

ESM Table 5: A summary of replication evidence in case/control and family collections for the 18 type 1 diabetes susceptibility loci discovered and replicated in Barrett *et al.* [1]. The case/control data mainly consist of the case/control component of the replication samples analysed in Barrett *et al.* [1], however, as 192 case samples were no longer available for analysis, we included available case and control samples not previously analysed in discovery or replication for the 18 susceptibility loci. We note that two-tailed *P*-values are reported for the case/control analyses and, as we attempted to replicate the evidence from the case/control component of the replication samples (Methods; ESM Table 2), one-tailed *P*-values for the family analyses. The reported odds ratios (ORs) and relative risks (RRs) are for the minor allele and the minor allele frequency (MAF) for rs2664170/*GAB3*/Xq28 is based on female samples. MAF –in controls and in unaffected parents from Great Britain, df – degree(s) of freedom and CI – confidence interval.

Region Candidate gene rsnumber Alleles	Independent cases and controls*		Current study
	Sample size	MAF OR (95% CI) for minor allele two-tailed <i>P</i> -value	4,429 independent families MAF RR (95% CI) for minor allele one-tailed <i>P</i> -value
1q32.1 <i>IL10</i> rs3024505 C>T	4,260 cases, 6,159 controls	0.17 0.87 (0.86-0.93) <i>P</i> = 3.9x10 ⁻⁴	0.15 0.89 (0.83-0.96) <i>P</i> = 9.5x10 ⁻⁴
4p15.2 rs10517086 G>A	4,172 cases, 6,462 controls	0.30 1.08 (1.02-1.15) <i>P</i> = 0.016	0.32 1.07 (1.02-1.13) <i>P</i> = 8.5x10 ⁻³
6q22.32 <i>C6orf173</i> rs9388489 A>G	4,249 cases, 6,115 controls	0.45 1.18 (1.11-1.25) <i>P</i> = 9.2x10 ⁻⁹	0.47 1.06 (1.01-1.12) <i>P</i> = 0.010
7p12.1 <i>COBL</i> rs4948088 C>A	4,300 cases, 6,293 controls	0.047 0.84 (0.73-0.97) <i>P</i> = 0.021	0.043 0.87 (0.76-1.01) <i>P</i> = 0.046
7p15.2 <i>SKAP2</i> rs7804356 T>C	4,278 cases, 6,608 controls	0.24 0.89 (0.84-0.96) <i>P</i> = 1.2x10 ⁻³	0.23 0.94 (0.89-1.00) <i>P</i> = 0.021

9p24.2 <i>GLIS3</i> rs7020673 G>C	4,303 cases, 6,261 controls	0.50 0.91 (0.86-0.96) $P = 7.1 \times 10^{-4}$	0.49 0.95 (0.90-1.00) $P = 0.017$
10q23.31 <i>RNLS</i> rs10509540 T>C	^s 2,513 cases, 4,668 controls from Great Britain	0.29 0.73 (0.67-0.79) $P = 1.8 \times 10^{-14}$	0.25 0.80 (0.75-0.84) $P = 9.0 \times 10^{-15}$
12p13.31 <i>CD69</i> rs4763879 G>A	4,229 cases, 6,009 controls	0.37 1.08 (1.02-1.15) $P = 9.6 \times 10^{-3}$	0.36 1.11 (1.05-1.17) $P = 5.0 \times 10^{-5}$
14q24.1 <i>ZFP36L1/C14orf181</i> rs1465788 G>A	4,287 cases, 6,089 controls	0.29 0.87 (0.81-0.93) $P = 2.0 \times 10^{-5}$	0.28 0.95 (0.90-1.01) $P = 0.055$
14q32.2 <i>C14orf64</i> rs4900384 A>G	4,246 cases, 6,164 controls	0.29 1.08 (1.02-1.15) $P = 0.010$	0.28 1.08 (1.02-1.14) $P = 1.4 \times 10^{-3}$
16p11.2 <i>IL27</i> rs4788084 G>A	4,271 cases, 6,593 controls	0.42 0.87 (0.82-0.92) $P = 3.0 \times 10^{-6}$	0.43 0.92 (0.88-0.97) $P = 4.6 \times 10^{-4}$
16q23.1 <i>CTRB2</i> rs7202877 T>G	4,266 cases, 6,566 controls	0.096 1.28 (1.17-1.40) $P = 6.5 \times 10^{-8}$	0.11 1.09 (1.01-1.18) $P = 6.5 \times 10^{-3}$
17q12 <i>GSDMB/ORMDL3</i> rs2290400 G>A	4,192 cases, 5,891 controls	0.50 0.88 (0.83-0.93) $P = 1.4 \times 10^{-5}$	0.48 0.89 (0.85-0.94) $P = 1.8 \times 10^{-6}$
17q21.2 <i>CCR7</i> rs7221109 C>T	4,337 cases, 6,343 controls	0.35 0.96 (0.90-1.02) $P = 0.14$	0.34 0.91 (0.86-0.96) $P = 1.8 \times 10^{-4}$
19q13.32 <i>PRKD2</i> rs425105 A>G	3,955 cases, 6,187 controls	0.16 0.84 (0.78-0.91) $P = 3.0 \times 10^{-5}$	0.15 0.88 (0.82-0.95) $P = 4.0 \times 10^{-4}$
20p13 <i>SIRPG</i> rs2281808 C>T	4,317 cases, 6,333 controls	0.36 0.90 (0.85-0.96) $P = 4.7 \times 10^{-4}$	0.36 0.89 (0.85-0.94) $P = 2.6 \times 10^{-5}$
22q12.2 <i>HORMAD2</i> rs5753037 C>T	4,254 cases, 6,480 controls	rs5753037 C>T 0.39 1.13 (1.07-1.20) $P = 2.9 \times 10^{-5}$	rs5753037 C>T 0.40 1.10 (1.05-1.16) $P = 7.0 \times 10^{-5}$
Xq28 <i>GAB3</i> rs2664170 A>G	4,714 cases, 7,438 controls	0.32 1.10 (1.04-1.15) $P = 1.9 \times 10^{-5}$	0.33 1.04 (1.00-1.09) $P = 0.025$

*Cases and controls are from Great Britain and Denmark unless otherwise stated.

^sCases and controls from Denmark dropped for rs10509540/*RNLS*/10q23.31 because of population heterogeneity in disease association between British and Danish case/control collections ($P = 4.1 \times 10^{-3}$).

References

- [1] Barrett JC, Clayton DG, Concannon P, et al. (2009) Genome-wide association study and meta-analysis find that over 40 loci affect risk of type 1 diabetes. *Nat Genet* 41: 703-707