SUPPLEMENTARY DATA

**Supplementary Table 1.** Characteristics of the study participants**.**

| | | | Cases | | Controls | |
|---|---|---|---|---|---|---|
| | | | fulminant | autoimmune | GWAS stage | Candidate gene |
| N | | | 257 | 409 | 419 | 357 |
| Sex | | male/female | 154/103 | 168/241 | 350/69 | 223/134 |
| Disease (years) | onset | mean | 43.5 | 20.5 | | |
| | | range | 1-92 | 4-34 | | |

**Supplementary Table 2.** SNP filtering for statistical analysis

| QC parameter | Threshold | numbers of SNPs excluded (Autosomal chromosomes) |
|---|---|---|
| SNP call rate | < 0.95 | 9157 |
| Minor allele frequency (MAF) | < 0.05 | 143057 |
| Hardy-Weinberg equilibrium P value in controls | < 0.001 | 2822 |
| Poor clustering | | 218 |

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SUPPLEMENTARY DATA

**Supplementary Table 3.**
A. SNPs in non-HLA regions showing a suggestive association with fulminant type 1 diabetes in the genome-wide association study ($P \leq 1.0 \times 10^{-4}$). SNPs with $P \leq 1.0 \times 10^{-5}$ are shown in bold.

| Chr | Cytoband | Position* | SNP | Risk/ Reference allele | Gene or nearby gene | P | OR† | 95%CI‡ | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | lower | upper |
| 1 | p36.32 | 4820420 | rs10915616 | C/T | *NPHP4* | $1.36 \times 10^{-5}$ | 2.39 | 1.60 | 3.58 |
| 1 | q42.13 | 226915712 | rs12041000 | G/A | *ADCK3* | $5.76 \times 10^{-5}$ | 1.58 | 1.26 | 1.98 |
| 2 | p25.3 | 3881302 | rs7591948 | A/C | *DCDC2C* | $4.08 \times 10^{-5}$ | 2.41 | 1.57 | 3.72 |
| 2 | p25.3 | 3906092 | rs4850005 | A/G | *LINC01304* | $2.42 \times 10^{-5}$ | 2.49 | 1.61 | 3.85 |
| 2 | p22.1 | 40979035 | rs6544376 | T/C | *LOC388942* | $9.38 \times 10^{-5}$ | 1.62 | 1.27 | 2.06 |
| 2 | p16.2 | 53653800 | rs6727876 | T/G | *ASB3* | $2.42 \times 10^{-5}$ | 1.61 | 1.29 | 2.01 |
| 2 | p16.2 | 53699166 | rs13414216 | T/C | *LOC100302652* | $7.69 \times 10^{-5}$ | 1.57 | 1.25 | 1.96 |
| 2 | p16.2 | 53791787 | rs2542588 | C/T | *LOC100302652* | $9.33 \times 10^{-5}$ | 1.56 | 1.25 | 1.94 |
| 2 | p16.1 | 55166432 | rs10172326 | A/G | *C2orf63* | $5.87 \times 10^{-5}$ | 1.58 | 1.26 | 1.98 |
| 2 | q11.1 | 95368615 | rs2320432 | G/A | *KCNIP3* | $1.62 \times 10^{-5}$ | 1.78 | 1.37 | 2.31 |
| 2 | q34 | 212714053 | rs13393014 | G/A | *IKZF2* | $3.80 \times 10^{-5}$ | 1.61 | 1.28 | 2.02 |
| 2 | q37.3 | 238930543 | rs11680343 | G/A | *HDAC4* | $3.96 \times 10^{-5}$ | 1.89 | 1.39 | 2.58 |
| **3** | **p26.1** | **5093886** | **rs3864055** | **T/C** | ***ARL8B*** | $\mathbf{5.93 \times 10^{-6}}$ | **1.79** | **1.39** | **2.31** |
| 3 | p14.3 | 55497931 | rs1160047 | A/G | *ERC2* | $3.66 \times 10^{-5}$ | 1.73 | 1.33 | 2.24 |
| 3 | q21.3 | 127431182 | rs4637240 | T/C | *TPRA1* | $4.34 \times 10^{-5}$ | 1.88 | 1.38 | 2.55 |
| 3 | q21.3 | 127441926 | rs3948104 | G/C | *TPRA1* | $1.89 \times 10^{-5}$ | 1.93 | 1.42 | 2.63 |
| 3 | q21.3 | 127474584 | rs2594220 | T/G | *TPRA1* | $8.16 \times 10^{-5}$ | 1.83 | 1.35 | 2.47 |
| 4 | p15.2 | 27495853 | rs905279 | T/C | *MIR4275* | $1.44 \times 10^{-5}$ | 1.64 | 1.31 | 2.05 |
| 4 | q31.22 | 147527718 | rs4639051 | A/G | *EDNRA* | $4.37 \times 10^{-5}$ | 2.44 | 1.57 | 3.80 |
| 4 | q34.3 | 181408638 | rs6857563 | G/T | *MGC45800* | $2.16 \times 10^{-5}$ | 1.62 | 1.30 | 2.02 |
| **4** | **q35.1** | **184755529** | **rs12644905** | **C/T** | ***ACSL1*** | $\mathbf{3.60 \times 10^{-6}}$ | **1.91** | **1.45** | **2.52** |
| 5 | p14.3 | 21839979 | rs16888321 | C/T | *CDH12* | $5.48 \times 10^{-5}$ | 2.15 | 1.47 | 3.15 |
| 5 | p14.3 | 21863845 | rs8180523 | G/A | *CDH12* | $4.34 \times 10^{-5}$ | 2.19 | 1.49 | 3.21 |
| 5 | q11.2 | 52890164 | rs1904163 | T/C | *ITGA1* | $7.51 \times 10^{-5}$ | 1.61 | 1.27 | 2.04 |
| 5 | q11.2 | 57044912 | rs2063260 | C/T | *LOC100130001* | $4.04 \times 10^{-5}$ | 2.08 | 1.46 | 2.97 |
| **6** | **p22.3** | **17120009** | **rs12203596** | **C/A** | ***FLJ23152*** | $\mathbf{5.90 \times 10^{-6}}$ | **2.84** | **1.78** | **4.53** |
| 6 | p22.3 | 24114366 | rs13215261 | A/G | *NRSN1* | $3.45 \times 10^{-5}$ | 2.15 | 1.49 | 3.11 |
| 6 | p22.2 | 26177054 | rs12664415 | T/C | *HIST1H2BE* | $1.96 \times 10^{-5}$ | 2.70 | 1.69 | 4.33 |
| 6 | p22.1 | 29644108 | rs3131854 | C/T | *MOG* | $7.34 \times 10^{-5}$ | 1.77 | 1.33 | 2.36 |
| 6 | p21.31 | 33764485 | rs6904991 | G/T | *LEMD2* | $4.71 \times 10^{-5}$ | 1.72 | 1.32 | 2.23 |
| 6 | q16.3 | 103607414 | rs9404439 | G/A | *HACE1* | $1.49 \times 10^{-5}$ | 1.81 | 1.38 | 2.38 |

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| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 6 | q21 | 105256293 | rs1189924 | T/G | *PREP* | $6.45 \times 10^{-5}$ | 1.58 | 1.26 | 1.97 |
| 6 | q22.1 | 117303435 | rs210966 | G/C | *ROS1* | $1.97 \times 10^{-5}$ | 1.75 | 1.35 | 2.28 |
| **6** | **q26** | **163922743** | **rs9356171** | **A/G** | ***C6orf118*** | **$9.19 \times 10^{-6}$** | **1.90** | **1.43** | **2.52** |
| 7 | p21.2 | 13877714 | rs17167612 | C/T | *ETV1* | $6.50 \times 10^{-5}$ | 2.34 | 1.53 | 3.59 |
| 7 | q22.1 | 101472937 | rs1008064 | C/T | *EMID2* | $7.45 \times 10^{-5}$ | 1.56 | 1.25 | 1.95 |
| 7 | q31.1 | 109189772 | rs10953597 | G/A | *EIF3IP1* | $6.19 \times 10^{-5}$ | 1.71 | 1.31 | 2.23 |
| 7 | q36.2 | 154439470 | rs6965651 | G/T | *DPP6* | $3.51 \times 10^{-5}$ | 1.60 | 1.28 | 2.01 |
| 8 | p23.2 | 3477514 | rs13250793 | A/C | *CSMD1* | $5.43 \times 10^{-5}$ | 1.69 | 1.31 | 2.18 |
| 8 | p23.2 | 3477767 | rs13248265 | G/T | *CSMD1* | $6.46 \times 10^{-5}$ | 1.68 | 1.30 | 2.16 |
| 8 | p23.2 | 4627847 | rs17070883 | C/A | *CSMD1* | $5.05 \times 10^{-5}$ | 1.88 | 1.38 | 2.56 |
| 8 | q11.21 | 51042700 | rs16915742 | A/G | *PXDNL* | $3.66 \times 10^{-5}$ | 1.73 | 1.33 | 2.24 |
| 8 | q11.23 | 53517084 | rs13279206 | G/A | *ATP6V1H* | $4.30 \times 10^{-5}$ | 1.63 | 1.29 | 2.06 |
| 8 | q11.23 | 53523733 | rs13270667 | G/A | *ATP6V1H* | $6.18 \times 10^{-5}$ | 1.62 | 1.28 | 2.04 |
| 8 | q22.2 | 98143304 | rs16896685 | A/G | *POP1* | $5.29 \times 10^{-5}$ | 1.71 | 1.32 | 2.22 |
| 8 | q22.2 | 98150406 | rs7000738 | C/T | *POP1* | $3.86 \times 10^{-5}$ | 1.70 | 1.32 | 2.18 |
| 8 | q24.3 | 140036525 | rs7011932 | T/C | *TRAPPC9* | $9.33 \times 10^{-5}$ | 1.56 | 1.25 | 1.94 |
| 9 | p24.1 | 7762216 | rs6477230 | G/A | *C9orf123* | $3.60 \times 10^{-5}$ | 2.52 | 1.61 | 3.97 |
| **9** | **p21.3** | **23166744** | **rs7871386** | **C/T** | ***ELAVL2*** | **$4.60 \times 10^{-6}$** | **2.54** | **1.69** | **3.83** |
| 10 | p14 | 8596272 | rs4747806 | C/T | *SFTA1P* | $5.54 \times 10^{-5}$ | 2.35 | 1.53 | 3.59 |
| 10 | q24.1 | 96325581 | rs3789940 | C/T | *DNTT* | $5.83 \times 10^{-5}$ | 1.59 | 1.27 | 1.99 |
| 11 | p15.1 | 20627519 | rs10833369 | G/T | *SLC6A5* | $3.54 \times 10^{-5}$ | 1.65 | 1.30 | 2.10 |
| **11** | **p14.1** | **27778324** | **rs5790666** | **-/G** | ***KIF18A*** | **$8.07 \times 10^{-7}$** | **2.32** | **1.65** | **3.26** |
| 11 | p12 | 41237630 | rs729210 | T/C | *LOC399881* | $3.23 \times 10^{-5}$ | 1.62 | 1.29 | 2.04 |
| 11 | p12 | 41267500 | rs4445616 | G/T | *LOC399881* | $4.39 \times 10^{-5}$ | 1.65 | 1.29 | 2.09 |
| 11 | p12 | 41267818 | rs10837603 | A/G | *LOC399881* | $9.74 \times 10^{-5}$ | 1.56 | 1.25 | 1.95 |
| 12 | p13.1 | 14189684 | rs10845905 | A/G | *ATF7IP* | $1.99 \times 10^{-5}$ | 1.63 | 1.30 | 2.05 |
| **12** | **q13.13** | **53151908** | **rs11170445** | **T/C** | ***CSAD*** | **$7.58 \times 10^{-9}$** | **1.96** | **1.56** | **2.46** |
| **12** | **q13.13** | **53187018** | **rs4606556** | **T/G** | ***ZNF740*** | **$9.84 \times 10^{-7}$** | **1.93** | **1.48** | **2.53** |
| **12** | **q13.13** | **53193038** | **rs2272299** | **A/G** | ***ITGB7*** | **$9.62 \times 10^{-6}$** | **1.86** | **1.41** | **2.45** |
| **12** | **q15** | **70516944** | **rs12582352** | **T/C** | ***PTPRB*** | **$3.74 \times 10^{-6}$** | **2.58** | **1.71** | **3.90** |
| 12 | q15 | 70543663 | rs919594 | C/T | *PTPRB* | $1.46 \times 10^{-5}$ | 2.42 | 1.61 | 3.64 |
| 12 | q22 | 93616192 | rs11107130 | T/C | *CRADD* | $2.12 \times 10^{-5}$ | 1.66 | 1.31 | 2.10 |
| 12 | q22 | 93622966 | rs7300268 | A/C | *CRADD* | $4.50 \times 10^{-5}$ | 1.62 | 1.28 | 2.04 |
| 12 | q22 | 93626791 | rs7968701 | T/C | *CRADD* | $3.33 \times 10^{-5}$ | 1.61 | 1.28 | 2.02 |
| 16 | p12.1 | 26144398 | rs11866894 | G/A | *C16orf82* | $9.14 \times 10^{-5}$ | 1.72 | 1.31 | 2.27 |
| 16 | p12.1 | 26147341 | rs12598369 | A/G | *C16orf82* | $6.16 \times 10^{-5}$ | 1.75 | 1.33 | 2.30 |
| 16 | q12.2 | 55697756 | rs36010 | A/C | *SLC6A2* | $5.50 \times 10^{-5}$ | 1.67 | 1.30 | 2.15 |
| 20 | q13.31 | 57723635 | rs6025742 | T/C | *C20orf85* | $9.03 \times 10^{-5}$ | 1.56 | 1.25 | 1.94 |

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SUPPLEMENTARY DATA

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **22** | **q11.21** | **20814301** | **rs178050** | **A/G** | ***PI4KA*** | **7.37 x $10^{-6}$** | **1.66** | **1.33** | **2.07** |
| 22 | q11.21 | 20899436 | rs178085 | A/G | *CRKL* | 1.92 x $10^{-5}$ | 1.62 | 1.30 | 2.03 |

* Nucleotide positions based on GRCh38.p7. † OR, odds ratio; ‡ CI, confidence interval.

B. SNPs in non-HLA region showing a suggestive association ($P \leq 1.0 \times 10^{-5}$) with fulminant type 1 diabetes in the genome-wide association study relative to the location of known susceptibility loci for autoimmune type 1 diabetes.

| Chr | Cytoband | Position | SNP | Gene or nearby gene | P | OR† (95%CI‡) | Type 1 diabetes | Other autoimmune disease |
|---|---|---|---|---|---|---|---|---|
| 1 | 1p13.2 | 113288123-114009223 | rs6679677 rs2476601 | *PHTF1 PTPN22* | | | T1D | ATD CRO JIA RA SLE AA VIT |
| 1 | 1q32.1 | 200599616-200896640 | rs6691977 | | | | T1D | |
| 1 | 1q32.1 | 206709013-206867593 | rs3024493 rs3024505 | *IL10* | | | T1D | CRO SLE UC IBD |
| 2 | 2q13 | 110225473-111045908 | rs4849135 | | | | T1D | |
| 2 | 2q24.2 | 162104363-162504293 | rs1990760 rs35667974 rs2111485 | *IFIH1* | | | T1D | PSO SLE UC IBD VIT |
| 2 | 2q33.2 | 203749263-203951852 | rs3087243 rs11571316 | *CTLA4* | | | T1D | ATD CEL RA |
| 2 | 2p23.3 | 24795892-25264789 | rs478222 | *EFR3B* | | | T1D | |
| 2 | 2q11.2 | 99926678-100432653 | rs9653442 | *AFF3* | | | T1D | RA |
| **3** | **3p26.1** | **5093886** | **rs3864055** | ***ARL8B*** | **5.93 x $10^{-6}$** | **1.79 (1.39-2.31)** | **FT1D** | |
| 3 | 3p21.31 | 46061249-46593299 | rs113010081 | *CCR5* | | | T1D | CEL UC |
| 4 | 4p15.2 | 26026175-26130530 | rs10517086 | | | | T1D | |
| 4 | 4q27 | 122017479-122644147 | rs17388568 rs4505848 rs75793288 rs6827756 | *IL21 ADAD1 IL2* | | | T1D | CEL CRO UC |
| 4 | 4q32.3 | 165571673-165682849 | rs2611215 | | | | T1D | |
| **4** | **4q35.1** | **184755529** | **rs12644905** | ***ACSL1*** | **3.60 x $10^{-6}$** | **1.91 (1.45-2.52)** | **FT1D** | |
| 5 | 5p13.2 | 35798580-36036080 | rs11954020 | *IL7R* | | | T1D T1DJ* | |
| **6** | **6p22.3** | **17120009** | **rs12203596** | ***FLJ23152*** | **5.90 x $10^{-6}$** | **2.84 (1.78-4.53)** | **FT1D** | |
| 6 | 6q15 | 90097116-90320436 | rs11755527 rs597325 rs72928038 | *BACH2* | | | T1D | ATD MS RA |
| 6 | 6q22.32 | 126129075-127098552 | rs9375435 rs9388489 rs1538171 | *CENPW* | | | T1D | |
| 6 | 6q23.3 | 137568592-137806067 | rs6920220 | *TNFAIP3* | | | T1D | RA SLE UC IBD |

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| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 6 | 6q25.3 | 158897742-159119181 | rs1738074 | *TAGAP* | | | T1D | CEL MS |
| **6** | **6q26** | **163922743** | **rs9356171** | ***C6orf118*** | **$9.19 \times 10^{-6}$** | **1.90 (1.43-2.52)** | **FT1D** | |
| 6 | 6q27 | 169879562-170130554 | rs924043 | | | | T1D | |
| 7 | 7p15.2 | 26618343-27162670 | rs7804356 | | | | T1D | |
| 7 | 7p12.2 | 50327041-50624014 | rs62447205 | *IKZF1* | | | T1D | |
| 7 | 7p12.1 | 50833203-51066332 | rs4948088 | *COBL* | | | T1D | |
| 9 | 9p24.2 | 4238265-4315442 | rs7020673<br>rs6476839<br>rs10758593 | *GLIS3* | | | T1D | |
| **9** | **9p21.3** | **23166744** | **rs7871386** | ***ELAVL2*** | **$4.60 \times 10^{-6}$** | **2.54 (1.69-3.83)** | **FT1D** | |
| 10 | 10p15.1 | 5988280-6146375 | rs2104286<br>rs61839660<br>rs7090530<br>rs10795791<br>rs12251307<br>rs41295121 | *RBM17*<br>*IL2RA* | | | T1D<br>T1DJ* | MS RA |
| 10 | 10p15.1 | 6388017-6503142 | rs11258747 | *PRKCQ* | | | T1D | |
| 10 | 10p11.22 | 32983821-33222119 | rs722988 | *NRP1* | | | T1D | |
| 10 | 10q23.31 | 88245291-88511262 | rs12416116<br>rs10509540 | *RNLS* | | | T1D | |
| 11 | 11p15.5 | 2026410-2051274 | rs7928968 | *INS* | | | T1D | |
| 11 | 11p15.5 | 2092701-2260001 | rs72853903<br>rs7111341<br>rs689 | *INS* | | | T1D<br>T1DJ | |
| **11** | **11p14.1** | **27778324** | **rs5790666** | ***KIF18A*** | **$8.07 \times 10^{-7}$** | **2.32 (1.65-3.26)** | **FT1D** | |
| 11 | 11q13.1 | 64076473-64456055 | rs694739 | *BAD* | | | T1D | CRO MS AA |
| 12 | 12p13.31 | 9366576-9820167 | rs4763879<br>rs10492166 | *CD69* | | | T1D | |
| **12** | **12q13.13** | **53151908** | **rs11170445** | ***CSAD*** | **$7.58 \times 10^{-9}$** | **1.96 (1.56-2.46)** | **FT1D** | |
| **12** | **12q13.13** | **53187018** | **rs4606556** | ***CSAD/ ZNF740*** | **$9.84 \times 10^{-7}$** | **1.93 (1.48-2.53)** | **FT1D** | |
| **12** | **12q13.13** | **53193038** | **rs2272299** | ***ITGB7*** | **$9.62 \times 10^{-6}$** | **1.86 (1.41-2.45)** | **FT1D** | |
| 12 | 12q13.13 | 53058065-53209207 | rs11170466 | *ITGB7* | | | T1D | |
| 12 | 12q13.2 | 55957562-56404651 | rs11171739<br>rs705704<br>rs2292239<br>rs11171710<br>rs705705 | *IKZF4*<br>*DGKA*<br>*ERBB3* | | | T1D<br>T1DJ | AA |
| **12** | **12q15** | **70516944** | **rs12582352** | ***PTPRB*** | **$3.74 \times 10^{-6}$** | **2.58 (1.71-3.90)** | **FT1D** | |
| 12 | 12q24.13 | 111278572- | rs3184504 | *NAA25* | | | T1D | CEL CRO JIA |

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| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | 112592683 | rs653178<br>rs17696736 | *SH2B3* | | | | PBC RA AA PSC VIT |
| 13 | 13q32.3 | 99240634-99534324 | rs9585056 | *GPR183* | | | T1D | |
| 14 | 14q24.1 | 68071518-68485527 | rs911263 | | | | T1D | PBC |
| 14 | 14q24.1 | 68696738-68851345 | rs1465788 | | | | T1D | |
| 14 | 14q32.2 | 97895009-98138364 | rs4900384<br>rs1456988 | | | | T1D | |
| 14 | 14q32.2 | 100817324-100862402 | rs941576<br>rs56994090 | *DLK1* | | | T1D | |
| 15 | 15q14 | 38522176-38701912 | rs12908309<br>rs72727394 | *RASGRP1* | | | T1D | CRO |
| 15 | 15q25.1 | 78709357-78968794 | rs3825932<br>rs12148472<br>rs34593439 | *CTSH* | | | T1D | CEL |
| 16 | 16p13.13 | 10923201-11372654 | rs12927355<br>rs193778<br>rs12708716 | *DEXI*<br>*CLEC16A* | | | T1D<br>T1DJ* | MS PBC |
| 16 | 16p11.2 | 28283985-29014657 | rs4788084<br>rs9924471<br>rs151234 | *IL27* | | | T1D | AS CRO IBD |
| 16 | 16q23.1 | 75182342-75487132 | rs8056814<br>rs7202877 | | | | T1D | |
| 17 | 17q12 | 39226421-40084508 | rs2290400<br>rs12453507 | *ORMDL3*<br>*GSDMB* | | | T1D | CRO UC IBD |
| 17 | 17q21.2 | 40563547-40722575 | rs7221109 | | | | T1D | UC |
| 17 | 17q21.31 | 45903164-46788073 | rs1052553 | | | | T1D | |
| 18 | 18p11.21 | 12738414-12925254 | rs2542151<br>rs1893217 | *PTPN2* | | | T1D | CEL CRO UC IBD |
| 18 | 18q22.2 | 69831437-69902924 | rs1615504<br>rs763361 | *CD226* | | | T1D | MS |
| 19 | 19p13.2 | 10280033-10517872 | rs12720356<br>rs34536443 | *TYK2* | | | T1D | CRO JIA MS PBC PSO RA IBD |
| 19 | 19q13.32 | 46648121-46811943 | rs402072<br>rs425105 | | | | T1D | |
| 20 | 19q13.33 | 48592641-48763133 | rs516246<br>rs602662 | *FUT2* | | | T1D | CRO IBD |
| 20 | 20p13 | 1508984-1741341 | rs6043409<br>rs2281808 | | | | T1D | |
| 21 | 21q22.3 | 42389067-42458550 | rs11203202<br>rs11203203 | *UBASH3A* | | | T1D | RA VIT |
| **22** | **22q11.21** | **20814301** | **rs178050** | ***PI4KA*** | **$7.37 \times 10^{-6}$** | **1.66 (1.33-2.07)** | **FT1D** | |
| 22 | 22q12.2 | 29670355-30273198 | rs5753037<br>rs4820830 | | | | T1D | |
| 22 | 22q12.3 | 37171803-37262764 | rs229533 | *C1QTNF6*<br>*RAC2* | | | T1D | |
| X | Xq28 | 154425779-155057576 | rs2664170 | | | | T1D | |

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## SUPPLEMENTARY DATA

The data for fulminant type 1 diabetes (FT1D) obtained in the present study are shown in bold.
The data for autoimmune type 1 diabetes (T1D) were obtained from ImmunoBase: http://www.t1dbase.org/disease/T1D/
The data for autoimmune type 1 diabetes in Japanese (T1DJ) individuals were obtained from the following reference: Diabetes Metab Res Rev 2011;27:844-848. The SNPs associated with T1DJ are underlined.
* The associated SNPs in T1DJ differe from those in ImmunoBase: IL7R, rs6897932; IL2RA, rs706778; and CLEC16A, rs2903692.
AA: alopecia areata, ATD: autoimmune thyroid disease, CEL: celiac disease, CRO: Crohn's disease, IBD: inflammatory bowel disease, JIA: juvenile idiopathic arthritis, MS: multiple sclerosis, PBC: primary biliary cirrhosis, PSO: psoriasis, RA: rheumatoid arthritis, SLE: systemic lupus erythematosus, UC: ulcerative colitis, VIT: vitiligo
† OR, odds ratio; ‡ CI, confidence interval.

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SUPPLEMENTARY DATA

**Supplementary Table 4.** Seven variants identified by genotype imputation that exhibit a stronger association than rs3782151

| SNP | Chr. | Position | Gene(s) or nearby gene(s) | Reference allele | Alternative allele | OR | P |
|---|---|---|---|---|---|---|---|
| rs7304044 | 12q13.13 | 53142385 | CSAD | G | A | 1.975 | 7.09E-09 |
| rs11170439 | 12q13.13 | 53147705 | CSAD | C | T | 1.952 | 8.69E-09 |
| rs140878838 | 12q13.13 | 53147884:53147885 | CSAD | C | CAT | 1.954 | 7.99E-09 |
| rs7305472 | 12q13.13 | 53153307 | CSAD | C | T | 1.949 | 8.82E-09 |
| rs11170448 | 12q13.13 | 53154203 | CSAD | A | G | 1.949 | 8.82E-09 |
| **rs3782151** | **12q13.13** | **53158877** | **CSAD** | **C** | **A** | **1.949** | **8.82E-09** |
| rs10876414 | 12q13.13 | 53165245 | CSAD | A | G | 1.957 | 8.12E-09 |
| rs1465056 | 12q13.13 | 53171673 | CSAD | T | C | 1.974 | 5.52E-09 |

Genotype imputation using the 1000 Genomes Project data was performed using IMPUTE2 software with the default parameters. rs3782151, which was genotyped in the present study, is shown in bold.

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SUPPLEMENTARY DATA

**Supplementary Table 5.** Conditional analysis by controlling for top hit SNPs, rs11170445 and rs3782151.

A. Conditioned by rs3782151

| Predictor | FvR Model P-value* | Odds Ratio | OR Lower | OR Upper |
|---|---|---|---|---|
| rs2272299 | 0.605 | 1.10 | 0.77 | 1.56 |
| rs4606556 | 0.302 | 1.21 | 0.84 | 1.73 |

B. Conditioned by rs11170445

| Predictor | FvR Model P-value* | Odds Ratio | OR Lower | OR Upper |
|---|---|---|---|---|
| rs2272299 | 0.568 | 1.11 | 0.78 | 1.57 |
| rs4606556 | 0.277 | 1.22 | 0.85 | 1.74 |

*Numeric regression analysis was carried out to obtain a full-vs-reduced-model (FvR Model) p-value using rs3782151 and rs11170445 as covariates.

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SUPPLEMENTARY DATA

**Supplementary Table 6.** Haplotype analysis of 13 SNPs in LD block 1 in the *CSAD-ITGB7* region.

| Haplotype | Fulminant type 1 diabetes (2n=514) | | Control (2n=838) | | OR (95%CI) * | P * |
|---|---|---|---|---|---|---|
| SNP #1-#13 | 2n | frequency | 2n | frequency | | |
| ACACTGAAGAGTC | 261 | 0.508 | 533 | 0.636 | 0.59 (0.47-0.74) | $3.32 \times 10^{-6}$ |
| G**T**G**A**CGCGTAAGC | 117 | 0.228 | 116 | 0.138 | 1.83 (1.38-2.44) | $2.49 \times 10^{-5}$ |
| G**T**A**A**TAAAGAGTG | 58 | 0.113 | 61 | 0.073 | 1.62 (1.11-2.36) | 0.0116 |
| G**T**A**A**TAAAGGGTG | 31 | 0.060 | 46 | 0.055 | 1.11 (0.69-1.77) | 0.6764 |
| GCACTGAAGAGTC | 18 | 0.035 | 56 | 0.067 | 0.51 (0.29-0.87) | 0.0126 |
| G**T**G**A**CGCGTAGTC | 15 | 0.029 | 12 | 0.014 | 2.07 (0.96-4.46) | 0.0578 |
| A**T**G**A**CGCGTAAGC | 7 | 0.014 | 8 | 0.010 | 1.43 (0.52-3.97) | 0.4877 |
| others | 7 | 0.014 | 6 | 0.010 | | |

Haplotypes of SNP #1-13 in LD block shown in Figure 2: #1, rs7965802; #2, **rs11170445**; #3, rs12161793; #4, **rs3782151**; #5, rs2272305; #6, rs2272306; #7, rs2293429; #8, rs3814777; #9, rs4606556; #10, rs2272298; #11, rs2272299; #12, rs2272300; and #13, rs2272301.
SNPs showing a genome-wide significant association with fulminant type 1 diabetes and their corresponding disease-associated allele are shown in bold.
The haplotypes were estimated using the PHASE program (version 2.1).
* Chi-squared test in two-by-two cross tables was used to examine the associations between haplotypes and fulminant type 1 diabetes. In this analysis, each haplotype was assumed to be one of the alleles at a biallelic locus, and the other haplotypes were assumed to be the other allele. For example, the first haplotype (ACACTGAAGAGTC) and the other haplotypes were designated “A allele” and “B allele”, respectively.

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SUPPLEMENTARY DATA

**Supplementary Table 7.** Effect of the HLA *DR-DQ* haplotypes on the association of rs3782151 in *CSAD* with fulminant type 1 diabetes.

A. Susceptible HLA haplotypes for fulminant type 1 diabetes. The top and middle panels show the association of HLA with the disease, and the bottom panel shows the association of the minor A allele of rs372151 with the disease relative to the HLA genotype.

| | | Control | | Fulminant type 1 diabetes | | OR* | [95%CI†] | P |
|---|---|---|---|---|---|---|---|---|
| | | 2n=838 | frequency | 2n=432 | frequency | | | |
| *DR-DQ* haplotype | *DRB1*04:05-DQB1*04:01* | 121 | 0.144 | 142 | 0.329 | 2.90 | [2.20-3.83] | $2.82 \times 10^{-14}$ |
| | *DRB1*09:01-DQB1*03:03* | 124 | 0.148 | 116 | 0.269 | 2.11 | [1.59-2.81] | $2.01 \times 10^{-7}$ |
| | | n=419 | frequency | n=216 | frequency | | | |
| Haplotype combination | S/ S‡ | 40 | 0.095 | 78 | 0.361 | 5.36 | [3.49-8.22] | $8.58 \times 10^{-16}$ |
| | S/ N§ | 165 | 0.394 | 102 | 0.472 | 1.38 | [0.99-1.92] | 0.058 |
| | N/ N | 214 | 0.511 | 36 | 0.167 | 0.19 | [0.13-0.29] | $8.66 \times 10^{-17}$ |
| | | 2n | frequency | 2n | frequency | | | |
| A allele of rs372151 | Total | 246/836 | 0.294 | 193/432 | 0.447 | 1.94 | [1.52-2.46] | $6.32 \times 10^{-8}$ |
| | Subjects with S/S | 22/80 | 0.275 | 70/156 | 0.449 | 2.15 | [1.20-3.85] | 0.010 |
| | Subjects with S/N | 101/328 | 0.308 | 94/204 | 0.461 | 1.92 | [1.34-2.76] | 0.000374 |
| | Subjects with N/N | 123/428 | 0.287 | 29/72 | 0.403 | 1.67 | [1.00-2.80] | 0.049 |
| | Heterogeneity | | | | | | | 0.916# |

* OR, odds ratio; † CI, confidence interval.
‡ S: susceptible haplotypes, *DRB1*04:05-DQB1*04:01* or *DRB1*09:01-DQB1*03:03*
§ N: non-susceptible haplotypes, haplotypes other than *DRB1*04:05-DQB1*04:01* and *DRB1*09:01-DQB1*03:03*
# The P value for heterogeneity assessed ~~by~~ using the random-effect (DerSimonian and Laird) method.

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SUPPLEMENTARY DATA

B. HLA-DR4 and DR9 haplotypes.

The upper panel shows the association of HLA genotypes with the disease, and the lower panel shows the association of the minor T allele of rs372151 with the disease relative to HLA genotypes.

| | | Control | | Fulminant type 1 diabetes | | OR* | [95%CI†] | P |
|---|---|---|---|---|---|---|---|---|
| | | n=419 | frequency | n=216 | frequency | | | |
| Haplotype combination | *DR4/DR4* | 11 | 0.026 | 31 | 0.144 | 6.22 | [3.06-12.63] | $1.78 \times 10^{-8}$ |
| | *DR9/DR9* | 12 | 0.029 | 21 | 0.097 | 3.65 | [1.76-7.58] | $2.25 \times 10^{-4}$ |
| | *DR4/DR9* | 17 | 0.041 | 26 | 0.120 | 3.24 | [1.71-6.11] | $1.50 \times 10^{-4}$ |
| | *DR4/others* | 82 | 0.196 | 54 | 0.250 | 1.37 | [0.93-2.03] | NS |
| | *DR9/others* | 83 | 0.198 | 48 | 0.222 | 1.16 | [0.77-1.73] | NS |
| | *Others/others* | 214 | 0.511 | 36 | 0.167 | 0.19 | [0.13-0.29] | $8.66 \times 10^{-17}$ |
| | | n | frequency | n | frequency | | | |
| A allele of rs372151 | Total | 246/836 | 0.294 | 191/432 | 0.442 | 1.90 | [1.49-2.42] | $1.51 \times 10^{-7}$ |
| | Subjects with *DR4/DR4* | 5/22 | 0.227 | 25/62 | 0.403 | 2.30 | [0.75-7.03] | NS |
| | Subjects with *DR9/DR9* | 7/24 | 0.292 | 20/42 | 0.476 | 2.21 | [0.76-6.43] | NS |
| | Subjects with *DR4/DR9* | 10/34 | 0.294 | 25/52 | 0.481 | 2.22 | [0.89-5.56] | NS |
| | Subjects with *DR4/others* | 46/164 | 0.280 | 51/108 | 0.472 | 2.30 | [1.38-3.82] | 0.001 |
| | Subjects with *DR9/others* | 55/164 | 0.335 | 41/96 | 0.427 | 1.48 | [0.88-2.48] | NS |
| | Subjects with *others* | 123/428 | 0.287 | 29/72 | 0.403 | 1.67 | [1.00-2.80] | 0.049 |
| | Heterogeneity | | | | | | | 0.969# |

* OR, odds ratio; † CI, confidence interval.

*DR4*: *DRB1*04:05-DQB1*04:01*, *DR9*: *DRB1*09:01-DQB1*03:03, others:* haplotypes other than *DR4 and DR9*

# The P value for heterogeneity assessed using the random-effect (DerSimonian and Laird) method.

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C. Relationship between a top-hit SNP in the HLA region, rs9268853, and disease-associated HLA haplotypes.

HLA-DR4 haplotype (*DRB1*04:05-DQB1*04:01*)

| | Control | | | Fulminant type 1 diabetes | | |
|---|---|---|---|---|---|---|
| | rs9268853 | | | rs9268853 | | |
| | with C allele | without C allele | P | with C allele | without C allele | P |
| with DR4 haplotype | 146 | 72 | $2.12 \times 10^{-22}$ | 179 | 43 | $5.60 \times 10^{-9}$ |
| without DR4 haplotype | 180 | 436 | | 114 | 96 | |

HLA-DR9 haplotype (*DRB1*09:01-DQB1*03:03*)

| | Control | | | Fulminant type 1 diabetes | | |
|---|---|---|---|---|---|---|
| | rs9268853 | | | rs9268853 | | |
| | with C allele | without C allele | P | with C allele | without C allele | P |
| with DR9 haplotype | 154 | 70 | $5.85 \times 10^{-26}$ | 148 | 42 | $7.66 \times 10^{-5}$ |
| without DR9 haplotype | 172 | 438 | | 145 | 97 | |

Data are number of subjects with or without C allele of rs9268853 relative to the presence or absence of disease-associated HLA haplotypes, *DR4* (*DRB1*04:05-DQB1*04:01*) and *DR9* (*DRB1*09:01-DQB1*03:03*).

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SUPPLEMENTARY DATA

**Supplementary Table 8.** Association of *CSAD* (rs3782151) and *ITGB7* (rs2272299) with classical autoimmune type 1 diabetes in European and Japanese populations.

| Population | *CSAD* (rs3782151) | | | | | | *ITGB7* (rs2272299) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Control | Type 1 | | OR [95%CI] * | | | Control | Type 1 | | OR [95%CI] | |
| | | | autoimmune | fulminant | autoimmune | fulminant | | | autoimmune | fulminant | autoimmune | fulminant |
| European§ | | 2n=11,826 | 2n=17,656 | | | | | 2n=11,826 | 2n=17,656 | | | |
| | C | 0.80 | 0.794 | | | | G | 0.951 | 0.944 | | | |
| | A | 0.20 | 0.206 | | 1.04 [0.98-1.10] | | A | 0.049 | 0.056 | | 1.15 [1.04-1.28] | |
| | | | | | (P=0.365) | | | | | | (P=0.0063) | |
| Japanese | | 2n =836 | 2n=820 | 2n=514 | | | | 2n=838 | 2n=818 | 2n=510 | | |
| | C | 0.706 | 0.648 | 0.549 | | | G | 0.851 | 0.778 | 0.755 | | |
| | A | 0.294 | 0.352 | 0.451 | 1.31 [1.06-1.60] | 1.97 [1.57-2.48] | A | 0.149 | 0.222 | 0.245 | 1.63 [1.27-2.10] | 1.85 [1.40-2.44] |
| | | | | | (P=0.011) | (P=4.60 x $10^{-9}$) | | | | | (P=0.0001) | (P=1.11 x $10^{-5}$) |
| Total † | A | | | | 1.05 [1.00-1.12]‡ | | A | | | | 1.21 [1.10-1.34]‡ | |
| | | | | | P=0.060 | | | | | | P=9.68 x $10^{-5}$ | |

The data show the allele frequencies, and data for fulminant type 1 diabetes in the Japanese population are shown for comparison purposes.
* OR: odds ratio; CI, confidence interval.
† Meta-analysis ~~by~~ using the Mantel-Haenszel method.
‡ Summary odds ratio [95% confidence interval], the P value for heterogeneity was >0.05 for both rs3782151 in *CSAD* and rs2272299 in *ITGB7*.
§The data were obtained from the Type 1 Diabetes Genetics Consortium (https://repository.niddk.nih.gov/studies/t1dgc/).

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SUPPLEMENTARY DATA

**Supplementary Table 9.** Frequencies of *CSAD-ITGB7* (rs3782151-rs2272299) haplotypes in Japanese participants.

| Haplotype | Control (C) 2n=836 | Fulminant (F) 2n=510 | Autoimmune (A) 2n=818 | OR [95%CI] * F vs. C | OR [95%CI] * A vs. C | OR [95%CI] * F vs. A | P F vs. C | P A vs. C | P F vs. A |
|---|---|---|---|---|---|---|---|---|---|
| A-A | 125 (0.150) | 125 (0.245) | 176 (0.215) | 1.85 [1.40-2.44] | 1.56 [1.21-2.01] | 1.18 [0.91-1.54] | $1.22 \times 10^{-5}$ | $5.42 \times 10^{-4}$ | NS |
| A-G | 121 (0.145) | 105 (0.206) | 113 (0.138) | 1.53 [1.15-2.04] | 0.95 [0.72-1.25] | 1.62 [1.21-2.17] | 0.004 | NS | 0.001 |
| C-G | 590 (0.706) | 280 (0.549) | 523 (0.639) | 0.51 [0.40-0.64] | 0.74 [0.60-0.91] | 0.69 [0.55-0.86] | $5.38 \times 10^{-9}$ | 0.004 | 0.001 |
| C-A | 0 (0) | 0 (0) | 6 (0.007) | | | | | | |

The haplotypes were estimated using the PHASE program (version 2.1).
The number of subjects is shown, and the frequency is indicated in parenthesis.
* OR, odds ratio; CI, confidence interval.

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SUPPLEMENTARY DATA

**Supplementary Table 10A.** Frequencies of *CSAD-ITGB7* (rs3782151-rs2272299) haplotypes in the European population.

| Haplotype | Control<br>2n=450 | Autoimmune type 1 diabetes<br>2n=458 | OR<br>[95%CI] * | P |
|---|---|---|---|---|
| A-A | 11<br>(0.024) | 34<br>(0.074) | 3.20<br>[1.60-6.40] | $5.47 \times 10^{-4}$ |
| A-G | 113<br>(0.251) | 86<br>(0.188) | 0.69<br>[0.50-0.95] | 0.021 |
| C-G | 326<br>(0.724) | 338<br>(0.738) | 1.07<br>[0.80-1.44] | NS |
| C-A | 0<br>(0) | 0<br>(0.000) | | |

The haplotypes were estimated using the PHASE program (version 2.1).
The number of subjects is shown, and the frequency is indicated in parenthesis.
* OR, odds ratio; CI, confidence interval.
Due to the near-absence of fulminant type 1 diabetes in European populations, only data for autoimmune type 1 diabetes are shown.
Samples were from Noso S et al. J Genet Syndr Gene Ther 2013;4:204.

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SUPPLEMENTARY DATA

**Supplementary Table 10B.** Comparison of *CSAD-ITGB7* (rs3782151-rs2272299) haplotype frequencies between Japanese and European populations.

| Haplotype | Controls | | OR | P | Autoimmune type 1 diabetes | | OR | P |
|---|---|---|---|---|---|---|---|---|
| | Japanese 2n=836 | European 2n=450 | [95%CI] * | | Japanese 2n=818 | European 2n=458 | [95%CI] * | |
| A-A | 125 (0.150) | 11 (0.024) | 7.02 [3.75-13.14] | $3.49 \times 10^{-12}$ | 176 (0.215) | 34 (0.074) | 3.42 [2.32-5.03] | $7.41 \times 10^{-11}$ |
| A-G | 121 (0.145) | 113 (0.251) | 0.50 [0.38-0.67] | $2.41 \times 10^{-6}$ | 113 (0.138) | 86 (0.188) | 0.69 [0.51-0.94] | 0.019 |
| C-G | 590 (0.706) | 326 (0.724) | 0.94 [0.71-1.18] | 0.48 | 523 (0.639) | 338 (0.738) | 0.63 [0.49-0.81] | $3.09 \times 10^{-4}$ |
| C-A | 0 (0) | 0 (0) | | | 6 (0.007) | 0 (0) | | |

The haplotypes were estimated using the PHASE program (version 2.1).
The number of subjects is shown, and the frequency is indicated in parenthesis.
* OR, odds ratio; CI, confidence interval.
Due to the near-absence of fulminant type 1 diabetes in European populations, only data for autoimmune type 1 diabetes are shown.

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SUPPLEMENTARY DATA

**Supplementary Table 11.** Variants identified by re-sequencing of the *CSAD* region in 32 individuals with fulminant type 1 diabetes who were homozygous for the disease-associated allele of the top- hit SNP, rs3782151.

| variant number | Chr. | position* | Gene or nearby gene | Type | Location | Amino Acid Change | Ref. | Variant | MAF Japanese† | MAF European‡ | dbSNP§ | MAF update Japanese ‖ | P for disease¶ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 001 | chr12 | 53158691 | *CSAD* | SNV | intronic | | A | G | 0.2163 | 0.0556 | ***rs12161793*** | 0.197 | $7.30 \times 10^{-6}$ |
| 002 | chr12 | 53158877 | *CSAD* | SNV | intronic | | G | T | 0.3846 | 0.2525 | ***rs3782151*** | 0.3407 | $4.60 \times 10^{-9}$ |
| 003 | chr12 | 53159448 | *CSAD* | INDEL | intronic | | T | - | | | | novel | |
| 004 | chr12 | 53159448 | *CSAD* | SNV | intronic | | T | C | 0.2163 | 0.0556 | ***rs2272305*** | | $9.28 \times 10^{-7}$ |
| 005 | chr12 | 53160499 | *CSAD* | SNV | intronic | | G | A | 0.1683 | 0.1869 | ***rs2272306*** | 0.1341 | 0.02 |
| 006 | chr12 | 53161148 | *CSAD* | SNV | **exonic** | **His288Arg** | T | C | | | | 0.0001 | |
| 007 | chr12 | 53161674 | *CSAD* | SNV | intronic | | A | T | 0.2163 | 0.0556 | rs11170451 | | |
| 008 | chr12 | 53164591 | *CSAD* | SNV | intronic | | G | A | | | | 0.0052 | |
| 009 | chr12 | 53164687 | *CSAD* | SNV | intronic | | C | T | | | | 0.0001 | |
| 010 | chr12 | 53165187 | *CSAD* | SNV | intronic | | T | A | | | | novel | |
| 011 | chr12 | 53165191 | *CSAD* | SNV | intronic | | A | T | | | | novel | |
| 012 | chr12 | 53165195 | *CSAD* | SNV | intronic | | G | A | | | | novel | |
| 013 | chr12 | 53165245 | *CSAD* | SNV | intronic | | A | G | 0.3846 | 0.2525 | rs10876414 | | |
| 014 | chr12 | 53166711 | *CSAD* | SNV | intronic | | G | A | 0.0048 | 0.0000 | rs11170452 | | |
| 015 | chr12 | 53169893 | *CSAD* | SNV | intronic | | G | A | | | | novel | |
| 016 | chr12 | 53169913 | *CSAD* | INDEL | intronic | | - | C | | | | novel | |
| 017 | chr12 | 53170081 | *CSAD* | SNV | **exonic** | synonymous | G | A | 0.02115 | 0.0505 | rs11170453 | 0.1988 | |
| 018 | chr12 | 53170150 | *CSAD* | SNV | intronic | | A | G | 0.0096 | 0.0000 | rs146549996 | 0.0034 | |
| 019 | chr12 | 53171195 | *CSAD* | INDEL | intronic | | - | G | | | | novel | |
| 020 | chr12 | 53171673 | *CSAD* | SNV | intronic | | T | C | 0.3846 | 0.2525 | rs1465056 | 0.3404 | |
| 021 | chr12 | 53171898 | *CSAD* | SNV | **exonic** | synonymous | G | A | | | | 0.0001 | |
| 022 | chr12 | 53174848 | *CSAD* | SNV | intronic | | A | C | | | | 0.0001 | |
| 023 | chr12 | 53175280 | *CSAD* | SNV | intronic | | G | A | 0.0192 | 0.0000 | rs75249111 | 0.0326 | |
| 024 | chr12 | 53176875 | *CSAD* | SNV | intronic | | G | C | 0.2163 | 0.0556 | rs11170454 | | |
| 025 | chr12 | 53177190 | *CSAD* | SNV | intronic | | T | C | | | | 0.0001 | |
| 026 | chr12 | 53177469 | *CSAD* | SNV | intronic | | A | T | | | | novel | |
| 027 | chr12 | 53178076 | *CSAD* | SNV | intronic | | A | C | 0.2163 | 0.0556 | rs12580404 | 0.1997 | |
| 028 | chr12 | 53178346 | *CSAD* | SNV | intronic | | T | G | 0.2163 | 0.0556 | rs10876417 | | |
| 029 | chr12 | 53180119 | *CSAD,ZNF740* | SNV | intronic, upstream | | A | C | 0.2163 | 0.0556 | ***rs2293429*** | 0.2023 | $2.11 \times 10^{-6}$ |
| 030 | chr12 | 53180260 | *CSAD,ZNF740* | SNV | intronic, upstream | | G | C | 0.2115 | 0.0556 | rs2293430 | | |
| 031 | chr12 | 53180261 | *CSAD,ZNF740* | SNV | intronic, upstream | | A | C | 0.2115 | 0.0556 | rs2293431 | | |
| 032 | chr12 | 53180484 | *CSAD,ZNF740* | SNV | intronic, upstream | | C | T | | | | novel | |

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| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 033 | chr12 | 53180582 | *CSAD,ZNF740* | SNV | intronic, upstream | C | T | 0.2163 | 0.0556 | rs34628172 | 0.2014 |
| 034 | chr12 | 53180706 | *CSAD,ZNF740* | SNV | intronic, upstream | G | A | 0.1635 | 0.1818 | rs3108403 | 0.1341 |
| 035 | chr12 | 53180708 | *CSAD,ZNF740* | SNV | intronic, upstream | C | A | 0.0385 | 0.0000 | rs138922341 | 0.0533 |
| 036 | chr12 | 53180823 | *CSAD,ZNF740* | SNV | utr_5, utr_5 | G | C | 0.0385 | 0.0000 | rs187048132 | 0.0537 |
| 037 | chr12 | 53180847 | *CSAD,ZNF740* | SNV | utr_5, intronic | A | C | 0.2163 | 0.0657 | rs59218377 | 0.1991 |

Accession number: JGAS00000000144, the DDBJ Japanese Genotype-phenotype Archive for genetic and phenotypic human data.
Chr., Chromosome, Ref., reference; SNV, single nucleotide variant; INDEL, insertion/deletion; utr, untranslated region.

[*] Genome Reference Consortium Human Build 38 patch release 7 (GRCh38.p7), annotation release 108.

[†] Frequency in Japanese in the 1000 Genomes Project browser (n=208, JTK: Japanese in Tokyo, Japan). https://www.ncbi.nlm.nih.gov/variation/tools/1000genomes/

[‡] Frequency in Europeans in the 1000 Genomes Project browser (n=198, CEU: Utah residents with Northern and Western European ancestry from the CEPH collection).

[§] The SNPs used for fine mapping are shown in bold and italics.
rs10876414 and rs1465056 were in complete linkage disequilibrium with the top-hit SNP, rs378215; these SNPs are shown for reference (underlined).
Because the samples used for re-sequencing were selected from patients homozygous for the disease-associated allele at rs378215, no variant was identified for these SNPs during the re-sequencing.

[‖] Frequency in Japanese in the database from the Tohoku Medical Megabank Organization (TMMO, n=3554). https://ijgvd.megabank.tohoku.ac.jp/
The term “novel” indicates that variants were identified by re-sequencing in this study.

[¶] P values for association with fulminant type 1 diabetes obtained in this study

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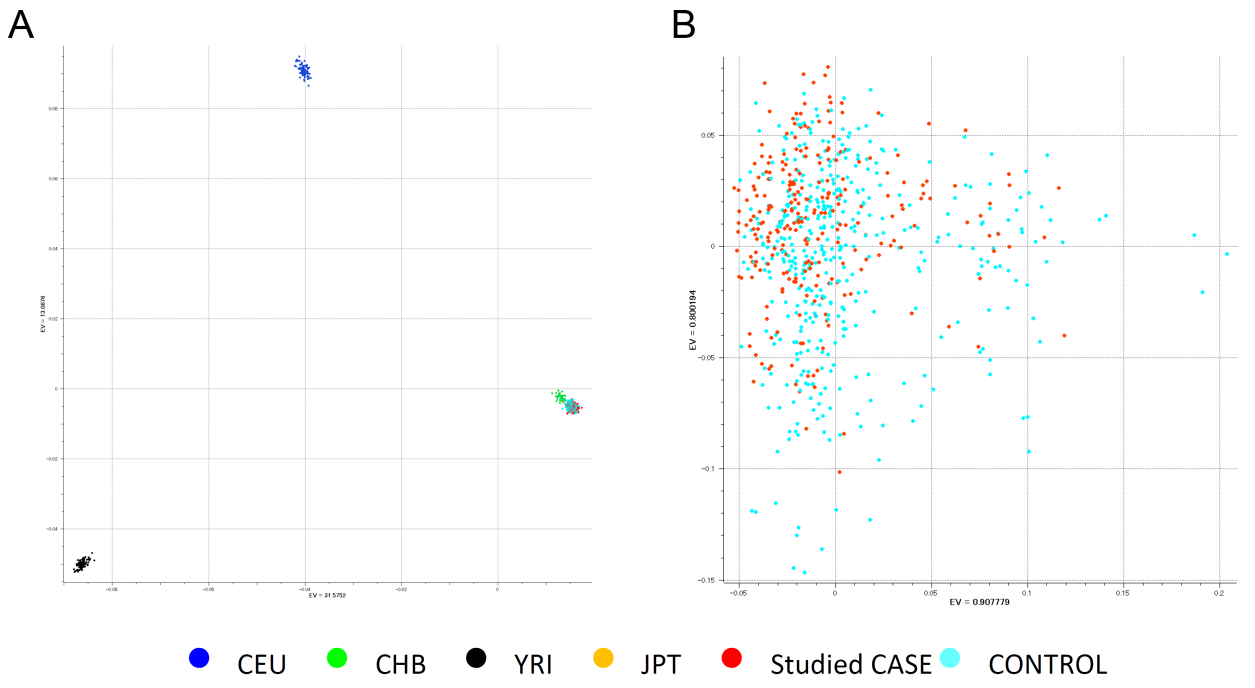
SUPPLEMENTARY DATA

**Supplementary Figure 1.** Principal component analysis of 676 samples used in the GWAS together with HapMap samples (43 JPT, 40 CHB, 91 YRI, and 91 CEU samples)




(A) all groups, (B) focused on Japanese samples in the present study.
CEU: Utah Residents (CEPH) with Northern and Western European ancestry; CHB: Han Chinese in Beijing, China; YRI: Yoruba in Ibadan, Nigeria; JPT: Japanese in Tokyo, Japan

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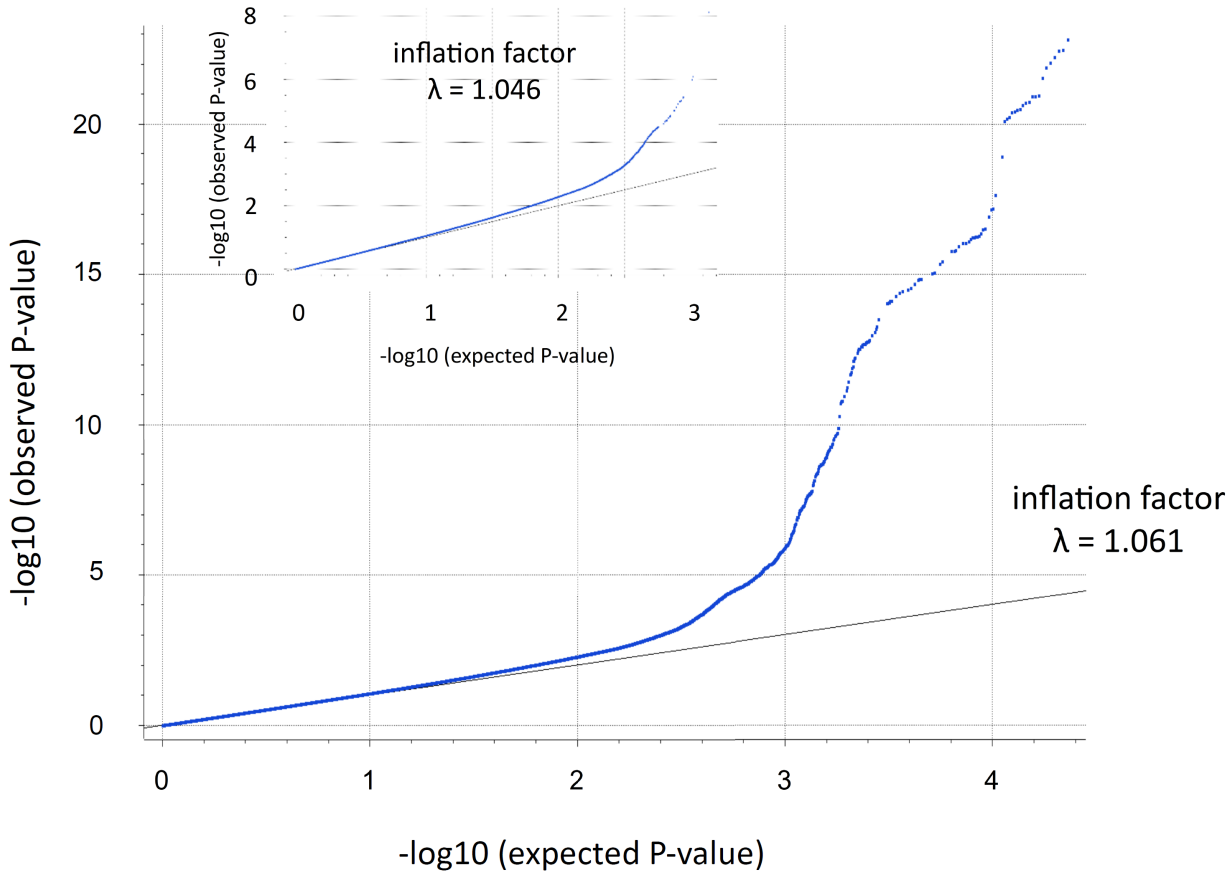
SUPPLEMENTARY DATA

**Supplementary Figure 2.** Quantile-quantile plot for test statistics (Cochran-Armitage trend test) for 425,767 SNPs that passed quality control. The quantile-quantile plot after removal of the loci in the HLA region is shown in the inset.

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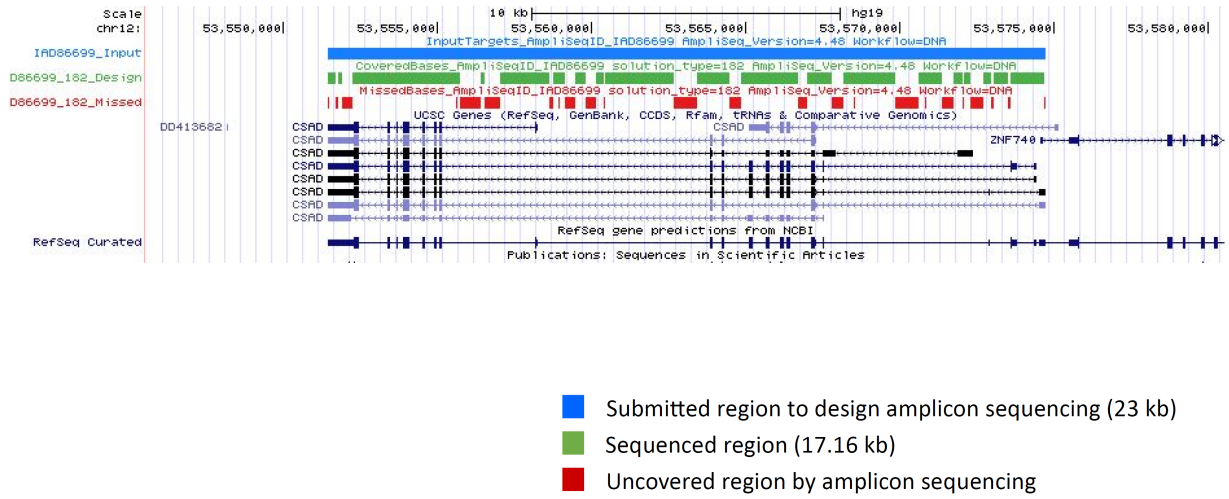
SUPPLEMENTARY DATA

**Supplementary Figure 3.** Exon-intron structure of the CSAD gene and re-sequenced region.




Submitted region to design amplicon sequencing (23 kb)

Sequenced region (17.16 kb)

Uncovered region by amplicon sequencing

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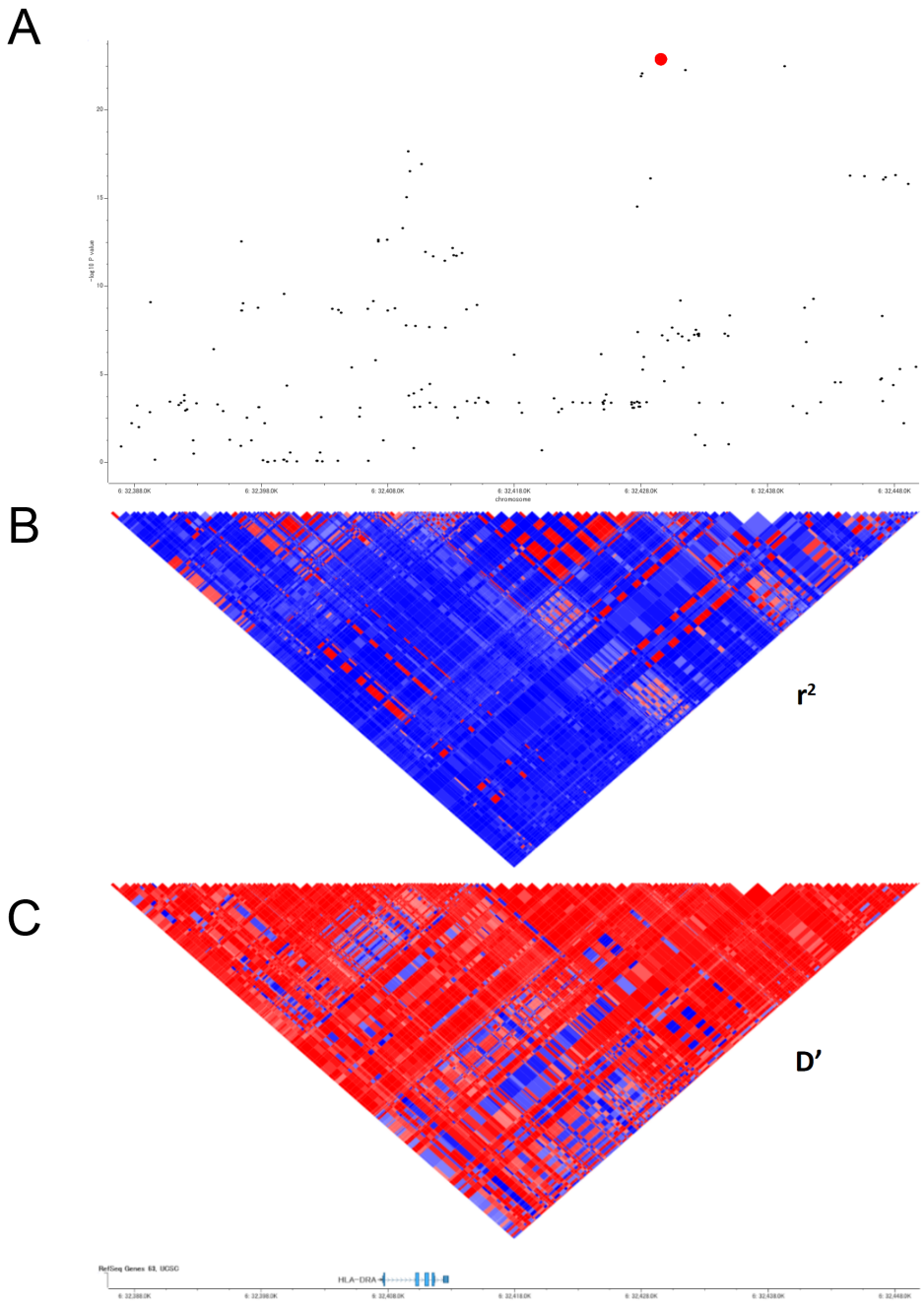
SUPPLEMENTARY DATA

**Supplementary Figure 4.** Linkage disequilibrium structure for the risk HLA-DR locus for fulminant type 1 diabetes in about 64 kb genetic region around GWAS top hit SNP rs9268853.




The top panel (A) shows the $-\log_{10}$ (P values) for 177 SNPs compared between 257 fulminant type 1 diabetes patients and 419 healthy individuals.

The second and third panels show a Haploview plot of linkage disequilibrium (LD) between markers measured by $r^2$ (B) and D'(C) in the 676 samples including 257 fulminant type 1 diabetes and 419 healthy individuals. The top hit SNP rs9268853 associated with fulminant type 1 diabetes with genome-wide significance is highlighted in red in the top panel

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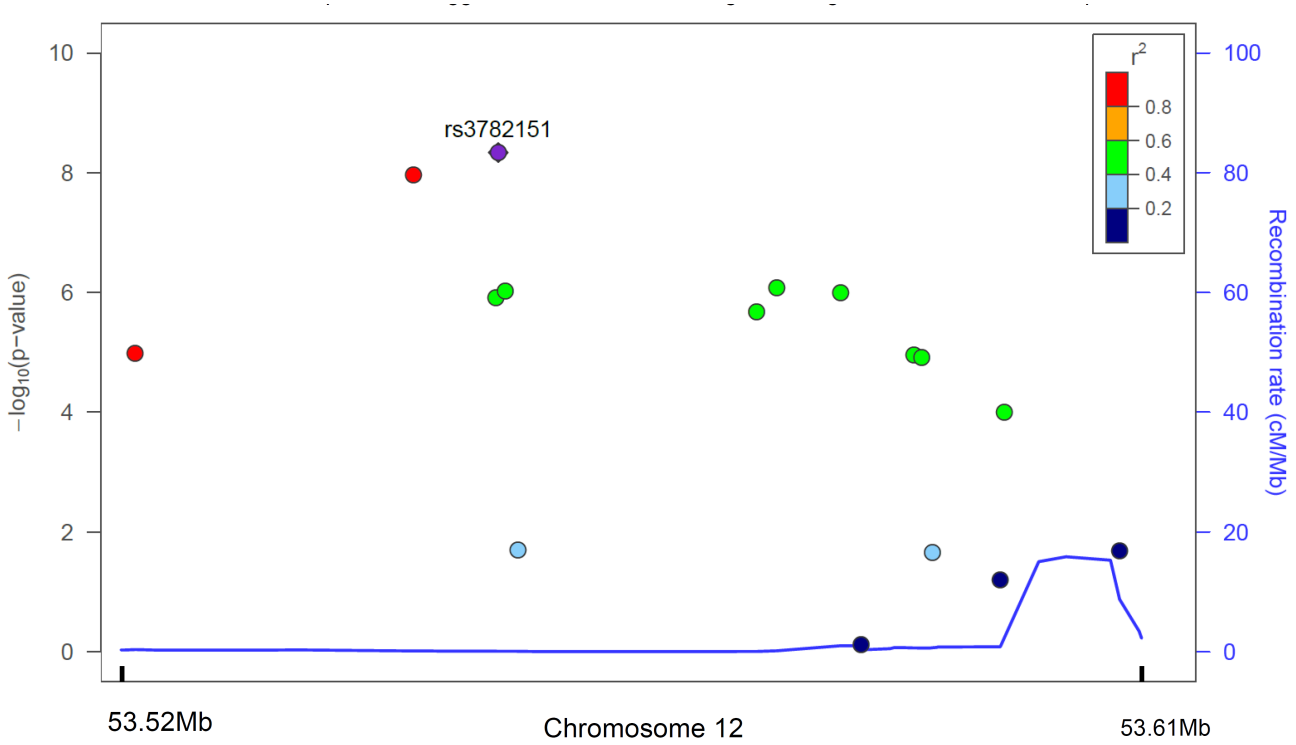
SUPPLEMENTARY DATA

**Supplementary Figure 5.** Locus zoom plot of 16 tagged SNPs in about 90 kb genetic region on chromosome 12q13.13




Locus zoom plot* compared between 257 fulminant type 1 diabetes patients and 419 healthy individuals, using 1000 Genomes LD Asian population (Nov 2014) and the hg19 genome build as references. An top-hit SNP rs3782151 is highlighted. Colors of each circle represent r2 values. Blue line shows recombination rate. * Pruim RJ, Welch RP, Sanna S, et al. Bioinformatics 2010;26:2336-2337

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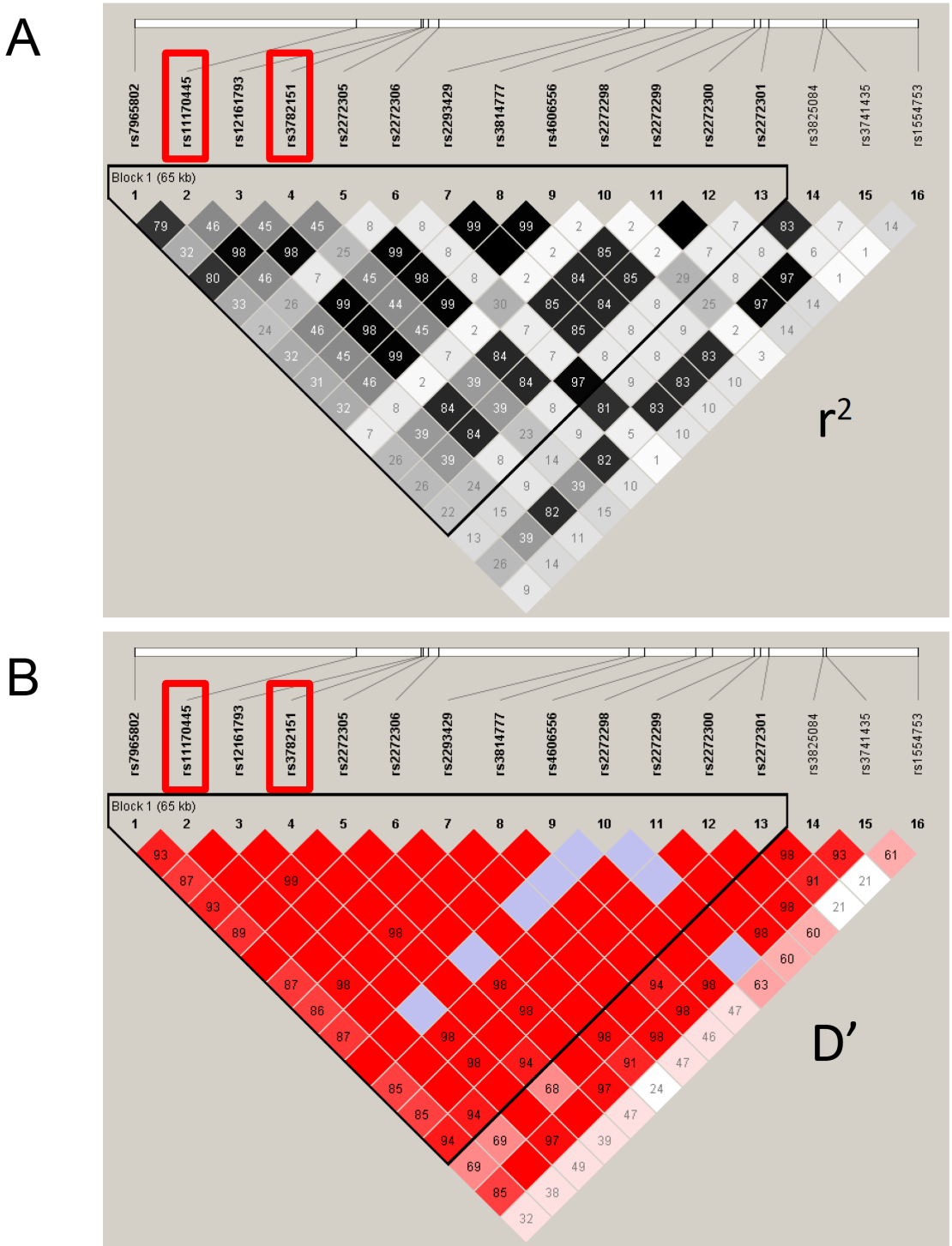
SUPPLEMENTARY DATA

**Supplementary Figure 6**. Linkage disequilibrium structure for the risk locus for fulminant type 1 diabetes in about 80 kb genetic region on chromosome 12q13.13 in samples with fulminant type 1 diabetes.




A Haploview plot of linkage disequilibrium (LD) between markers measured by $r^2$ (A) and D'(B) in the 257 samples with fulminant type 1 diabetes

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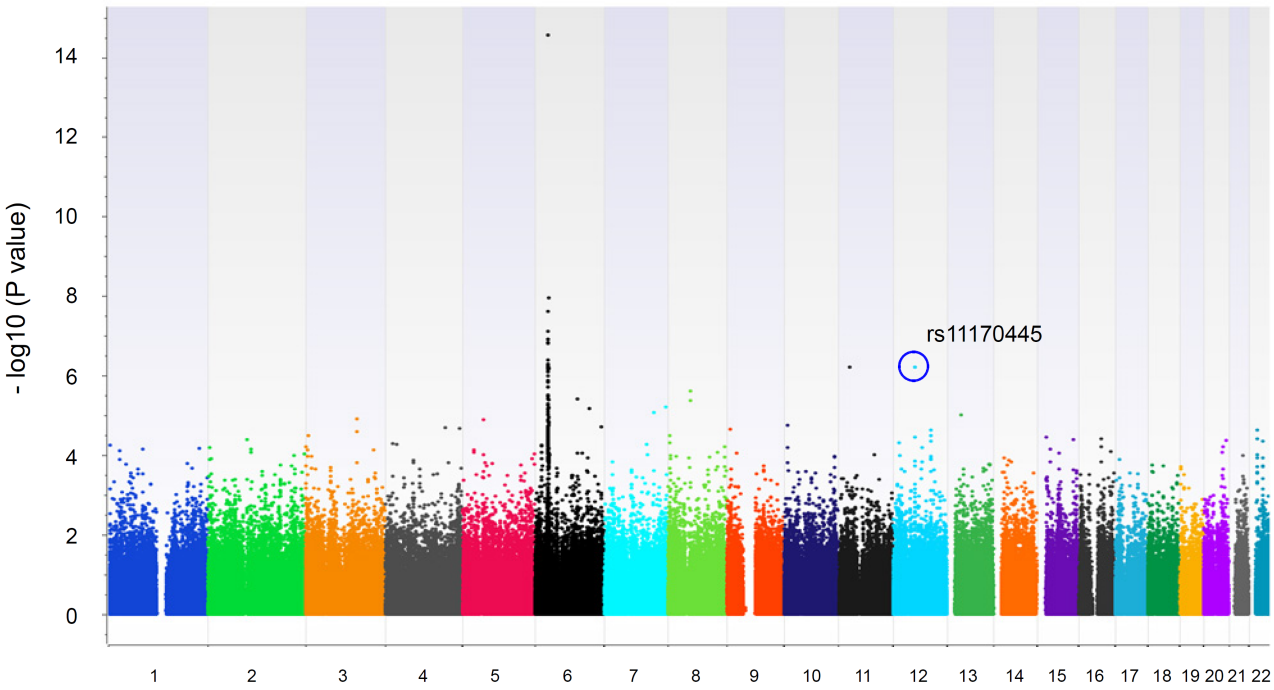
SUPPLEMENTARY DATA

**Supplementary Figure 7.** Genome-wide Manhattan plot applying a regression analysis with top hit SNP rs9268853 in the HLA as covariate. A top-hit SNP, rs11170445, associated with fulminant type 1 diabetes with genome-wide significance outside of HLA in Fig. 1 is highlighted.

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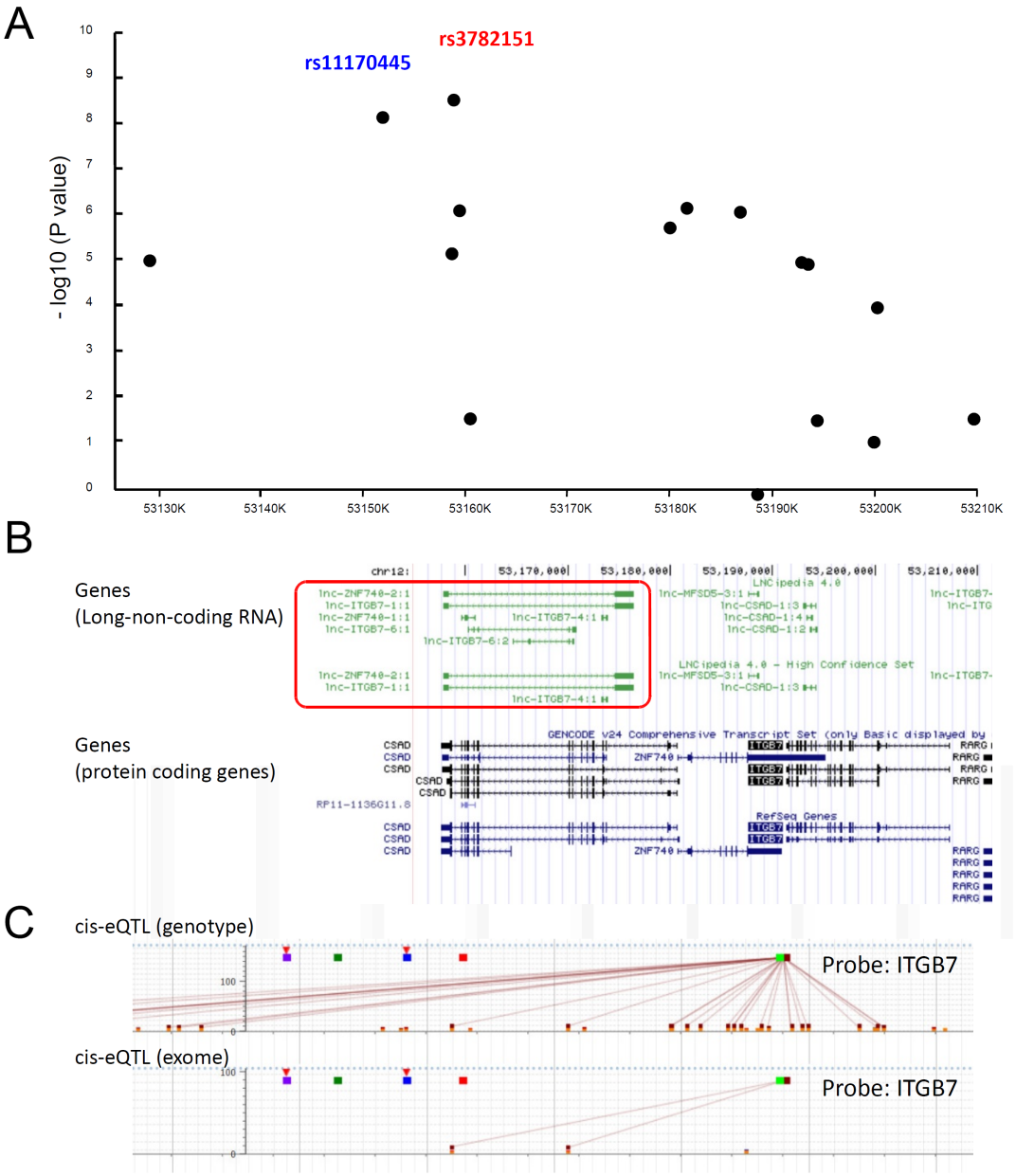
SUPPLEMENTARY DATA

**Supplementary Figure 8.** Location of disease-associated SNPs in the *CSAD/lnc-ITGB7-1* region and their effects on ITGB7 expression.




The top panel is the same as described in Figure 3 and shows the -log$_{10}$ (P values) from 16 tagged SNPs from the *CSAD-ITGB7* region.

The second panel is the genomic locations of the genes in this region. The top hit SNP rs3782151 is located in *CSAD* and in *lnc-ITGB7-1*, which encodes a long non-coding-RNA (RP11-1136G11.7) also known as lnc-ITGB7-1:1.

The third panel shows the cis-eQTL of *ITGB7* in the *CSAD/lnc-ITGB7-1* region (Human Genetic Variation Database [HGVD] Browser [http://www.hgvd.genome.med.kyoto-u.ac.jp/cgi-bin/searchBydbsnp.cgi]). SNPs in the *CSAD/lnc-ITGB7-1* region are cis-eQTLs of *ITGB7*. eQTLs with a significant effect on *ITGB7* expression are connected with the ITGB7 probe (green box) using lines.

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