Supplemental Data

HLA-C Level Is Regulated by a Polymorphic

Oct1 Binding Site in the *HLA-C* Promoter Region

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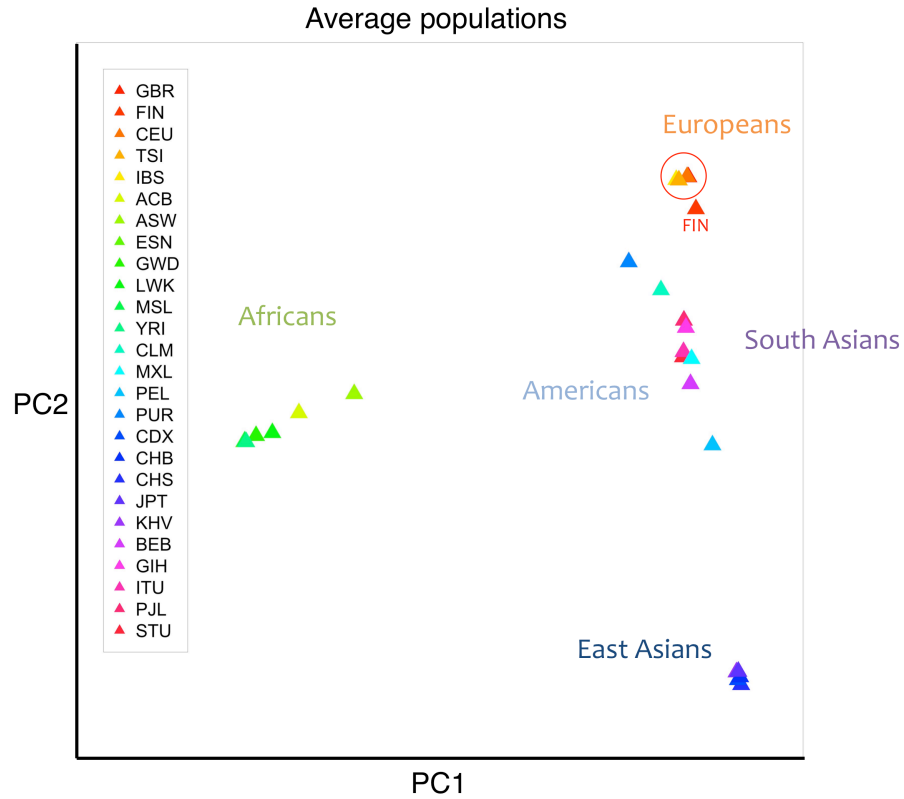
Supplemental figures and table

Figure S1. R plot of the first two principal components (PC) of population stratification using Eigensoft [1]. Individuals of European ancestry were used in this study because of their homogenous genetic background (inside the red circle are GBR, CEU, TSI and IBS). The FIN (Finland) were excluded due to their divergence from the rest of the Europeans.

A

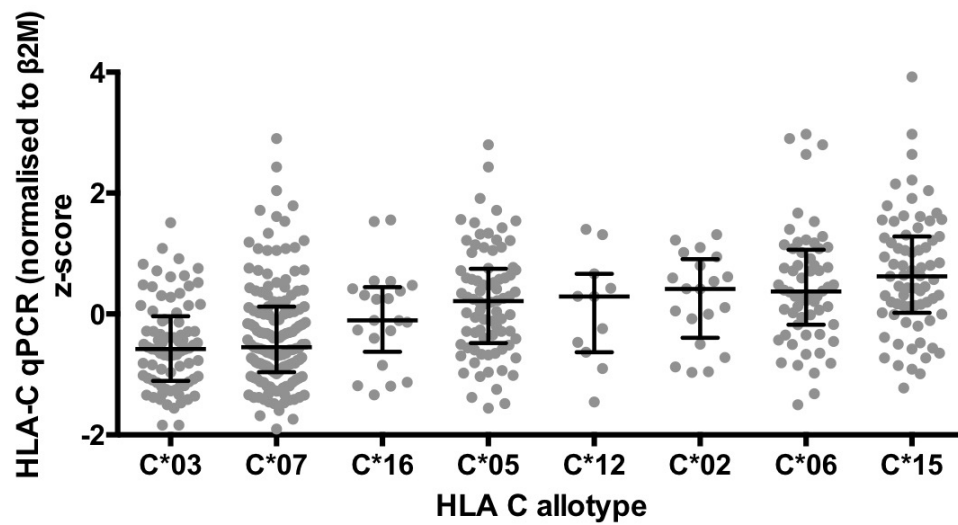

273 European British

$p = 1.8 \times 10^{-20}$
$R^2 = 0.29$
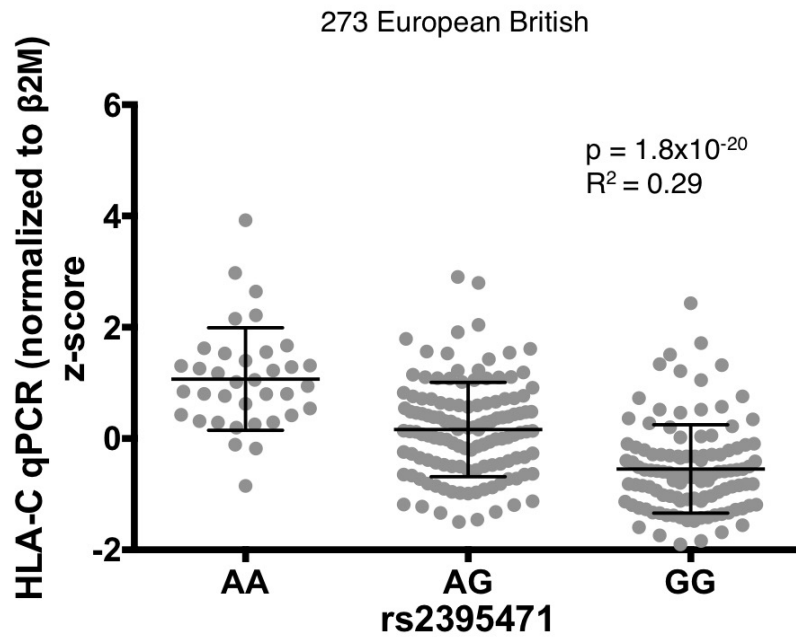
B

Figure S2. (A) Association between rs2395471 and *HLA-C* qPCR in peripheral

blood mononuclear cells, transformed to z-score to ensure normality, in 273 donors of

European descent from Great Britain [2; 3]. The p value and R^2 (the level of variation explained by the SNP) are provided. (B) Gradient of *HLA-C* mRNA expression across allelic type in the same cohort. Genotyping in this cohort was performed using the OmniExpress Illumina genotyping chip and imputed against the 1KG phase 1 reference dataset as previously described [4]. Only variants with an info score > 0.8 were included in the analysis. Association testing was performed using a linear-mixed effects model (the '--mlma' method) in GCTA [5], that takes into account population structure. Consent for participation in these studies was obtained from each donor and is detailed in the original publication [2]. The mean with standard deviation is represented.
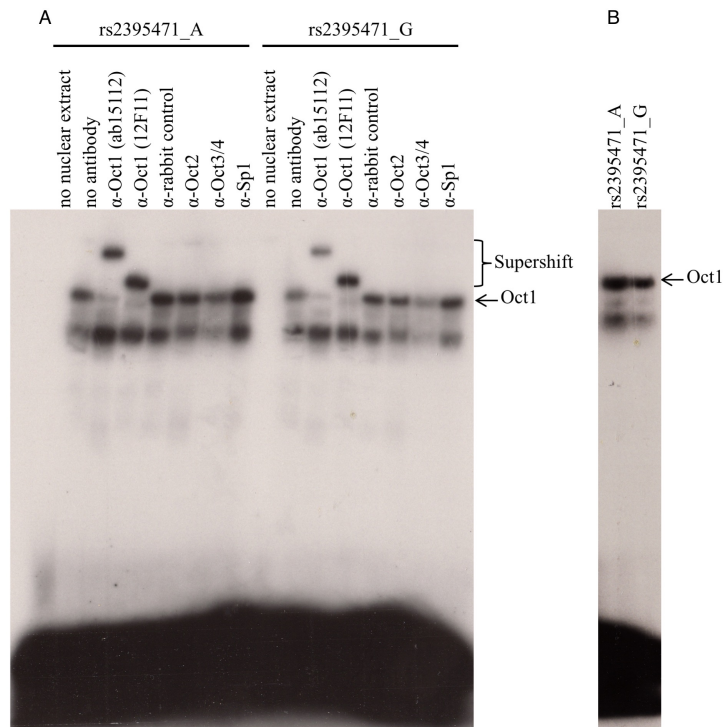
Figure S3. The Oct1 transcription factor binds to the genomic region containing rs2395471. The same EMSA experiments as shown in Figure 3A and B were replicated using Jurkat T cell line nuclear extracts. Panels A and B show similar results to those shown in Figure 3A and B, confirming that Oct1 binds to the genomic region containing rs2395471, and that rs2395471_G binds more weakly to Oct1 relative to rs2395471_A.

HLA-C alleles (2 digits)	Average expression (MFI)
01	254
02	167
03	116
04	201
05	154
06	226
07	114
08	176
12	193
14	294
15	223
16	181
17	115
18	239

Table S1. Average expression (MFI) of *HLA-C* alleles derived from Apps et al. [6].

We imputed HLA-C expression levels here by summing the average expression values for

each HLA-C allele present in each given individual. For example, an *HLA-C*01/HLA-C*02* individual would have an average expression of 421 (254 + 167).

Supplemental references

1. Price, A.L., Patterson, N.J., Plenge, R.M., Weinblatt, M.E., Shadick, N.A., and Reich, D. (2006). Principal components analysis corrects for stratification in genome-wide association studies. Nat Genet 38, 904-909.
2. Fairfax, B.P., Makino, S., Radhakrishnan, J., Plant, K., Leslie, S., Dilthey, A., Ellis, P., Langford, C., Vannberg, F.O., and Knight, J.C. (2012). Genetics of gene expression in primary immune cells identifies cell type-specific master regulators and roles of HLA alleles. Nat Genet 44, 502-510.
3. Kulkarni, S., Qi, Y., O'HUigin, C., Pereyra, F., Ramsuran, V., McLaren, P., Fellay, J., Nelson, G., Chen, H., Liao, W., et al. (2013). Genetic interplay between HLA-C and MIR148A in HIV control and Crohn disease. Proc Natl Acad Sci U S A 110, 20705-20710.
4. Naranbhai, V., Fairfax, B.P., Makino, S., Humburg, P., Wong, D., Ng, E., Hill, A.V., and Knight, J.C. (2015). Genomic modulators of gene expression in human neutrophils. Nat Commun 6, 7545.
5. Yang, J., Lee, S.H., Goddard, M.E., and Visscher, P.M. (2011). GCTA: a tool for genome-wide complex trait analysis. Am J Hum Genet 88, 76-82.
6. Apps, R., Qi, Y., Carlson, J.M., Chen, H., Gao, X., Thomas, R., Yuki, Y., Del Prete, G.Q., Goulder, P., Brumme, Z.L., et al. (2013). Influence of HLA-C expression level on HIV control. Science 340, 87-91.