Supplementary Information for Wallace *et al.*, Statistical colocalisation of monocyte gene expression and genetic risk variants for type 1 diabetes

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# Equivalence of Fieller and maximum likelihood test statistics

We being by reparameterising the model in terms of $\theta = \tan^{-1}(\eta)$, with the null hypothesis expressed as

$$\mathrm{H}_0 : \beta_1 = \beta \cos(\theta); \beta_2 = \beta \sin(\theta).$$

Then

$$\mathbf{b}_1 \sim N(\boldsymbol{\beta}_1, \mathbf{V}_1) \qquad\qquad \mathbf{b}_2 \sim N(\boldsymbol{\beta}_2, \mathbf{V}_2),$$

$$-2 \log L(\mathbf{b}1, \mathbf{b}2 | \beta, \theta) = (\mathbf{b}1 - \beta \cos(\theta))^T \mathbf{V}_1 (\mathbf{b}1 - \beta \cos(\theta)) + (\mathbf{b}2 - \beta \sin(\theta))^T \mathbf{V}_2 (\mathbf{b}2 - \beta \sin(\theta))$$

and the maximum likelihood estimate of $\boldsymbol{\beta}$ is

$$\widetilde{\boldsymbol{\beta}} = \left( \cos^2 \theta \mathbf{V}_1^{-1} + \sin^2 \theta \mathbf{V}_2^{-1} \right)^{-1} \left( \cos \theta \mathbf{V}_1^{-1} \mathbf{b}_1 + \sin \theta \mathbf{V}_2^{-1} \mathbf{b}_2 \right)$$

$$\mathrm{E}(\widetilde{\boldsymbol{\beta}}) = \boldsymbol{\beta}$$

$$\mathrm{Var}(\widetilde{\boldsymbol{\beta}}) = \left( \cos^2 \theta \mathbf{V}_1^{-1} + \sin^2 \theta \mathbf{V}_2^{-1} \right)^{-1} = \mathbf{V}_+, \tag{1}$$

so that

$$-2 \log L = \mathbf{b}1^T \mathbf{V}_1^{-1} \mathbf{b}1 + \mathbf{b}2^T \mathbf{V}_2^{-1} \mathbf{b}2 - 2\beta^2 \mathbf{V}_+ \widetilde{\boldsymbol{\beta}} + \boldsymbol{\beta}^T \mathbf{V}_+ \boldsymbol{\beta}. \tag{2}$$

Using a profile likelihood approach, we replace $\boldsymbol{\beta}$ by $\widetilde{\boldsymbol{\beta}}$ to obtain

$$
\begin{aligned}
-2 \log L = {}& \mathbf{b}1^T \mathbf{V}_1^{-1} \mathbf{b}1 + \mathbf{b}2^T \mathbf{V}_2^{-1} \mathbf{b}2 - \widetilde{\boldsymbol{\beta}}^T \mathbf{V}_+ \widetilde{\boldsymbol{\beta}} \\
={}& \mathbf{b}_1^T \left( \mathbf{V}_1^{-1} - \cos^2 \theta \mathbf{V}_1^{-1} \mathbf{V}_+ \mathbf{V}_1^{-1} \right) \mathbf{b}1 + \mathbf{b}_2^T \left( \mathbf{V}_2^{-1} - \sin^2 \theta \mathbf{V}_2^{-1} \mathbf{V}_+ \mathbf{V}_2^{-1} \right) \mathbf{b}2 \\
& - 2 \sin \theta \cos \theta \mathbf{b}1^T \left( \mathbf{V}_1^{-1} \mathbf{V}_+ \mathbf{V}_2^{-1} \right) \mathbf{b}2 \\
={}& \mathbf{b}_1^T \left( \mathbf{V}_1^{-1} - \mathbf{V}_1^{-1} \mathbf{V}_+ (\mathbf{V}_+ - \sin^2 \theta \mathbf{V}_2^{-1}) \right) \mathbf{b}1 + \mathbf{b}_2^T \left( \mathbf{V}_2^{-1} - \mathbf{V}_2^{-1} \mathbf{V}_+ (\mathbf{V}_+ - \cos^2 \theta \mathbf{V}_1^{-1}) \right) \mathbf{b}2 \\
& - 2 \sin \theta \cos \theta \mathbf{b}1^T \left( \mathbf{V}_1^{-1} \mathbf{V}_+ \mathbf{V}_2^{-1} \right) \mathbf{b}2 \\
={}& \sin^2 \theta \mathbf{b}_1^T \mathbf{V}_1^{-1} \mathbf{V}_+ \mathbf{V}_2^{-1} \mathbf{b}_1 + \cos^2 \theta \mathbf{b}_2^T \mathbf{V}_2^{-1} \mathbf{V}_+ \mathbf{V}_1^{-1} \mathbf{b}_2 - 2 \sin \theta \cos \theta \mathbf{b}_1^T \mathbf{V}_1^{-1} \mathbf{V}_+ \mathbf{V}_2^{-1} \mathbf{b}_2^T \\
={}& (\sin \theta \mathbf{b}_1 - \cos \theta \mathbf{b}_2)^T \mathbf{V}_1^{-1} \mathbf{V}_+ \mathbf{V}_2^{-1} (\sin \theta \mathbf{b}_1 - \cos \theta \mathbf{b}_2)
\end{aligned}
$$

since all matrices are symmetric and using (1) .

Note the similarity with Fieller's chisquare statistic which, under this parameterisation, is

$$X^2 = (\sin\theta\mathbf{b}_1 - \cos\theta\mathbf{b}_2)^T \left(\sin^2\theta\mathbf{V}_1 + \cos^2\theta\mathbf{V}_2\right)^{-1} (\sin\theta\mathbf{b}_1 - \cos\theta\mathbf{b}_2)^T. \qquad (3)$$

Now,

$$\left(\mathbf{V}_1^{-1}\mathbf{V}_+\mathbf{V}_2^{-1}\right)^{-1} = \mathbf{V}_2\mathbf{V}_+^{-1}\mathbf{V}_2 = \sin^2\theta\mathbf{V}_1 + \cos^2\theta\mathbf{V}_2$$

Thus, $X^2$ (3) $= -2\log L$ (2) and the likelihood statistic and Fieller's statistic alternatively derived here are identical.

## Posterior distribution of $\theta$

The full joint likelihood is given by

$$
\begin{aligned}
L(\boldsymbol{\beta}_1, \boldsymbol{\beta}_2|\theta, \beta) &= \frac{1}{(2\pi)^{p/2} \left(|\mathbf{V}_1||\mathbf{V}_2|\right)^{1/2}} \\
&\quad \cdot \exp\left(-\frac{1}{2}\left[(\mathbf{b}_1 - \cos\theta\boldsymbol{\beta})^T \mathbf{V}_1^{-1} (\mathbf{b}_1 - \cos\theta\boldsymbol{\beta}) + (\mathbf{b}_2 - \sin\theta\boldsymbol{\beta})^T \mathbf{V}_2^{-1} (\mathbf{b}_2 - \sin\theta\boldsymbol{\beta})\right]\right) \\
&= \frac{1}{(2\pi)^{p/2} \left(|\mathbf{V}_1||\mathbf{V}_2|\right)^{1/2}} \\
&\quad \cdot \exp\left(-\frac{1}{2}\left[(\boldsymbol{\beta} - \boldsymbol{\mu})^T \mathbf{M}^{-1} (\boldsymbol{\beta} - \boldsymbol{\mu}) - \boldsymbol{\mu}^T\mathbf{M}^{-1}\boldsymbol{\mu} + \mathbf{b}_1^T\mathbf{V}_1^{-1}\mathbf{b}_1 + \mathbf{b}_2^T\mathbf{V}_2^{-1}\mathbf{b}_2\right]\right)
\end{aligned}
$$

where

$$\mathbf{M} = \left(\cos^2\theta\mathbf{V}_1^{-1} + \sin^2\theta\mathbf{V}_2^{-1}\right)^{-1}$$

$$\boldsymbol{\mu} = \left(\cos\theta\mathbf{b}_1\mathbf{V}_1^{-1} + \sin\theta\mathbf{b}_2\mathbf{V}_2^{-1}\right)\mathbf{M} = \widetilde{\boldsymbol{\beta}}.$$

The posterior for $\theta$ is given by

$$\mathcal{P}(\theta) \propto \int_{-\infty}^{\infty} L(\boldsymbol{\beta}_1, \boldsymbol{\beta}_2|\theta, \boldsymbol{\beta})\pi(\theta)\pi(\boldsymbol{\beta})d\boldsymbol{\beta}$$

where $\pi(\theta) \propto 1$ and $\pi(\boldsymbol{\beta}) \propto \mathbf{1}$ are uninformative priors for $\theta$ and $\boldsymbol{\beta}$ respectively. Thus

$$\mathcal{P}(\theta) \propto \frac{|M|^{1/2}}{(2\pi)^{p/2} (|V_1||V_2|)^{1/2}} \exp\left(-\frac{1}{2}\left[\mathbf{b}_1^T \mathbf{V}_1^{-1} \mathbf{b}_1 + \mathbf{b}_2^T \mathbf{V}_2^{-1} \mathbf{b}_2 - \boldsymbol{\mu}^T \mathbf{M}^{-1} \boldsymbol{\mu}\right]\right).$$

## Justification of a flat prior for $\theta$

We have used a non-informative prior for $\theta$. To consider the case of suitable alternative priors, its worth considering the simpler case of Feiller's theorem (i.e. univariate $\beta_1$, $\beta_2$).

If we take $\beta_1$ and $\beta_2$ as having Gaussian priors with zero mean, $\beta_1/\beta_2$ has a Cauchy$(0, k)$ prior where $k$ is the ratio of the prior variances of $\beta_1$ and $\beta_2$. Thus writing

$$\tan(\theta) = \frac{\beta_1}{\beta_2}$$

the density of $\theta$ is

$$\frac{k(1 + \tan^2(\theta))}{2\pi(1 + k^2 tan^2(\theta))}.$$

This is uniform when $k = 1$. Of course, $k$ is itself unknown. We have experimented with a range of $k$, and found inference differed very little (Supplementary Figure 1). Therefore we have used $k = 1$ in the results presented in this paper.

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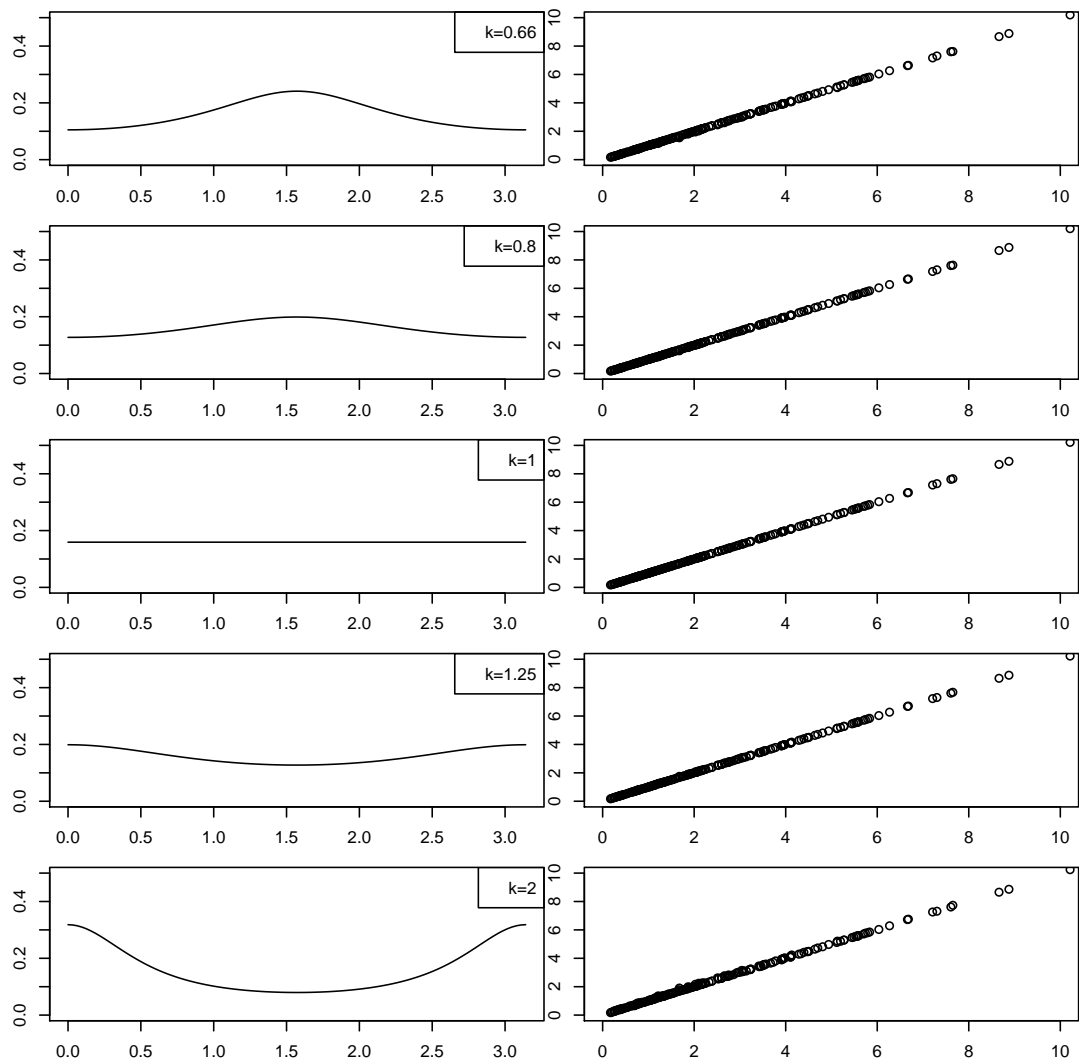
# Supplementary Figures
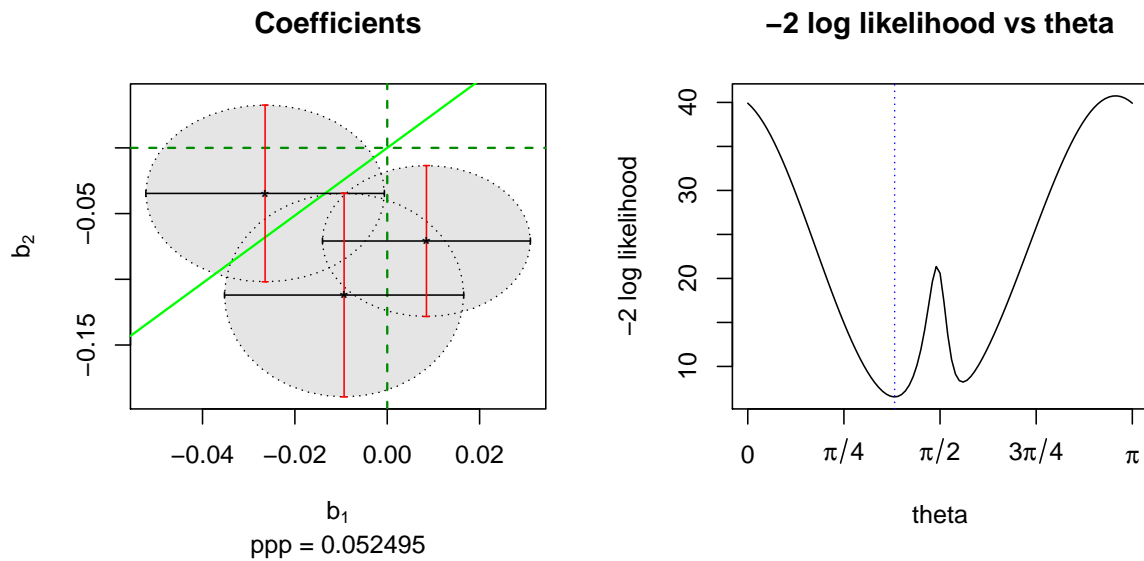


**Supplementary Figure 1.** Coefficients from two regressions (left panel) and a typical bimodal log-likelihood (right panel). The maximum likelihood estimate of $\theta$ may be understood graphically as the line through the origin which minimises the distance from the each pair of coefficients (allowing for some weighting according to their variance estimate, which is shown as the shaded ellipse). The log-likelihood of these data under a range of $\theta$ from 0 to $\pi$ is shown and has two local minima, *i.e.* the likelihood is bimodal. Note also that the shape of the minima are not symmetric, meaning that it the likelihood there cannot be adequately described by a quadratic approximation.
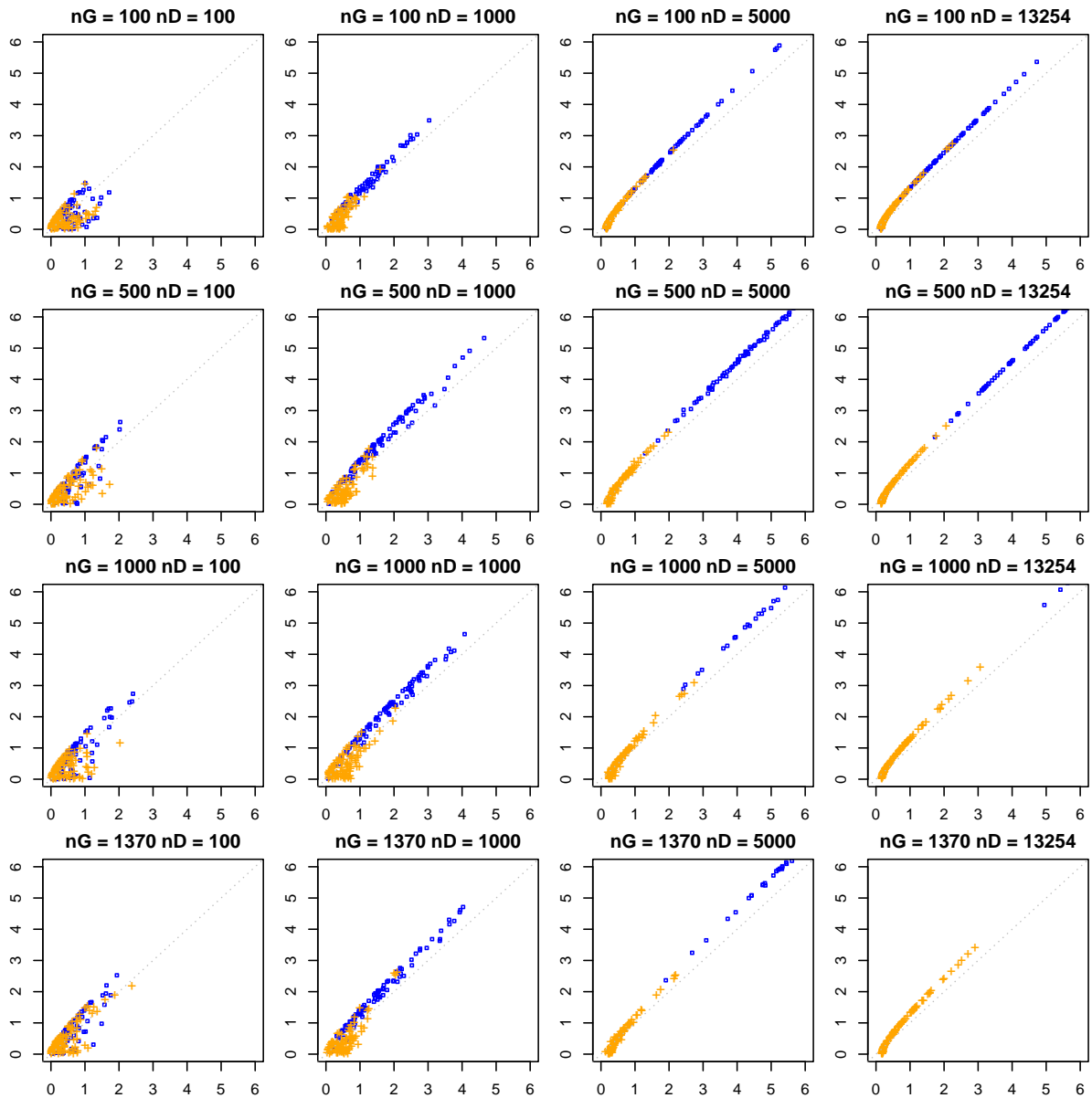
**Supplementary Figure 2.** Effect of sample size on the equivalence of the asymptotic and posterior predictive $p$ values. We repeatedly resampled with replacement nG individuals from the GHS dataset and nD individuals from the T1D case/control dataset for two probes - ILMN_2168217 (orange crosses) which was consistent with colocalisation and ILMN_1690921 (blue squares) which was not - to ensure we covered small and large $p$ values. The figures show the posterior predictive $p$ values on the x axis, and the asymptotic $p$ values on the y axis, both using a $\log_{10}$ scale. While the two are in close correspondence for smaller $p$ values and larger sample sizes, for larger $p$ values (in the regions consistent with the null hypothesis) and smaller sample sizes, there can be considerable disagreement. Plots are truncated at $p > 10^{-6}$ to allow the effects at larger $p$ values to be seen clearly. Note this truncation means points for ILMN_1690921 are missing in the later plots, but they continue to follow the trend indicated by the points which are within the plotted region.

**Supplementary Figure 3.** Effects of changing $k$ in prior for $\theta$ on posterior predictive $p$ values from colocalisation test. The left column shows the shape of the prior across $theta \in [0, \pi]$, and the right column the -log10 posterior predictive $p$ values from the model assuming that prior (vertical axis) compared with a model assuming a flat prior ($k = 1$, horizontal axis).

# Supplementary Tables

**Supplementary Table 1.** Forty-nine T1D associated regions in which evidence for eQTLs was assessed in GHS data. Positions are according to genome build 36.

| Chromosome | Start | End | Size (kb) |
|---|---|---|---|
| 1p13.2 | 113620000 | 114460000 | 840 |
| 1q31.2 | 190728079 | 190816535 | 88 |
| 1q32.1 | 204869063 | 205116454 | 247 |
| 2q11.2 | 99883121 | 100415547 | 532 |
| 2q24.2 | 162669119 | 163101007 | 432 |
| 2q32.2 | 191596469 | 191738798 | 142 |
| 2q33.2 | 204381054 | 204528303 | 147 |
| 3p21.31 | 45955677 | 46629136 | 673 |
| 4p15.2 | 25637903 | 25745871 | 108 |
| 4q27 | 123128865 | 123833732 | 705 |
| 6q15 | 90863556 | 91103018 | 239 |
| 6q22.32 | 126479722 | 127461527 | 982 |
| 6q23.3 | 137915383 | 138379949 | 465 |
| 6q25.3 | 159237500 | 159446677 | 209 |
| 7p15.2 | 26624487 | 27171807 | 547 |
| 7p12.2 | 50337181 | 50662811 | 330 |
| 7p12.1 | 50866662 | 51640000 | 773 |
| 9p24.2 | 4218550 | 4311558 | 93 |
| 10p15.1 | 6069732 | 6237542 | 168 |
| 10p15.1 | 6475380 | 6585110 | 110 |
| 10q22.3 | 80629523 | 80761569 | 132 |
| 10q23.31 | 89998027 | 90268360 | 270 |
| 11p15.5 | 2025000 | 2264880 | 240 |
| 12p13.31 | 9512800 | 9867423 | 355 |
| 12q13.2 | 54637613 | 55091576 | 454 |

| Chromosome | Start | End | Size (kb) |
|---|---|---|---|
| 12q13.3 | 55268557 | 56819824 | 1551 |
| 12q24.12 | 109772109 | 111723111 | 1951 |
| 13q32.3 | 98723873 | 98915794 | 191 |
| 14q24.1 | 68237491 | 68387815 | 150 |
| 14q32.2 | 97427667 | 97601359 | 174 |
| 14q32.2 | 100357784 | 100398492 | 41 |
| 15q14 | 36604000 | 36786000 | 182 |
| 15q25.1 | 76773860 | 77050416 | 277 |
| 16p13.13 | 10923546 | 11560000 | 636 |
| 16p11.2 | 28191236 | 28944416 | 753 |
| 16q23.1 | 73760231 | 74086012 | 326 |
| 17q12 | 34634168 | 35508018 | 874 |
| 17q21.2 | 35990900 | 36132000 | 141 |
| 18p11.21 | 12726556 | 12916278 | 190 |
| 18q22.2 | 65630495 | 65722590 | 92 |
| 19p13.2 | 10256447 | 10489468 | 233 |
| 19q13.32 | 51843218 | 52015224 | 172 |
| 20p13 | 1444473 | 1707590 | 263 |
| 21q22.3 | 42681878 | 42761422 | 80 |
| 22q12.2 | 28137855 | 28999883 | 862 |
| 22q12.3 | 35868086 | 35892057 | 24 |
| 22q13.1 | 35898616 | 35996732 | 98 |
| Xp22.2 | 12820442 | 12934000 | 114 |
| Xq28 | 153480831 | 154098953 | 618 |

**Supplementary Table 2.** Probes which associate with SNPs located in the T1D regions in the GHS monocyte dataset. Evidence for association in CTS is also presented where available. SNP is the most associated SNP in the region, Alleles lists the major and minor alleles, respectively, and Fold is the change in normalised expression level per copy of the minor allele in GHS ($^G$) and CTS ($^C$). CTS indicates whether the probe is present in CTS. Where the probe is present, the most associated SNP was either directly available ($r2 =$NA) or imputed with an estimated $r^2$ shown. $p$ values are given for the association in GHS ($p^G$), CTS ($p^C$) or overall ($p^O$), calculated by Fisher's combination of $p^G$ and $p^O$. † SNP not available in HapMap to enable imputation.

| Region | cis/ trans | Gene | Probe | SNP | Alleles | Fold$^G$ | p$^G$ | CTS? | Fold$^C$ | $r^2$ | p$^C$ | p$^O$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2q11.2 | cis | AFF3 | ILMN_1775235 | rs11681966 | C/A | -0.0764 | 1.72e-10 | yes | -0.05194 | 0.98 | 2.17e-03 | 1.10e-11 |
| 6q25.3 | cis | EZR | ILMN_1795937 | rs10455834 | A/G | 0.1206 | 1.95e-09 | yes | 0.13463 | 1.00 | 7.68e-06 | 4.91e-13 |
| 6q25.3 | cis | RSPH3 | ILMN_1788223 | rs10455840 | C/T | -0.4175 | 7.25e-70 | yes | -0.46737 | NA | 1.72e-30 | 2.86e-97 |
| 7p15.2 | cis | – | ILMN_1869943 | rs2522828 | C/T | 0.2077 | 1.27e-70 | no | – | – | – | – |
| 7p15.2 | cis | HOXA9 | ILMN_1739582 | rs10259620 | G/A | -0.1066 | 1.32e-23 | yes | -0.13299 | NA | 1.49e-13 | 1.63e-34 |
| 10q23.31 | cis | RNLS | ILMN_1718520 | rs1035796 | C/T | -0.0393 | 6.59e-11 | yes | -0.05491 | NA | 4.28e-07 | 1.10e-15 |
| 12p13.31 | cis | CLECL1 | ILMN_1782729 | rs7970116 | G/A | 0.6008 | 4.66e-182 | yes | 0.88127 | 1.00 | 3.97e-84 | 1.13e-262 |
| 12q13.2 | cis | LOC650646 | ILMN_1726647 | rs1873914 | G/C | 0.9725 | 5.39e-195 | no | – | – | – | – |
| 12q13.2 | trans | – | ILMN_2180866 | rs1873914 | G/C | 0.9933 | 5.62e-194 | no | – | – | – | – |
| 12q13.2 | trans | BEND4 | ILMN_1740094 | rs1873914 | G/C | 0.3072 | 3.59e-159 | yes | 0.32735 | NA | 5.92e-60 | 1.07e-215 |
| 12q13.2 | trans | DCAF16 | ILMN_1753440 | rs1873914 | G/C | 0.1531 | 3.47e-34 | yes | 0.17358 | NA | 9.11e-34 | 4.87e-65 |
| 12q13.2 | cis | RPS26 | ILMN_1678522 | rs1873914 | G/C | 0.8949 | 2.29e-184 | no | – | – | – | – |

| Region | $c/t$ | Gene | Probe | SNP | Alleles | Fold$^\text{G}$ | p$^\text{G}$ | CTS? | Fold$^\text{C}$ | $r^2$ | p$^\text{C}$ | p$^\text{O}$ |
|--------|-------|------|-------|-----|---------|------|------|------|------|------|------|------|
| 12q13.2 | *trans* | *RPS26* | ILMN_1737991 | rs1873914 | G/C | 0.8122 | 6.87e-197 | no | – | – | – | – |
| 12q13.2 | *cis* | *RPS26* | ILMN_1750636 | rs1873914 | G/C | 1.0564 | 9.31e-184 | yes | 1.01223 | NA | 1.40e-82 | 7.98e-263 |
| 12q13.2 | *cis* | *RPS26* | ILMN_2209027 | rs1873914 | G/C | 0.9294 | 1.70e-186 | yes | 0.89618 | NA | 2.42e-85 | 2.57e-268 |
| 12q13.2 | *cis* | *RPS26* | ILMN_2310703 | rs1873914 | G/C | 1.0144 | 5.13e-204 | yes | 0.92379 | NA | 4.27e-76 | 1.41e-276 |
| 12q13.2 | *cis* | *RPS26P31* | ILMN_1695585 | rs1873914 | G/C | 0.9321 | 9.84e-208 | no | – | – | – | – |
| 12q13.2 | *trans* | *RPS26P35* | ILMN_1677697 | rs1873914 | G/C | 0.8964 | 6.54e-146 | no | – | – | – | – |
| 12q13.2 | *cis* | *SUOX* | ILMN_2383455 | rs1873914 | G/C | -0.0456 | 5.49e-15 | yes | -0.05598 | NA | 1.48e-04 | 3.47e-17 |
| 12q13.2 | *cis* | *SUOX* | ILMN_1803745 | rs705702 | A/G | -0.0691 | 1.04e-18 | yes | -0.06086 | 0.97 | 1.83e-04 | 9.69e-21 |
| 12q13.2 | *cis* | *STAT2* | ILMN_1690921 | rs871130 | C/T | -0.2005 | 4.10e-18 | yes | -0.16924 | 1.00 | 1.11e-03 | 2.18e-19 |
| 12q13.3 | *cis* | *RBMS2* | ILMN_1755411 | rs7313074 | A/G | 0.1666 | 1.95e-70 | yes | 0.17501 | 1.00 | 2.49e-03 | 8.14e-71 |
| 12q13.3 | *cis* | *STAT6* | ILMN_1763198 | rs324019 | G/A | 0.2867 | 6.61e-143 | yes | † | – | – | – |
| 12q13.3 | *cis* | *TSPAN31* | ILMN_1725079 | rs12368653 | G/A | 0.0504 | 7.91e-13 | yes | 0.02885 | NA | 2.27e-02 | 5.87e-13 |
| 12q13.3 | *cis* | *FAM119B* | ILMN_1723846 | rs4646536 | A/G | 0.2780 | 5.69e-156 | yes | 0.31147 | NA | 8.18e-66 | 2.37e-218 |
| 12q13.3 | *cis* | *TSFM* | ILMN_2097954 | rs10877019 | C/T | -0.0476 | 7.68e-19 | yes | -0.04434 | 1.00 | 3.55e-05 | 1.44e-21 |
| 12q24.12 | *cis* | *C12orf24* | ILMN_2180371 | rs2238149 | T/C | -0.0510 | 9.69e-11 | yes | -0.04557 | 0.97 | 7.45e-03 | 2.09e-11 |
| 12q24.12 | *cis* | *ALDH2* | ILMN_1793859 | rs10744777 | T/C | 0.1005 | 1.29e-15 | yes | 0.10706 | 0.82 | 1.19e-08 | 8.19e-22 |
| 12q24.12 | *cis* | *TMEM116* | ILMN_2052871 | rs7114 | A/G | 0.1130 | 7.05e-31 | yes | 0.12726 | 1.00 | 1.03e-13 | 7.26e-42 |
| 12q24.12 | *cis* | *MAPKAPK5* | ILMN_2322935 | rs12579336 | A/G | 0.1150 | 1.41e-12 | yes | 0.08411 | 1.00 | 2.22e-02 | 1.00e-12 |

| Region | c/t | Gene | Probe | SNP | Alleles | Fold$^G$ | p$^G$ | CTS? | Fold$^C$ | $r^2$ | p$^C$ | p$^O$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 13q32 | *cis* | *CLYBL* | ILMN_1663538 | rs17656454 | A/G | -0.0850 | 1.67e-14 | yes | -0.10080 | NA | 2.56e-06 | 1.95e-18 |
| 13q32 | *cis* | *GPR183* | ILMN_2168217 | rs7325697 | C/T | -0.0846 | 6.83e-11 | yes | -0.22196 | 0.95 | 2.05e-04 | 4.61e-13 |
| 16p13.13 | *cis* | *DEXI* | ILMN_1738866 | rs3901386 | T/C | 0.1137 | 3.78e-38 | yes | 0.09734 | NA | 1.76e-07 | 6.84e-43 |
| 16p13.13 | *trans* | *LOC642755* | ILMN_1655244 | rs3893660 | A/G | 0.0742 | 2.64e-25 | no | – | – | – | – |
| 16p13.13 | *trans* | *LOC642755* | ILMN_1793287 | rs3893660 | A/G | 0.1135 | 1.94e-33 | no | – | – | – | – |
| 16p13.13 | *cis* | *LITAF* | ILMN_1713934 | rs11646660 | C/T | -0.1832 | 7.49e-09 | yes | -0.11659 | NA | 6.16e-02 | 1.04e-08 |
| 16p11.2 | *cis* | *CCDC101* | ILMN_1684789 | rs231976 | C/G | 0.1261 | 3.85e-59 | yes | 0.10751 | 0.98 | 6.15e-15 | 3.98e-71 |
| 16p11.2 | *cis* | *CCDC101* | ILMN_1701477 | rs7193402 | T/C | -0.0822 | 6.99e-32 | yes | -0.08333 | NA | 2.90e-12 | 2.01e-41 |
| 16p11.2 | *cis* | *TUFM* | ILMN_1738369 | rs8049439 | T/C | 0.1695 | 5.07e-65 | yes | 0.16078 | NA | 2.35e-20 | 2.31e-82 |
| 16p11.2 | *cis* | *SPNS1* | ILMN_1681016 | rs8045689 | T/C | 0.2630 | 2.36e-111 | yes | 0.16594 | NA | 1.14e-15 | 7.81e-124 |
| 17q12 | *cis* | *CRKRS* | ILMN_1707448 | rs4404103 | A/G | -0.1290 | 4.18e-14 | yes | -0.11365 | NA | 1.60e-09 | 3.49e-21 |
| 17q12 | *cis* | *PGAP3* | ILMN_1805636 | rs9675194 | C/T | 0.0457 | 2.27e-09 | yes | 0.04701 | 1.00 | 1.39e-03 | 8.64e-11 |
| 17q21.2 | *cis* | *SMARCE1* | ILMN_1747857 | rs11078951 | G/T | 0.1206 | 2.41e-60 | yes | 0.11209 | 1.00 | 3.72e-13 | 1.50e-70 |
| 18p11.21 | *cis* | *CEP192* | ILMN_1703754 | rs6505770 | C/T | 0.0858 | 8.24e-25 | yes | 0.08339 | NA | 5.40e-09 | 3.36e-31 |
| 18q22.2 | *cis* | *CD226* | ILMN_1687825 | rs1790947 | G/T | -0.1200 | 6.96e-16 | yes | -0.00594 | 1.00 | 2.95e-01 | 7.61e-15 |
| 19p13.2 | *cis* | *ICAM4* | ILMN_1681296 | rs2569702 | T/C | -0.1659 | 1.03e-25 | yes | -0.27639 | 0.96 | 3.18e-25 | 3.77e-48 |
| 19p13.2 | *cis* | *ICAM3* | ILMN_2212763 | rs2304240 | G/A | 0.1999 | 2.26e-23 | yes | 0.25110 | NA | 4.00e-24 | 9.66e-45 |
| 19q13.32 | *cis* | *FKRP* | ILMN_2368617 | rs2871987 | C/T | 0.0683 | 3.05e-22 | yes | 0.05070 | NA | 6.61e-06 | 1.26e-25 |

**Supplementary Table 2.** *(continued)*

| Region | c/t | Gene | Probe | SNP | Alleles | Fold$^G$ | p$^G$ | CTS? | Fold$^C$ | $r^2$ | p$^C$ | p$^O$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 19q13.32 | *cis* | *PRKD2* | ILMN_1753805 | rs2871987 | C/T | 0.0667 | 3.87e-16 | yes | 0.06808 | NA | 2.05e-08 | 4.30e-22 |
| 19q13.32 | *cis* | *SLC1A5* | ILMN_1707720 | rs8105903 | A/C | 0.0762 | 4.22e-20 | yes | 0.02417 | NA | 2.00e-01 | 3.98e-19 |
| 20p13 | *cis* | – | ILMN_1841622 | rs8182997 | T/C | -0.0986 | 6.58e-10 | no | – | – | – | – |
| 20p13 | *cis* | *SIRPD* | ILMN_1769886 | rs2243603 | G/C | 0.0870 | 3.41e-22 | yes | 0.11855 | 1.00 | 3.71e-07 | 8.25e-27 |
| 22q12.2 | *cis* | *NEFH* | ILMN_1705153 | rs165734 | C/T | 0.1216 | 2.34e-40 | yes | 0.09644 | 1.00 | 8.43e-06 | 2.05e-43 |
| 22q12.2 | *cis* | *NIPSNAP1* | ILMN_1805916 | rs2530670 | C/G | 0.0456 | 2.21e-14 | yes | 0.03288 | 1.00 | 3.14e-02 | 2.49e-14 |
| 22q12.2 | *cis* | *UCRC* | ILMN_2366714 | rs131298 | G/A | 0.0845 | 3.52e-17 | yes | 0.08495 | 0.96 | 3.50e-15 | 8.89e-30 |
| 22q12.2 | *cis* | *MTMR3* | ILMN_1803925 | rs12537 | C/T | 0.0820 | 5.11e-37 | yes | 0.08171 | NA | 2.95e-10 | 1.61e-44 |
| 22q12.2 | *cis* | *MTMR3* | ILMN_1739641 | rs16987156 | C/T | 0.1369 | 1.99e-26 | yes | 0.10234 | 1.00 | 4.40e-07 | 6.56e-31 |
| 22q12.2 | *cis* | *MTMR3* | ILMN_2380605 | rs16987156 | C/T | 0.1097 | 1.52e-09 | yes | 0.10492 | 1.00 | 2.35e-05 | 1.14e-12 |
| Xp22.2 | *cis* | *TLR8* | ILMN_1657892 | rs9780736 | G/A | 0.1125 | 2.06e-29 | yes | 0.07805 | NA | 4.35e-07 | 7.31e-34 |
| Xq28 | *cis* | *FAM3A* | ILMN_1808356 | rs7879049 | A/G | 0.1612 | 1.14e-35 | yes | 0.19278 | NA | 9.23e-12 | 1.12e-44 |

**Supplementary Table 3.** Colocalisation results comparing monocyte expression signals in GHS/Cardiogenics with T1D association. G-C indicates whether the probe is found in Cardiogenics (otherwise 'no probe'), whether there appears a significant effect in Cardiogenics (otherwise 'n/sig'), and finally whether the signal colocalises with GHS ('yes' or 'no'). T1 and T2 indicate the traits under test - monocyte expression in GHS or Cardiogenics (CTS), or T1D in WTCCC, T1DGC or both cohorts combined (T1D). nSNP is the number of SNPs included in the regressions of each trait. Both the asymptotic ($p$ asymp) and positive predictive $p$ (ppp) values are shown for individual tests. $pT1$ and $pT2$ are the overall $p$ values for all the SNPs in the regressions of T1 and T2 respectively. $p$ is a final combined $p$ value for colocalisation for monocyte expression and T1D risk, either a Fisher's combined $p$ value of the ppp for GHS-WTCCC and CTS-T1DGC, or the minimum of the GHS vs WTCCC, T1DGC and T1D ppp when GHS and Cardiogenics signals do not colocalise. T1D-expression colocalisation tests, *i.e.* whether increased expression correlates with T1D susceptibility ('+') or protection ('-') in GHS vs WTCCC. † indicates cases where only one SNP is required to capture both the eQTL and T1D signal. In this case, the data are consistent with the null and a formal colocalisation test is neither needed nor possible.

| Region | Probe | Gene | G-C | p | T1 | T2 | sign($\eta$) | nSNP | p (asymp) | ppp | pT1 | pT2 |
|--------|-------|------|-----|---|----|----|----------|------|-----------|-----|-----|-----|
| 12q24.12 | ILMN_2052871 | *TMEM116* | no | 1.01e-23 | GHS | WTCCC | - | 4 | 1.76e-13 | 5.58e-13 | 2.62e-39 | 5.75e-15 |
| | | | | | GHS | T1DGC | + | 4 | 4.62e-14 | 1.75e-13 | 1.59e-39 | 9.57e-14 |
| | | | | | GHS | T1D | - | 5 | 2.49e-24 | 1.01e-23 | 3.37e-40 | 1.51e-24 |
| | | | | | GHS | CTS | + | 5 | 5.03e-04 | 8.36e-04 | 1.76e-41 | 1.11e-21 |

**Supplementary Table 3.** *(continued)*

| Region | Probe | Gene | G-C | p | T1 | T2 | sign($\eta$) | nSNP | p (asymp) | ppp | pT1 | pT2 |
|--------|-------|------|-----|---|----|----|--------------|------|-----------|-----|-----|-----|
| 12q24.12 | ILMN_2180371 | *C12orf24* | yes | 3.91e-22 | GHS | WTCCC | + | 6 | 7.66e-12 | 1.99e-11 | 1.20e-69 | 5.36e-13 |
| | | | | | CTS | T1DGC | + | 3 | 8.13e-14 | 3.61e-13 | 7.48e-22 | 4.10e-14 |
| | | | | | GHS | CTS | + | 5 | 6.35e-01 | 6.07e-01 | 4.92e-53 | 5.56e-16 |
| 12q24.12 | ILMN_1793859 | *ALDH2* | yes | 6.81e-20 | GHS | WTCCC | - | 3 | 1.77e-11 | 6.11e-11 | 6.28e-19 | 4.46e-15 |
| | | | | | CTS | T1DGC | + | 2 | 5.68e-12 | 2.27e-11 | 1.62e-11 | 2.55e-15 |
| | | | | | GHS | CTS | + | 2 | 5.56e-02 | 1.12e-01 | 4.60e-22 | 8.57e-11 |
| 12q13.2 | ILMN_1690921 | *STAT2* | yes | 5.06e-15 | GHS | WTCCC | + | 4 | 6.58e-10 | 2.18e-09 | 7.01e-17 | 1.82e-09 |
| | | | | | CTS | T1DGC | - | 4 | 5.94e-08 | 6.17e-08 | 3.50e-08 | 5.01e-12 |
| | | | | | GHS | CTS | + | 4 | 1.91e-02 | 2.98e-02 | 2.90e-16 | 3.07e-08 |
| 18p11.21 | ILMN_1703754 | *CEP192* | yes | 1.39e-12 | GHS | WTCCC | - | 4 | 1.38e-05 | 3.31e-05 | 4.65e-174 | 4.23e-05 |
| | | | | | CTS | T1DGC | - | 5 | 4.69e-10 | 1.33e-09 | 2.13e-30 | 1.39e-09 |
| | | | | | GHS | CTS | + | 3 | 2.73e-02 | 4.71e-02 | 5.77e-176 | 1.27e-30 |
| 22q12.2 | ILMN_1739641 | *MTMR3* | no | 1.70e-12 | GHS | WTCCC | + | 2 | 5.44e-05 | 2.14e-04 | 3.82e-28 | 1.92e-04 |
| | | | | | GHS | T1DGC | - | 2 | 1.49e-09 | 8.40e-09 | 7.80e-29 | 5.07e-09 |
| | | | | | GHS | T1D | - | 2 | 2.48e-13 | 1.70e-12 | 8.51e-29 | 1.93e-12 |
| | | | | | GHS | CTS | + | 2 | 1.24e-03 | 3.81e-03 | 1.61e-27 | 8.47e-10 |
| 12q24.12 | ILMN_2322935 | *MAPKAPK5* | no | 3.68e-12 | GHS | WTCCC | - | 5 | 9.14e-08 | 1.33e-07 | 1.42e-10 | 1.84e-14 |
| | | | | | GHS | T1DGC | - | 4 | 2.70e-12 | 3.68e-12 | 1.46e-12 | 3.21e-14 |
| | | | | | GHS | T1D | - | 7 | 8.72e-09 | 2.48e-09 | 1.68e-09 | 1.61e-23 |
| | | | | | GHS | CTS | + | 4 | 1.18e-03 | 1.77e-03 | 1.76e-11 | 3.13e-05 |

**Supplementary Table 3.** *(continued)*

| Region | Probe | Gene | G-C | p | T1 | T2 | sign($\eta$) | nSNP | p (asymp) | ppp | pT1 | pT2 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 16p13.13 | ILMN_1713934 | *LITAF* | yes | 2.00e-11 | GHS | WTCCC | + | 2 | 9.06e-09 | 4.97e-08 | 5.33e-09 | 2.87e-08 |
| | | | | | CTS | T1DGC | + | 4 | 7.42e-06 | 1.39e-05 | 3.79e-06 | 7.59e-06 |
| | | | | | GHS | CTS | + | 3 | 1.45e-01 | 1.96e-01 | 8.00e-20 | 9.08e-07 |
| 22q12.2 | ILMN_1805916 | *NIPSNAP1* | no | 1.14e-10 | GHS | WTCCC | + | 2 | 1.56e-05 | 7.25e-05 | 2.07e-14 | 8.25e-05 |
| | | | | | GHS | T1DGC | + | 2 | 4.27e-08 | 1.74e-07 | 3.17e-14 | 4.25e-09 |
| | | | | | GHS | T1D | + | 3 | 3.88e-11 | 1.14e-10 | 1.95e-13 | 5.35e-12 |
| | | | | | GHS | CTS | + | 3 | 2.07e-04 | 3.99e-04 | 9.61e-14 | 8.31e-05 |
| 22q12.2 | ILMN_1705153 | *NEFH* | yes | 1.39e-09 | GHS | WTCCC | + | 3 | 1.12e-03 | 2.53e-03 | 1.55e-58 | 9.17e-04 |
| | | | | | CTS | T1DGC | + | 2 | 4.87e-09 | 2.23e-08 | 2.37e-14 | 8.59e-10 |
| | | | | | GHS | CTS | + | 2 | 6.52e-01 | 6.37e-01 | 2.32e-69 | 3.51e-18 |
| 22q12.2 | ILMN_1803925 | *MTMR3* | yes | 9.34e-09 | GHS | WTCCC | - | 4 | 7.67e-03 | 1.25e-02 | 2.37e-42 | 1.43e-03 |
| | | | | | CTS | T1DGC | - | 4 | 1.33e-08 | 3.30e-08 | 7.26e-11 | 2.63e-09 |
| | | | | | GHS | CTS | + | 2 | 5.89e-01 | 6.06e-01 | 3.68e-42 | 4.33e-10 |
| 22q12.2 | ILMN_2380605 | *MTMR3* | yes | 1.04e-08 | GHS | WTCCC | + | 3 | 1.62e-04 | 4.16e-04 | 1.98e-11 | 2.54e-04 |
| | | | | | CTS | T1DGC | - | 3 | 4.75e-07 | 1.11e-06 | 5.43e-10 | 1.02e-08 |
| | | | | | GHS | CTS | + | 4 | 5.83e-02 | 7.54e-02 | 9.28e-11 | 1.11e-08 |
| 20p13 | ILMN_1769886 | *SIRPD* | yes | 1.33e-07 | GHS | WTCCC | - | 4 | 1.21e-03 | 2.44e-03 | 9.58e-25 | 2.02e-03 |
| | | | | | CTS | T1DGC | - | 2 | 5.33e-07 | 2.75e-06 | 4.64e-08 | 2.88e-06 |
| | | | | | GHS | CTS | + | 4 | 3.90e-02 | 5.59e-02 | 5.99e-29 | 3.80e-11 |

**Supplementary Table 3.** *(continued)*

| Region | Probe | Gene | G-C | p | T1 | T2 | sign($\eta$) | nSNP | p (asymp) | ppp | pT1 | pT2 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 22q12.2 | ILMN_2366714 | *UCRC* | yes | 3.00e-07 | GHS | WTCCC | - | 4 | 1.92e-04 | 3.94e-04 | 5.19e-16 | 1.70e-04 |
| | | | | | CTS | T1DGC | - | 2 | 1.04e-05 | 4.01e-05 | 6.84e-20 | 5.07e-09 |
| | | | | | GHS | CTS | + | 4 | 3.16e-01 | 3.08e-01 | 3.20e-16 | 9.16e-18 |
| 20p13 | ILMN_1841622 | | no probe | 5.39e-07 | GHS | WTCCC | - | 3 | 2.30e-04 | 5.96e-04 | 5.47e-26 | 7.06e-04 |
| | | | | | GHS | T1DGC | + | 2 | 5.23e-05 | 1.94e-04 | 2.84e-24 | 1.56e-06 |
| | | | | | GHS | T1D | + | 4 | 1.99e-07 | 5.39e-07 | 3.41e-25 | 6.58e-08 |
| 12q13.2 | ILMN_2310703 | *RPS26* | no | 9.23e-07 | GHS | WTCCC | + | 4 | 3.54e-03 | 6.41e-03 | 0.00e+00 | 1.49e-10 |
| | | | | | GHS | T1DGC | + | 4 | 5.08e-03 | 8.97e-03 | 0.00e+00 | 1.01e-11 |
| | | | | | GHS | T1D | + | 4 | 1.69e-06 | 9.23e-07 | 0.00e+00 | 5.44e-23 |
| | | | | | GHS | CTS | + | 3 | 3.26e-07 | 1.62e-06 | 0.00e+00 | 8.58e-226 |
| 17q12 | ILMN_1805636 | *PGAP3* | yes | 1.21e-06 | GHS | WTCCC | - | 2 | 3.43e-04 | 9.12e-04 | 4.98e-09 | 9.92e-05 |
| | | | | | CTS | T1DGC | + | 2 | 1.66e-05 | 7.62e-05 | 4.75e-06 | 7.65e-05 |
| | | | | | GHS | CTS | + | 2 | 4.83e-03 | 1.25e-02 | 1.04e-08 | 1.95e-05 |
| 16p13.13 | ILMN_1793287 | *LOC642755* | no probe | 1.54e-06 | GHS | WTCCC | - | 4 | 5.41e-03 | 9.07e-03 | 2.66e-43 | 4.95e-07 |
| | | | | | GHS | T1DGC | - | 5 | 6.78e-07 | 1.54e-06 | 6.72e-46 | 1.37e-08 |
| | | | | | GHS | T1D | - | 4 | 9.95e-07 | 2.45e-06 | 6.68e-43 | 4.19e-14 |
| 12q13.2 | ILMN_1677697 | *RPS26P35* | no probe | 2.27e-06 | GHS | WTCCC | + | 4 | 3.43e-03 | 6.23e-03 | 0.00e+00 | 1.49e-10 |
| | | | | | GHS | T1DGC | + | 5 | 1.50e-02 | 2.27e-02 | 0.00e+00 | 4.07e-11 |
| | | | | | GHS | T1D | + | 3 | 5.36e-07 | 2.27e-06 | 0.00e+00 | 1.01e-23 |

**Supplementary Table 3.** *(continued)*

| Region | Probe | Gene | G-C | p | T1 | T2 | sign($\eta$) | nSNP | p (asymp) | ppp | pT1 | pT2 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 17q12 | ILMN_1707448 | *CRKRS* | yes | 3.23e-06 | GHS | WTCCC | - | 3 | 2.68e-04 | 7.26e-04 | 1.03e-13 | 9.20e-04 |
| | | | | | CTS | T1DGC | + | 3 | 1.05e-04 | 2.71e-04 | 3.19e-12 | 1.15e-04 |
| | | | | | GHS | CTS | + | 3 | 4.38e-01 | 4.53e-01 | 1.03e-13 | 3.15e-13 |
| 12q13.2 | ILMN_1750636 | *RPS26* | no | 3.25e-06 | GHS | WTCCC | + | 4 | 3.68e-03 | 6.64e-03 | 0.00e+00 | 1.49e-10 |
| | | | | | GHS | T1DGC | + | 5 | 1.63e-02 | 2.45e-02 | 0.00e+00 | 4.11e-11 |
| | | | | | GHS | T1D | + | 4 | 4.23e-06 | 3.25e-06 | 0.00e+00 | 6.58e-23 |
| | | | | | GHS | CTS | + | 4 | 9.63e-05 | 2.09e-04 | 0.00e+00 | 9.60e-290 |
| 12q13.2 | ILMN_1726647 | *LOC650646* | no probe | 3.56e-06 | GHS | WTCCC | + | 4 | 3.18e-03 | 5.80e-03 | 0.00e+00 | 1.49e-10 |
| | | | | | GHS | T1DGC | + | 4 | 8.32e-03 | 1.42e-02 | 0.00e+00 | 1.01e-11 |
| | | | | | GHS | T1D | + | 4 | 3.87e-06 | 3.56e-06 | 0.00e+00 | 5.44e-23 |
| 12q13.2 | ILMN_1695585 | *RPS26P31* | no probe | 5.37e-06 | GHS | WTCCC | + | 5 | 4.29e-03 | 7.03e-03 | 0.00e+00 | 3.14e-10 |
| | | | | | GHS | T1DGC | + | 4 | 6.95e-03 | 1.20e-02 | 0.00e+00 | 1.01e-11 |
| | | | | | GHS | T1D | + | 4 | 2.56e-06 | 5.37e-06 | 0.00e+00 | 5.44e-23 |
| 12q13.2 | ILMN_2209027 | *RPS26* | no | 7.10e-06 | GHS | WTCCC | + | 4 | 1.42e-03 | 2.71e-03 | 0.00e+00 | 6.57e-11 |
| | | | | | GHS | T1DGC | + | 4 | 6.30e-03 | 1.10e-02 | 0.00e+00 | 9.90e-12 |
| | | | | | GHS | T1D | + | 4 | 3.18e-06 | 7.10e-06 | 0.00e+00 | 6.58e-23 |
| | | | | | GHS | CTS | + | 5 | 2.76e-22 | 1.45e-21 | 0.00e+00 | 0.00e+00 |
| 12q13.2 | ILMN_1737991 | *RPS26* | no probe | 7.66e-06 | GHS | WTCCC | + | 5 | 4.05e-03 | 6.66e-03 | 0.00e+00 | 2.37e-10 |
| | | | | | GHS | T1DGC | + | 4 | 4.64e-03 | 8.25e-03 | 0.00e+00 | 1.01e-11 |
| | | | | | GHS | T1D | + | 4 | 1.83e-06 | 7.66e-06 | 0.00e+00 | 5.44e-23 |

**Supplementary Table 3.** *(continued)*

| Region | Probe | Gene | G-C | p | T1 | T2 | sign($\eta$) | nSNP | p (asymp) | ppp | pT1 | pT2 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 12q13.2 | ILMN_1678522 | *RPS26* | no probe | 8.32e-06 | GHS | WTCCC | + | 5 | 2.51e-03 | 4.24e-03 | 0.00e+00 | 2.37e-10 |
| | | | | | GHS | T1DGC | + | 4 | 6.40e-03 | 1.11e-02 | 0.00e+00 | 1.01e-11 |
| | | | | | GHS | T1D | + | 4 | 2.39e-06 | 8.32e-06 | 0.00e+00 | 5.44e-23 |
| 16p11.2 | ILMN_1684789 | *CCDC101* | yes | 1.50e-05 | GHS | WTCCC | + | 4 | 4.75e-03 | 8.58e-03 | 2.02e-83 | 3.37e-03 |
| | | | | | CTS | T1DGC | + | 4 | 5.48e-05 | 1.18e-04 | 3.98e-19 | 1.64e-06 |
| | | | | | GHS | CTS | + | 2 | 4.52e-01 | 5.31e-01 | 1.87e-80 | 2.79e-19 |
| 16p11.2 | ILMN_1738369 | *TUFM* | yes | 2.01e-05 | GHS | WTCCC | - | 3 | 6.12e-03 | 1.24e-02 | 5.91e-82 | 4.66e-03 |
| | | | | | CTS | T1DGC | - | 3 | 4.21e-05 | 1.11e-04 | 1.03e-21 | 4.86e-07 |
| | | | | | GHS | CTS | NA | 1 | | | 1.60e-82 | 1.02e-23 |
| 16p11.2 | ILMN_1681016 | *SPNS1* | yes | 2.07e-05 | GHS | WTCCC | - | 4 | 4.81e-02 | 7.16e-02 | 2.96e-95 | 3.48e-02 |
| | | | | | CTS | T1DGC | - | 3 | 7.07e-06 | 2.00e-05 | 3.04e-16 | 2.34e-06 |
| | | | | | GHS | CTS | + | 3 | 3.07e-01 | 3.74e-01 | 3.86e-175 | 8.44e-16 |
| 7p15.2 | ILMN_1869943 | | no probe | 2.56e-05 | GHS | WTCCC | + | 4 | 1.44e-01 | 1.92e-01 | 8.13e-120 | 1.92e-01 |
| | | | | | GHS | T1DGC | - | 4 | 1.05e-05 | 2.56e-05 | 1.10e-113 | 3.10e-05 |
| | | | | | GHS | T1D | - | 4 | 2.83e-04 | 5.99e-04 | 8.13e-120 | 7.99e-04 |
| 7p15.2 | ILMN_1739582 | *HOXA9* | yes | 3.33e-05 | GHS | WTCCC | - | 3 | 1.04e-01 | 1.53e-01 | 5.23e-24 | 4.78e-02 |
| | | | | | CTS | T1DGC | - | 4 | 6.31e-06 | 1.56e-05 | 7.84e-21 | 7.18e-06 |
| | | | | | GHS | CTS | + | 2 | 3.05e-01 | 4.12e-01 | 1.59e-25 | 1.56e-16 |

**Supplementary Table 3.** *(continued)*

| Region | Probe | Gene | G-C | p | T1 | T2 | sign($\eta$) | nSNP | p (asymp) | ppp | pT1 | pT2 |
|--------|-------|------|-----|---|----|----|--------------|------|-----------|-----|-----|-----|
| 19q13.32 | ILMN_1707720 | *SLC1A5* | n/sig | 1.17e-04 | GHS | WTCCC | - | 3 | 2.29e-02 | 3.83e-02 | 4.90e-25 | 1.51e-03 |
| | | | | | GHS | T1DGC | + | 4 | 8.73e-04 | 1.78e-03 | 8.80e-24 | 1.51e-03 |
| | | | | | GHS | T1D | - | 5 | 5.78e-05 | 1.17e-04 | 8.35e-27 | 3.35e-05 |
| | | | | | GHS | CTS | + | 3 | 3.82e-01 | 4.36e-01 | 1.84e-25 | 4.77e-03 |
| 12q13.2 | ILMN_2383455 | *SUOX* | yes | 1.21e-04 | GHS | WTCCC | - | 4 | 1.79e-05 | 3.36e-05 | 1.97e-15 | 6.57e-11 |
| | | | | | CTS | T1DGC | - | 2 | 2.10e-01 | 2.87e-01 | 5.13e-04 | 8.66e-12 |
| | | | | | GHS | CTS | + | 2 | 3.14e-01 | 3.83e-01 | 2.85e-16 | 9.71e-04 |
| 12q13.2 | ILMN_1740094 | *BEND4* | yes | 1.35e-04 | GHS | WTCCC | + | 4 | 3.82e-03 | 6.85e-03 | 0.00e+00 | 1.49e-10 |
| | | | | | CTS | T1DGC | + | 3 | 6.82e-04 | 1.59e-03 | 2.69e-133 | 3.19e-12 |
| | | | | | GHS | CTS | + | 4 | 6.20e-03 | 1.07e-02 | 0.00e+00 | 3.25e-133 |
| 12q13.3 | ILMN_1763198 | *STAT6* | yes | 1.48e-04 | GHS | WTCCC | + | 4 | 3.48e-03 | 6.39e-03 | 1.05e-119 | 7.51e-03 |
| | | | | | CTS | T1DGC | - | 4 | 9.51e-04 | 1.87e-03 | 2.55e-97 | 2.23e-03 |
| | | | | | GHS | CTS | + | 4 | 7.92e-02 | 1.10e-01 | 1.90e-195 | 3.51e-99 |
| Xp22.2 | ILMN_1657892 | *TLR8* | yes | 3.06e-04 | GHS | WTCCC | - | 3 | 1.83e-03 | 4.10e-03 | 1.12e-34 | 2.51e-03 |
| | | | | | CTS | T1DGC | - | 3 | 3.90e-03 | 6.46e-03 | 5.63e-08 | 7.02e-04 |
| | | | | | GHS | CTS | + | 3 | 5.81e-02 | 9.25e-02 | 2.65e-37 | 4.61e-08 |
| 12q13.3 | ILMN_1755411 | *RBMS2* | yes | 4.15e-04 | GHS | WTCCC | + | 3 | 1.18e-03 | 2.72e-03 | 2.29e-110 | 2.58e-03 |
| | | | | | CTS | T1DGC | - | 2 | 8.49e-03 | 1.36e-02 | 8.70e-03 | 2.45e-03 |
| | | | | | GHS | CTS | + | 4 | 3.54e-02 | 5.31e-02 | 2.11e-114 | 2.17e-55 |

**Supplementary Table 3.** *(continued)*

| Region | Probe | Gene | G-C | p | T1 | T2 | sign($\eta$) | nSNP | p (asymp) | ppp | pT1 | pT2 |
|--------|-------|------|-----|---|----|----|--------------|------|-----------|-----|-----|-----|
| 13q32 | ILMN_1663538 | *CLYBL* | yes | 7.22e-04 | GHS | WTCCC | + | 4 | 3.62e-02 | 5.73e-02 | 1.64e-19 | 5.03e-02 |
| | | | | | CTS | T1DGC | - | 4 | 6.51e-04 | 1.19e-03 | 2.68e-14 | 2.70e-05 |
| | | | | | GHS | CTS | + | 4 | 2.05e-02 | 2.99e-02 | 1.96e-24 | 1.12e-13 |
| 16p13.13 | ILMN_1655244 | *LOC642755* | no probe | 1.01e-03 | GHS | WTCCC | - | 3 | 2.32e-01 | 2.78e-01 | 3.57e-29 | 4.22e-05 |
| | | | | | GHS | T1DGC | - | 4 | 5.50e-04 | 1.01e-03 | 1.33e-30 | 6.97e-08 |
| | | | | | GHS | T1D | - | 3 | 2.36e-02 | 3.92e-02 | 1.59e-24 | 7.30e-15 |
| 12q13.3 | ILMN_1723846 | *FAM119B* | yes | 1.39e-03 | GHS | WTCCC | - | 2 | 4.37e-04 | 1.47e-03 | 1.02e-319 | 1.18e-03 |
| | | | | | CTS | T1DGC | - | 2 | 4.54e-02 | 9.58e-02 | 2.64e-136 | 2.26e-03 |
| | | | | | GHS | CTS | + | 2 | 7.54e-01 | 6.73e-01 | 1.95e-321 | 1.02e-135 |
| 19p13.2 | ILMN_1681296 | *ICAM4* | yes | 1.45e-03 | GHS | WTCCC | - | 4 | 5.93e-02 | 8.68e-02 | 7.08e-48 | 6.75e-02 |
| | | | | | CTS | T1DGC | - | 4 | 8.63e-04 | 1.70e-03 | 0.00e+00 | 1.94e-03 |
| | | | | | GHS | CTS | + | 6 | 7.23e-02 | 8.71e-02 | 3.31e-46 | 1.30e-53 |
| 19p13.2 | ILMN_2212763 | *ICAM3* | yes | 1.95e-03 | GHS | WTCCC | + | 4 | 1.13e-01 | 1.59e-01 | 7.16e-14 | 1.87e-01 |
| | | | | | CTS | T1DGC | + | 2 | 3.80e-04 | 1.29e-03 | 1.98e-30 | 2.70e-04 |
| | | | | | GHS | CTS | + | 3 | 1.92e-02 | 3.28e-02 | 5.08e-24 | 1.50e-29 |
| 16p13.13 | ILMN_1738866 | *DEXI* | yes | 2.45e-03 | GHS | WTCCC | - | 3 | 9.92e-03 | 1.83e-02 | 7.81e-45 | 1.29e-07 |
| | | | | | CTS | T1DGC | - | 3 | 7.91e-03 | 1.45e-02 | 7.89e-08 | 4.32e-08 |
| | | | | | GHS | CTS | + | 3 | 1.43e-02 | 2.63e-02 | 8.67e-46 | 1.19e-09 |

| Region | Probe | Gene | G-C | p | T1 | T2 | sign($\eta$) | nSNP | p (asymp) | ppp | pT1 | pT2 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 12q13.3 | ILMN_2097954 | *TSFM* | n/sig | 2.73e-03 | GHS | WTCCC | + | 2 | 9.21e-04 | 2.73e-03 | 5.38e-19 | 1.20e-03 |
| | | | | | GHS | T1DGC | + | 4 | 2.19e-01 | 2.32e-01 | 4.73e-18 | 1.37e-02 |
| | | | | | GHS | T1D | + | 3 | 2.66e-03 | 5.15e-03 | 8.35e-19 | 1.53e-04 |
| | | | | | GHS | CTS | + | 2 | 9.85e-02 | 1.83e-01 | 1.07e-19 | 4.54e-02 |
| 6q25.3 | ILMN_1795937 | *EZR* | yes | 4.86e-03 | GHS | WTCCC | - | 2 | 1.18e-02 | 2.88e-02 | 9.20e-09 | 1.15e-02 |
| | | | | | CTS | T1DGC | - | 3 | 9.64e-03 | 1.99e-02 | 6.37e-07 | 2.22e-02 |
| | | | | | GHS | CTS | + | 4 | 3.95e-02 | 5.31e-02 | 7.10e-10 | 2.12e-07 |
| 19q13.32 | ILMN_2368617 | *FKRP* | yes | 7.32e-03 | GHS | WTCCC | - | 4 | 1.72e-02 | 2.55e-02 | 2.29e-26 | 1.51e-03 |
| | | | | | CTS | T1DGC | - | 4 | 2.79e-02 | 3.59e-02 | 5.69e-10 | 2.71e-05 |
| | | | | | GHS | CTS | + | 4 | 9.48e-02 | 1.04e-01 | 3.73e-27 | 2.08e-13 |
| Xq28 | ILMN_1808356 | *FAM3A* | yes | 1.01e-02 | GHS | WTCCC | + | 4 | 6.32e-02 | 9.21e-02 | 8.16e-66 | 6.27e-02 |
| | | | | | CTS | T1DGC | - | 4 | 8.43e-03 | 1.44e-02 | 7.45e-34 | 5.73e-03 |
| | | | | | GHS | CTS | + | 5 | 6.77e-02 | 8.77e-02 | 7.68e-51 | 2.90e-22 |
| 12q13.2 | ILMN_1803745 | *SUOX* | yes | 1.71e-02 | GHS | WTCCC | - | 3 | 1.96e-02 | 3.25e-02 | 1.56e-19 | 6.50e-08 |
| | | | | | CTS | T1DGC | - | 4 | 6.47e-02 | 7.53e-02 | 1.01e-07 | 8.08e-12 |
| | | | | | GHS | CTS | + | 4 | 1.84e-01 | 1.96e-01 | 2.79e-19 | 7.66e-08 |
| 12q13.3 | ILMN_1725079 | *TSPAN31* | n/sig | 2.38e-02 | GHS | WTCCC | + | 3 | 8.07e-01 | 6.98e-01 | 1.25e-12 | 3.19e-01 |
| | | | | | GHS | T1DGC | + | 2 | 1.83e-01 | 2.61e-01 | 4.54e-13 | 2.13e-03 |
| | | | | | GHS | T1D | + | 3 | 1.39e-02 | 2.38e-02 | 2.19e-14 | 1.28e-04 |
| | | | | | GHS | CTS | + | 4 | 5.02e-01 | 4.93e-01 | 9.01e-14 | 7.62e-03 |

| Region | Probe | Gene | G-C | p | T1 | T2 | sign($\eta$) | nSNP | p (asymp) | ppp | pT1 | pT2 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 12p13.31 | ILMN_1782729 | *CLECL1* | no | 8.04e-02 | GHS | WTCCC | + | 6 | 6.96e-02 | 8.93e-02 | 0.00e+00 | 1.06e-04 |
| | | | | | GHS | T1DGC | + | 2 | 3.70e-02 | 8.04e-02 | 0.00e+00 | 3.41e-02 |
| | | | | | GHS | T1D | + | 5 | 6.39e-02 | 8.59e-02 | 0.00e+00 | 5.99e-04 |
| | | | | | GHS | CTS | + | 3 | 3.18e-02 | 1.47e-06 | 0.00e+00 | 0.00e+00 |
| 2q11.2 | ILMN_1775235 | *AFF3* | no | 8.15e-02 | GHS | WTCCC | + | 2 | 4.38e-01 | 4.70e-01 | 5.39e-10 | 4.13e-05 |
| | | | | | GHS | T1DGC | + | 2 | 6.50e-01 | 5.94e-01 | 5.39e-10 | 3.81e-03 |
| | | | | | GHS | T1D | + | 3 | 5.72e-02 | 8.15e-02 | 2.58e-09 | 4.16e-08 |
| | | | | | GHS | CTS | + | 5 | 4.40e-03 | 7.03e-03 | 9.19e-09 | 1.51e-07 |
| 12q13.2 | ILMN_1753440 | *DCAF16* | yes | 1.09e-01 | GHS | WTCCC | + | 3 | 4.32e-01 | 4.71e-01 | 5.96e-41 | 5.36e-10 |
| | | | | | CTS | T1DGC | + | 5 | 3.45e-02 | 4.82e-02 | 9.70e-49 | 1.23e-10 |
| | | | | | GHS | CTS | + | 2 | 4.00e-01 | 4.82e-01 | 1.65e-41 | 3.97e-47 |
| 19q13.32 | ILMN_1753805 | *PRKD2* | yes | 1.14e-01 | GHS | WTCCC | - | 2 | 5.67e-01 | 5.77e-01 | 1.08e-29 | 3.37e-02 |
| | | | | | CTS | T1DGC | - | 4 | 2.98e-02 | 4.19e-02 | 2.29e-16 | 1.79e-05 |
| | | | | | GHS | CTS | + | 3 | 8.63e-01 | 7.50e-01 | 8.63e-30 | 5.26e-17 |
| 16p11.2 | ILMN_1701477 | *CCDC101* | yes | 1.35e-01 | GHS | WTCCC | + | 2 | 3.17e-01 | 4.22e-01 | 6.43e-40 | 9.83e-02 |
| | | | | | CTS | T1DGC | + | 2 | 3.42e-02 | 7.07e-02 | 2.41e-13 | 7.43e-05 |
| | | | | | GHS | CTS | + | 3 | 7.87e-01 | 7.16e-01 | 3.46e-40 | 3.27e-13 |
| 17q21.2 | ILMN_1747857 | *SMARCE1* | no | 1.39e-01 | GHS | WTCCC | - | 4 | 1.20e-01 | 1.56e-01 | 3.11e-102 | 9.93e-06 |
| | | | | | GHS | T1DGC | - | 3 | 2.38e-01 | 3.04e-01 | 1.68e-102 | 1.77e-03 |
| | | | | | GHS | T1D | - | 3 | 9.32e-02 | 1.39e-01 | 1.68e-102 | 4.98e-08 |
| | | | | | GHS | CTS | + | 4 | 3.08e-04 | 6.10e-04 | 4.42e-104 | 4.63e-23 |

**Supplementary Table 3.** *(continued)*

| Region | Probe | Gene | G-C | p | T1 | T2 | sign($\eta$) | nSNP | p (asymp) | ppp | pT1 | pT2 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 6q25.3 | ILMN_1788223 | *RSPH3* | yes | 1.96e-01 | GHS | WTCCC | + | 3 | 2.17e-01 | 2.88e-01 | 2.42e-165 | 1.32e-01 |
| | | | | | CTS | T1DGC | + | 2 | 9.01e-02 | 1.69e-01 | 1.76e-26 | 3.53e-02 |
| | | | | | GHS | CTS | + | 4 | 8.55e-02 | 1.16e-01 | 2.36e-163 | 1.67e-65 |
| 13q32 | ILMN_2168217 | *GPR183* | yes | 2.14e-01 | GHS | WTCCC | - | 4 | 2.75e-01 | 3.09e-01 | 1.07e-12 | 9.33e-02 |
| | | | | | CTS | T1DGC | - | 2 | 9.68e-02 | 1.77e-01 | 1.30e-05 | 4.51e-06 |
| | | | | | GHS | CTS | + | 5 | 2.58e-01 | 2.19e-01 | 7.31e-13 | 1.25e-05 |
| 10q23.31 | ILMN_1718520 | *RNLS* | yes | 2.52e-01 | GHS | WTCCC | + | 3 | 9.77e-02 | 1.25e-01 | 2.21e-13 | 1.92e-02 |
| | | | | | CTS | T1DGC | + | 2 | 6.29e-01 | 5.48e-01 | 2.58e-07 | 1.11e-03 |
| | | | | | GHS | CTS | + | 3 | 5.99e-01 | 5.66e-01 | 7.92e-14 | 2.73e-05 |
| 18q22.2 | ILMN_1687825 | *CD226* | n/sig | † | GHS | WTCCC | NA | 1 | | | 2.14e-16 | 5.87e-02 |
| | | | | | GHS | T1DGC | - | 2 | 2.82e-01 | 3.87e-01 | 1.01e-17 | 6.15e-06 |
| | | | | | GHS | T1D | NA | 1 | | | 2.14e-16 | 3.31e-07 |
| | | | | | GHS | CTS | - | 7 | 1.26e-01 | 1.56e-01 | 2.56e-15 | 1.64e-01 |

**Supplementary Information: confirmation of the *CD226* monocyte eQTL**

*Genomic DNA and RNA extraction and cDNA synthesis*

Genomic DNA (gDNA) and RNA samples from three individuals selected for heterozygosity at the T1D most associated *CD226* SNP, rs763361, were extracted from unstimulated positively-selected CD14+ monocyte samples (Miltenyi Biotec) kindly provided by Paul Lyon. RNA samples were then cleaned-up using RNeasy kit with DNase treatment (QIAGEN) following the manufacturers' instructions. RNA purity and quality were assessed using Agilent 2100 Bioanalyzer and Agilent RNA 6000 Nano assay (Agilent Technologies, USA) according to manufacturers' instructions. Quantification of RNA was measured using Nanodrop 1000 spectrophotometer (Thermo Scientific). 1 μg of total RNA was used per reverse transcription reaction for synthesizing cDNA using the Superscript™ III RT kit (Invitrogen). cDNA was primed with 1 μl of 500 ng/μl oligo dT primer (18-mer). To control the absence of gDNA, a corresponding reverse transcriptase (RT)-negative control template was set up for each reverse transcription reaction without the addition of reverse transcriptase. The presence of gDNA in RT-negative samples was assessed by quantitative PCR and none of the samples were found to have gDNA contamination (data not shown).

*Allele-specific gene expression analysis*

Primers were designed against conserved sequences flanking the ASE reporter SNP, rs763361 (forward *CD226* primer 5'-CCCAATAACTATAGAAGTCCCATCTC-3' and reverse *CD226* primer 5'-GGTAGACCTTGGGTAGTGGAAA-3'). Both gDNA

and cDNA from the genotype-selected individuals were amplified using AmpliTaq Gold protocol (ABI) according to manufacturer's protocol using 2.5 mM $MgCl_2$ with an annealing temperature of 55ºC. The PCR products were gel-purified using QIAquick Gel Extraction Kit (QIAGEN), then transformed into competent cells. Over 384 bacterial colonies were picked from the agar plates for each gDNA and cDNA samples and directly inserted into the AmpliTaq Gold PCR mix with 2.5 mM $MgCl_2$, an annealing temperature of 55ºC and the recommended T3 (5'-ATTAACCCTCACTAAAGGGA-3') and T7 (5'-TAATACGACTCACTATAGGG-3') primers. The colonies were then screened by sequencing using the reverse *CD226* primer. The sequencing reactions were performed using Applied Biosystems' BigDye chemistry (version 3.1), resolved using an ABI 3730xl Analyzer and the number of sequences with the A or the G allele of rs763361 were counted. Statistical analysis was performed using a 2 x 2 contingency table to calculate two-tailed *P*-values.

| Sample id | rs763361 3'UTR G>A | gDNA | cDNA | Mantel-Haenszel test |
|---|---|---|---|---|
| C524 | Allele A (sus) | 88 (52.1) 152 (43.6) | 46 (30.5) 137 (38.4) | |
| | Allele B (prot) | 81 (47.9) 197 (56.4) | 105 (69.5) 220 (61.6) | |
| | *P*-value | | | $1.04 \times 10^{-3}$ |
| | | | | |
| C507 | Allele A (sus) | 81 (45.5) | 66 (35.5) | |

| | | | | |
|---|---|---|---|---|
| | | 145 (43.5) | 114 (31.1) | |
| | Allele B (prot) | 97 (54.5) 188 (56.5) | 120 (64.5) 253 (68.9) | |
| | *P*-value | | | $1.2\times10^{-4}$ |
| | | | | |
| C526 | Allele A (sus) | 82 (45.3) 178 (48.2) | 62 (42.8) 139 (37.1) | |
| | Allele B (prot) | 99 (54.7) 191 (51.8) | 83 (57.2) 236 (62.9) | |
| | *P*-value | | | $5.79\times10^{-3}$ |

Supplementary Table: CD14+ monocytes, *CD226* C-BASE ASE assay. Each cell shows n (%) with the top line operator 1 who used 192 colonies per sample and the bottom line operator 2 who used 384 colonies per sample. The p value shown is from the Mantel-Haenszel test which combines information over the two strata defined by operator.