

ESM Table 3: Tests of heterogeneity of genotype frequencies and disease association across family collections (listed in ESM Table 1).

| Region Candidate gene rsnumber Alleles | Genotype frequency heterogeneity tests | Disease association heterogeneity tests |
|--|---|--|
| 1q32.1 <i>IL10</i> rs3024505 C>T | 0.25 | 0.42 |
| 4p15.2 rs10517086 G>A | 0.12 | 0.36 |
| 6q22.32 <i>C6orf173</i> rs9388489 A>G | 6.9x10 ⁻⁴ | 0.82 |
| 7p12.1 <i>COBL</i> rs4948088 C>A | 5.6x10 ⁻⁸ | 0.14 |
| 7p15.2 <i>SKAP2</i> rs7804356 T>C | 4.3x10 ⁻⁸ | 0.084 |
| 9p24.2 <i>GLIS3</i> rs7020673 G>C | 0.025 | 0.61 |
| 10q23.31 <i>RNLS</i> rs10509540 T>C | 0.071 | 0.015 |
| 12p13.31 <i>CD69</i> rs4763879 G>A | 8.0x10 ⁻³ | 0.57 |
| 14q24.1 <i>ZFP36L1/C14orf181</i> rs1465788 G>A | 4.0x10 ⁻¹⁵ | 0.010 |
| 14q32.2 <i>C14orf64</i> rs4900384 A>G | 4.4x10 ⁻⁴⁶ | 0.30 |
| 16p11.2 <i>IL27</i> rs4788084 G>A | 1.3x10 ⁻¹⁴ | 0.57 |
| 16q23.1 <i>CTRB2</i> rs7202877 T>G | 5.6x10 ⁻⁸ | 0.026 |
| 17q12 <i>GSDMB/ORMDL3</i> rs2290400 G>A | 1.3x10 ⁻¹¹ | 0.34 |
| 17q21.2 <i>CCR7</i> | 1.9x10 ⁻¹⁴ | 0.39 |

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| rs7221109 C>T | | |
| 19q13.32 <i>PRKD2</i> rs425105 A>G | 0.51 | 0.57 |
| 20p13 <i>SIRPG</i> rs2281808 C>T | 3.1×10^{-14} | 0.91 |
| 22q12.2 <i>HORMAD2</i> rs5753037 C>T | 5.4×10^{-9} | 0.43 |
| Xq28 <i>GAB3</i> rs2664170 A>G | 4.4×10^{-5} | 0.31* |

*Only females analysed, only transmissions from the mother were considered for the chromosome X disease association heterogeneity test.