Supplementary Figure 1. Comparison of the allelic effects of eQTL variants between cell types.

(a) Effect sizes of eQTL variants were plotted for each pair of cell types (permutation q-value $\leq 0.05$ in both cell types). Red dot indicates a variant with opposite allelic effects. (b) For each pair of cell types, correlation coefficient of mean gene expression was plotted against the number of eGenes which have eQTL variants with opposite effects.
Supplementary Figure 2. Consistent cell-specific eQTL effects between European datasets and ours.

We utilized summary statistics from European eQTL analysis using CD4$^+$ T cells and monocytes$^1$. Both of European and our datasets were derived from single cell-type eQTL analysis. We considered the results were replicated when a significant eQTL variant in one dataset was also detected as a significant eQTL variant in the other dataset for the same gene with the same direction of allelic effect. The threshold of significance was FDR $\leq 0.05$ for European datasets; and different permutation q-values for our datasets. (a, b) Replication of our results (CD4$^+$ T cells for (a); and monocytes for (b)) by the results of European eQTL analysis. For the top eQTL variants (variants with the lowest P-values) of each gene in our datasets, we examined the ratio that can be replicated by the results of European datasets. (c, d) Replication of the results of European eQTL analysis by our results (CD4$^+$ T cells for (c); and monocytes for (d)). For the top eQTL variants of each gene in European datasets, we examined the ratio that can be replicated by our datasets.
Activity probabilities of eQTL effects for all combinations of cell types ($2^6=64$ patterns) were estimated by analyzing all of six datasets simultaneously using MT-eQTL. (a) Absolute values of effect sizes (beta in linear regression) of eQTL variants that are significant in single cell-type analysis (permutation q-value $\leq 0.05$) or significant only in joint eQTL analysis (local FDR $\leq 0.05$) were plotted. Boxplots denote three quartiles, distribution with whiskers, and outliers as dots. (b) The number of genes whose eQTLs are active only in one cell type (local FDR $\leq 0.05$). (c) Total probability of the number of active cell types. Both of pre and post TSS-conditioned data were analyzed (Supplementary Fig. 5). Consistent with GTEx study\(^2\), we observed U-shaped pattern in the total probabilities for the number of cell types with active eQTL, which suggested the most likely profiles were eQTL that were active in one cell type or in all cell types.
Supplementary Figure 4. Proportion of shared eQTL effects between cell types.

The proportion of shared eQTL effects were calculated as the ratio of the variant-gene pairs which are significant in both cell-type 1 (X-axis) and cell-type 2 (Y-axis) over all pairs which are significant in cell-type 1. The threshold of significance was permutation q-value $\leq 0.05$ for single cell-type eQTL analysis; and local FDR $\leq 0.05$ for joint eQTL analysis.
Supplementary Figure 5. Cell-specific eQTL effects detected by TSS conditioning.

(a) Schematic explanation of transcription start site (TSS) conditioning analysis. The regions that ranged from 1 Kb upstream to 1 Kb downstream from TSS were defined as TSS regions. For each gene in each cell type, we first identified the top eQTL variant (a variant with the lowest P-value) within the TSS region. We next extracted the residual of the linear-regression of this variant against the normalized expression value, and finally the residual was re-analyzed for eQTL. (b, c) A typical example of TSS conditioning observed in NLRP3 region. P-values in eQTL analysis before (top) and after (bottom) TSS-conditioning were plotted. The enhancer regions of memory CD4+ T cells (obtained from Roadmap Epigenome Project) were presented above. The plots only for CD4+ T cells were shown in (b), where each variant was colored by the enhancer or TSS regions and the top eQTL variant was shifted from the TSS region (top) to the enhancer region (bottom) after TSS-conditioning. Layered plots for different cell-types (CD4+ T cells, CD8+ T cells and others) were shown in (c), where each variant was colored by the cell types and the cell-specific eQTL effect became prominent in CD4+ T cells after TSS-conditioning (bottom).
Supplementary Figure 6. Enrichment of eQTL variants before and after TSS conditioning in epigenomic regions.

The top eQTL variant for each eGene (permutation q-value ≤ 0.05) in each cell-type before (a) and after (b) TSS conditioning were analyzed for enrichments in each chromatin state. All variants which were tested for eQTL were used as baseline data. We obtained the chromatin state data of 15-state model for each cell type from Roadmap epigenome project. IDs and epigenome mnemonics were as follows: E037 (BLD.CD4.MPC) for CD4+ T cells; E048 (BLD.CD8.MPC) for CD8+ T cells; E032 (BLD.CD19.PPC) for B cells; E046 (BLD.CD56.PC) for NK cells; E029 (BLD.CD14.PC) for monocytes; and E062 (BLD.PER.MONUC.PC) for PB. The black dashed lines (− log10(P-value) = 3.2) and the grey dashed lines (− log10(P-value) = 1.3) are the cutoff for Bonferroni significance and nominal P-value of 0.05, respectively.
Supplementary Figure 7. Comparison between RTC scores and the posterior probabilities of colocalisation of eQTL and GWAS signals.

The probabilities of colocalisation between GWAS variants of RA and cell-specific eQTL variants were assessed by a Bayesian test (See online methods). Summary statistics of meta-analysis of two GWAS dataset in Japanese population were utilized in this test. Target regions were defined within 500 kilobases of the associated variants (P-value in the current GWAS meta-analysis ≤ 1 x 10^{-5} and P-value in GWAS Catalog ≤ 5 x 10^{-8}). The pairs of the RTC scores and the posterior probabilities of colocalisation (PP.H4 in Supplementary Table 6) of all cell types were plotted.
Supplementary Figure 8. eQTL effects of rs7617215 in all cell types.

Expression of CCR1, CCR3, CCR2, and CCR5 in the six cell types from each individual were plotted according to rs7617215 genotype (T: risk allele). rs7617215 was identified as a significant eQTL (permutation q-value ≤ 0.05, indicated by red boxes) only for CCR2 in monocytes and CCR3 in PB. Boxplots denote three quartiles, distribution with whiskers, and outliers as dots.
Supplementary Figure 9. CCR3 is less likely the candidate causal gene in Behcet disease than CCR2.
P-values in eQTL analysis of CCR3 in CD4+ T cells, monocytes, and unfractionated peripheral blood (PB) were plotted (top). P-values in the conditional analysis by rs7616215 (GWAS variant of Bechet disease, indicated by arrow and diamond shape) were also plotted (bottom). The regulatory trait concordance (RTC) score for CCR3 in PB was 0.48, whereas that of CCR2 in monocytes was 0.98 (Figure 2b).
(a) For each trait, we prepared 10,000 sets of randomly sampled variants which were matched to its GWAS variants for the distance from TSS, MAF, and the number of LD variants. We here showed the data of type I diabetes as an example of this analysis. We first counted the number of GWAS variants which were LD with eQTL variants (a red number in shaded column and a red vertical line in the histogram) and the number of randomly sampled variants which were LD with eQTL variants (blue numbers in shaded column and their distributions were shown in the histogram). When N out of 10,000 random sets had more eQTL variants in LD than GWAS variants, we empirically determined the enrichment P-value = N/10,000. (b) We also performed another enrichment analysis by directly comparing different cell types as done in (a). For each pair of cell types, we calculated the differences of the number of GWAS variants or randomly selected variants which were LD with eQTL variants (shaded column on the table). We empirically determined the enrichment P-value by contrasting two differences (red and blue numbers in shaded column). This strategy enabled us to compare the enrichment between different cell types, even though the total numbers of eQTL variants were different between cell types (cell-type B had more eQTL variants than cell-type A in this example).
Supplementary Figure 11. Direct comparison of enrichment of eQTL variants in GWAS variants between cell types.

The strategy of enrichment analysis was shown in Supplementary Figure 10b. For each trait, an arrow was plotted when its GWAS variants were significantly more enriched in the eQTL variants of one cell type (on the right axis) than those of the other cell type (on the left axis) (P-value ≤ 0.05). We marked the cell types by red boxes which showed enrichment compared with all the other cell types. The total number of independent GWAS variants was shown in parentheses. Although the same diseases were analyzed as in Figure 3, only diseases with at least one significant pair were plotted in this figure: rheumatoid arthritis (RA), Behcet disease (BD), multiple sclerosis (MS), ulcerative colitis (UC), Crohn's disease (CD), type 1 diabetes (T1D), type 2 diabetes (T2D), Alzheimer's disease (AD), Parkinson disease (PD), schizophrenia (SZ), and prostate cancer (PCa). GWAS p-value ≤ 5x10^{-8} and eQTL permutation q-value ≤ 0.05.
Supplementary Figure 12. Strategy of constructing prediction models of gene expression.

(a) The method to design and evaluate the models of gene expression prediction. In this example, we showed the prediction of i-th gene expression in cell type X in the k-th round of 10-fold cross-validation (CV). (i) We performed eQTL analysis of cell type X using the training set only. (ii) We merged the eQTL data with the active chromatin state data of cell type X (obtained from Roadmap Epigenomic Project). (iii) We selected multiple sets of eQTL variants based on the P-value thresholds (0.05, 1x10^{-2}, 1x10^{-3}, 1x10^{-4}, 1x10^{-5}, and 1x10^{-6}) and active chromatin states (eight states in 15-state model + 12 states in 18-state model). (iv) For each model constructed in step iii, we calculated polygenic score using genotype of samples in the testing set. (v) For each model, we compared the predicted gene expression (polygenic score) with the observed gene expression and evaluated its prediction performance by Pearson's correlation coefficient ($R_{k,n,i}$).

(b) Strategy of variant selection for prediction model (training set eQTL data + active chromatin state data)

- Model ID
- P-value
- Chromatin state

(i) eQTL analysis of cell type X in training set

(ii) Active chromatin states of cell type X

(iii) Strategy of variant selection for prediction model

(iv) Polygenic score (PS) calculation in testing set

(v) Evaluation of prediction performance in testing set

Best model
- $R_{k,i}$ (mean of $R_{k,n,i}$) is used to evaluate the total prediction performance in cross validation.
- The best model is defined as the one with the highest $R_{k,i}$ in cross validation.
- In this example, model 2 was selected as the best model.

Final model
- eQTL analysis using ALL SAMPLES
- P-values
- Effect sizes
- Variant selection for polygenic score calculation based on the BEST MODEL in cross validation.

P-value threshold: 0.01
Chromatin state: Enh

$R_i$ is defined as $R_{n,i}$ of the best model.
- This index will be used in Fig. 5 and Supplementary Fig. 14.
- In this example, $R_i = 0.4$. 
(b) The method to construct the final model. In this example, we showed the prediction of $i$-th gene expression. For each model, we averaged $R (R_{k,n,i})$ of ten rounds, and the model with the highest mean $R (R_{n,i})$ was selected as the best model. Based on the parameters of the BEST MODEL (P-value threshold and chromatin state) and statistics of eQTL analysis using ALL SAMPLES, we constructed the final prediction model of $i$-th gene. This final model was used for the gene expression prediction of GWAS datasets.
Supplementary Figure 13. Evaluation of our prediction model for gene expression using the Geuvadis project data.

(a) Schematic explanation of the evaluation method. We obtained the genotype and gene expression data for 344 Europeans from the Geuvadis project. We split them into the training set (N=100) and the testing set (N=244). The sample size of training set was set around the same level as that of our study. In the training set, prediction models were constructed by polygenic score with chromatin state data (our model). For comparison, three other prediction models (polygenic score without chromatin state data, LASSO and elastic net) were also constructed. The prediction performances were evaluated in the testing set using Pearson's correlation coefficient R between the predicted gene expression (polygenic score) and the observed gene expression (hold-out validation). (b) The prediction performances of different models were plotted for each eGene (permutation q value ≤ 0.1) (c) The prediction performances with different degrees of eQTL significance. Permutation q values for eGenes calculated only in the training samples were used as an indicator of eQTL significance. Only the results of our model were shown. Boxplots denote three quartiles, distribution with whiskers, and outliers as dots.
Supplementary Figure 14. Performance of each chromatin state in cross-validation

Performances of gene expression prediction were evaluated by cross-validation (CV). For each gene in each cell type, we plotted the mean correlation coefficient of the best prediction model in CV ($R_i$, as explained in Supplementary Figure 12). Data were sorted according to the chromatin state. "No data" indicates genes whose best model did not utilize chromatin state data. Boxplots denote three quartiles, distribution with whiskers, and outliers as dots.
Supplementary Figure 15. Combined Z-scores in the association studies using predicted gene expression.

(a) Combined Z-scores in the association studies using predicted gene expression. Positive $Z_{\text{Case-control}}$ indicates that upregulation of the assessed gene increases the risk of RA. Positive $Z_{\text{Age of onset}}$ indicates that upregulation of the assessed gene delays the onset of RA. For each gene, the absolute values of Z-scores were compared, and the data of the cell type with the highest value was plotted. When the absolute value of the Z-score was $\geq 3$, the corresponding data was plotted using a cell-specific color and labeled with the gene name. (b) The same data as in (a) were plotted according to the cell types. When either of absolute value of Z score was $\geq 3$, the corresponding data was plotted with red or blue color. Bonferroni significance was indicated by dashed lines and genes with Bonferroni significance were labeled with their names. The results of Pearson's correlation analysis between $Z_{\text{Case-control}}$ and $Z_{\text{Age of onset}}$ were shown at the top of each plot.
Supplementary Figure 16. Evaluation of the performance of exon expression prediction using the Geuvadis project data.

The performance of exon expression prediction was analyzed using Geuvadis data. We tested three P-value thresholds for variant selection (1x10^{-4}, 1x10^{-5}, and 1x10^{-6}). As illustrated in Supplementary Figure 13a, we constructed prediction models (polygenic score) in the training set (N=100), and examined the prediction performance by Pearson's correlation coefficient (R) between the predicted exon expression (polygenic score) and the observed exon expression in the testing set (N=244) (hold-out validation). We selected variants with P-values less than or equal to each P-value threshold in exon-level eQTL analysis using training set, and used their effect sizes for calculating polygenic score in testing set.
Supplementary Figure 17. Comparison of predicted gene and exon expression in RA.
We applied our pipelines to predict exon expression using two RA GWAS datasets (the same datasets as used in gene expression prediction) and meta-analyses of case-control association studies were performed. We then compared meta-analysis Z scores ($Z_{\text{Case-control}}$) derived from gene and exon-level predicted expression. When pairs of gene and exon had inconsistent direction of dysregulation and $Z_{\text{Case-control}}$ of gene or exon $\geq$ 3, they were indicated by red dots.
Supplemental Tables:

Supplementary Table 1. Basic information for each cell type.

1) Permutation q-value ≤ 0.05. 2) q-value ≤ 0.01.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CD4</th>
<th>CD8</th>
<th>B</th>
<th>NK</th>
<th>Mono</th>
<th>PB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean sorted cell count</td>
<td>5.83x10^5</td>
<td>5.03x10^5</td>
<td>4.92x10^5</td>
<td>5.31x10^5</td>
<td>5.35x10^5</td>
<td>-</td>
</tr>
<tr>
<td>Mean read count (post-QC)</td>
<td>4.68x10^7</td>
<td>4.56x10^7</td>
<td>4.80x10^7</td>
<td>4.69x10^7</td>
<td>4.91x10^7</td>
<td>5.09x10^7</td>
</tr>
<tr>
<td>Mean mapping rate</td>
<td>97.4%</td>
<td>97.2%</td>
<td>96.2%</td>
<td>97.2%</td>
<td>97.4%</td>
<td>97.4%</td>
</tr>
<tr>
<td>N of eGenes^1</td>
<td>3,156</td>
<td>2,717</td>
<td>2,973</td>
<td>2,653</td>
<td>3,759</td>
<td>3,386</td>
</tr>
<tr>
<td>N of eQTL variants^1</td>
<td>231,557</td>
<td>199,372</td>
<td>224,376</td>
<td>191,041</td>
<td>284,015</td>
<td>229,862</td>
</tr>
<tr>
<td>N of eGenes^1 (TSS-conditioning analysis)</td>
<td>488</td>
<td>407</td>
<td>456</td>
<td>403</td>
<td>717</td>
<td>521</td>
</tr>
<tr>
<td>N of eQTL variants^1 (TSS-conditioning analysis)</td>
<td>25,634</td>
<td>22,114</td>
<td>27,012</td>
<td>22,011</td>
<td>34,855</td>
<td>26,197</td>
</tr>
<tr>
<td>N of genes with sQTL variants^2</td>
<td>783</td>
<td>705</td>
<td>710</td>
<td>640</td>
<td>813</td>
<td>919</td>
</tr>
<tr>
<td>N of sQTL variants^2</td>
<td>22,051</td>
<td>20,130</td>
<td>21,891</td>
<td>17,729</td>
<td>21,907</td>
<td>27,874</td>
</tr>
<tr>
<td>N of eExons^1</td>
<td>14,410</td>
<td>12,211</td>
<td>13,793</td>
<td>12,904</td>
<td>19,596</td>
<td>15,615</td>
</tr>
<tr>
<td>N of exon-level eQTL variants^1</td>
<td>329,575</td>
<td>284,250</td>
<td>323,119</td>
<td>280,676</td>
<td>390,113</td>
<td>321,210</td>
</tr>
</tbody>
</table>

Supplementary Table 2. Enrichment of cell-specific eQTL variants within transcription factor binding sites. (Supplemental excel file)

Supplementary Table 3. List of candidate causal genes identified by combining GWAS catalog and eQTL data of each cell type. (Supplemental excel file)

Supplementary Table 4. List of candidate causal genes identified by combining GWAS catalog and exon-level eQTL data of each cell type. (Supplemental excel file)

Supplementary Table 5. List of candidate causal genes identified by combining GWAS catalog and TSS-conditioned eQTL data of each cell type. (Supplemental excel file)

Supplementary Table 6. Bayesian test for colocalisation between GWAS variants of RA and eQTL variants of each cell type. (Supplemental excel file)

Supplementary Table 7. eQTL variants and their effect sizes used to predict gene expression of CD4^+ T cells. (Supplemental excel file)

Supplementary Table 8. eQTL variants and their effect sizes used to predict gene expression of CD8^+ T cells.
Supplementary Table 9. eQTL variants and their effect sizes used to predict gene expression of B cells.

Supplementary Table 10. eQTL variants and their effect sizes used to predict gene expression of NK cells.

Supplementary Table 11. eQTL variants and their effect sizes used to predict gene expression of monocytes.

Supplementary Table 12. eQTL variants and their effect sizes used to predict gene expression of PB.

Supplementary Table 13. Genes with Bonferroni significance in the case-control analysis using predicted gene expression.

Supplementary Table 14. Quality control of genotype data.

1) both in cases and controls. 2) Hardy-Weinberg Equilibrium P-values were calculated only for controls in RA GWAS dataset. 3) IMPUTE info measure

<table>
<thead>
<tr>
<th>Parameter</th>
<th>eQTL</th>
<th>RA Cohort 1</th>
<th>RA Cohort 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample size</td>
<td>105</td>
<td>5,683</td>
<td>7,359</td>
</tr>
<tr>
<td>Case</td>
<td>-</td>
<td>2,303</td>
<td>2,342</td>
</tr>
<tr>
<td>Control</td>
<td>-</td>
<td>3,380</td>
<td>5,017</td>
</tr>
</tbody>
</table>

Pre-imputation QC

Sample-QC
- Call rate                          | 0.98 | 0.98       | 0.98       |
- Closely related samples (IBD)      | Excluded | Excluded   | Excluded   |
- Outlier from East Asian cluster    | Excluded | Excluded   | Excluded   |
                by PCA with 1000G phase 1 v3 samples | Excluded | Excluded   | Excluded   |

SNP-QC
- Call rate                          | 0.95 | 0.99¹      | 0.99¹      |
- MAF                                 | 0.01 | 0.05       | 0.05       |
- HWE P-value²                        | 1x10⁻⁶| 1x10⁻⁶     | 1x10⁻⁶     |

Post-imputation QC

MAF                                   | 0.05 | -          | -          |
Average maximum posterior probability  | 0.9  | 0.9        | 0.9        |
INFO³                                 | 0.4  | 0.4        | 0.4        |
REFERENCES
