 0.79 |
| 7 | 99956391 | rs370340323 | G | C | 0 | 0.01 | PILRB2 | NA |
| 7 | 104753398 |  | G | A | 0 | 0.01 | KMT2E2 | NA |
| 9 | 73151387 | rs148192709 | T | C | 0.01 | 0.01 | TRPM32 | 0.40 |
| 9 | 107589317 | \* | T | C | 0 | 0.01 | ABCA12 | NA |
| 10 | 24922388 | rs61758700 | C | T | 0.01 | 0.01 | ARHGAP212 | 0.73 |
| 12 | 112194227 |  | A | G | 0 | 0.01 | ACAD102 | NA |
| 12 | 112194234 | \* | G | A | 0 | 0.01 | ACAD102 | NA |
| 13 | 31898021 | rs142935066 | G | C | 0.01 | 0 | B3GALTL1,2 | 0.69 |
| 19 | 5831608 | rs61739551 | A | G | 0.01 | 0 | FUT62 | NA |
| 19 | 6707129 | rs117793540 | A | G | 0 | 0.01 | C31,2 | 0.95 |
| 19 | 45721556 | rs143444923 | A | G | 0 | 0.02 | EXOC3L22 | NA |
| 20 | 44639214 | rs143024943 | T | C | 0 | 0.01 | MMP92 | 0.30 |
| 20 | 44640275 | rs144098289 | A | G | 0.01 | 0 | MMP92 | NA |
| 22 | 32914209 | rs140962261 | A | C | 0.01 | 0 | SYN32 | 0.95 |

1 genes with variants that reached genome-wide significant in Fritsche et al. 2013 [1]. 2 genes with variants that reached genome-wide significant in Fritsche et al. 2016 [2]. \* Variants that were novel (not reported in 1000Genomes, EVS6500, dbSNP v138 or ExAC databases).

1. Fritsche LG, Chen W, Schu M, Yaspan BL, Yu Y, Thorleifsson G, Zack DJ, Arakawa S, Cipriani V, Ripke S, Igo RP, Buitendijk GHS, Sim X, Weeks DE, Guymer RH, Merriam JE, Francis PJ, Hannum G, Agarwal A, Armbrecht AM, Audo I, Aung T, Barile GR, Benchaboune M, Bird AC, Bishop PN, Branham KE, Brooks M, Brucker AJ, Cade WH, Cain MS, Campochiaro PA, Chan C-, Cheng C-, Chew EY, Chin KA, Chowers I, Clayton DG, Cojocaru R, Conley YP, Cornes BK, Daly MJ, Dhillon B, Edwards AO, Evangelou E, Fagerness J, Ferreyra HA, Friedman JS, Geirsdottir A, George RJ, Gieger C, Gupta N, Hagstrom SA, Harding SP, Haritoglou C, Heckenlively JR, Holz FG, Hughes G, Ioannidis JPA, Ishibashi T, Joseph P, Jun G, Kamatani Y, Katsanis N, N Keilhauer C, Khan JC, Kim IK, Kiyohara Y, Klein BEK, Klein R, Kovach JL, Kozak I, Lee CJ, Lee KE, Lichtner P, Lotery AJ, Meitinger T, Mitchell P, Mohand-Saïd S, Moore AT, Morgan DJ, Morrison MA, Myers CE, Naj AC, Nakamura Y, Okada Y, Orlin A, Ortube MC, Othman MI, Pappas C, Park KH, Pauer GJT, Peachey NS, Poch O, Priya RR, Reynolds R, Richardson AJ, Ripp R, Rudolph G, Ryu E, Sahel J-, Schaumberg DA, Scholl HPN, Schwartz SG, Scott WK, Shahid H, Sigurdsson H, Silvestri G, Sivakumaran TA, Smith RT, Sobrin L, Souied EH, Stambolian DE, Stefansson H, Sturgill-Short GM, Takahashi A, Tosakulwong N, Truitt BJ, Tsironi EE, Uitterlinden AG, Van Duijn CM, Vijaya L, Vingerling JR, Vithana EN, Webster AR, Wichmann H-, Winkler TW, Wong TY, Wright AF, Zelenika D, Zhang M, Zhao L, Zhang K, Klein ML, Hageman GS, Lathrop GM, Stefansson K, Allikmets R, Baird PN, Gorin MB, Wang JJ, Klaver CCW, Seddon JM, Pericak-Vance MA, Iyengar SK, Yates JRW, Swaroop A, Weber BHF, Kubo M, Deangelis MM, Léveillard T, Thorsteinsdottir U, Haines JL, Farrer LA, Heid IM, Abecasis GR. Seven new loci associated with age-related macular degeneration. Nat.Genet. 2013; 45:433-9.

2. Fritsche LG, Igl W, Bailey JNC, Grassmann F, Sengupta S, Bragg-Gresham JL, Burdon KP, Hebbring SJ, Wen C, Gorski M. A large genome-wide association study of age-related macular degeneration highlights contributions of rare and common variants. Nat.Genet. 2016; 48:134-43.