Supplementary Table 1. Primers, annealing temperatures, and restriction endonucleases used for genotyping.

Polymorphisms	Sense primer	Antisense primer	Annealing temperature	Restriction enzyme
CD28 Int3T>C	5'TTTTCTGGGTAAGAGAAGCAGCGC 3'	5'GAACCTACTCAAGCATGGGG 3'	58^{O}C	*Eco 47R*III
CTLA4 - 318C>T	5'AAATGAATTGGACTGGATGGT 3'	5'TTACGAGAAAGGAAGCCGTG 3'	60 ^{O}C	*Mse* I
*CTLA*4 +49 A>G	5'CACGGCTTCCTTTCTCGTAA 3'	5'CCCTGGAATACAGAGCCAGC 3'	63^{O}C	*Bbv* I
ICOS 3'UTR 1564 T>C	5' TTACCAAGACTTTAGATGCTTTCTT 3'	5'GAATCTTTCTAGCCAAATCATATTC 3'	55^{O}C	*Alu* I
PDCD1 +7785 C>T	5' AGACGGAGTATGCCACCATTGTC 3'	5' AAATGCGCTGACCCGGGCTCAT 3'	50 ^{O}C	*PvuII*
FAS -670 G>A	5' CTACCTAAGAGCTATCTACCGTTC 3'	5' GGCTGTCCATGTTGTGGCTGC 3'	62 ^{O}C	*Mva I*

Penalized Logistic Regression.

For all calculations we used the R package "stepPrl" created by Park & Hastie (2006). The logistic regression model is represented by the following formula:

$$\log\frac{P\{Y=1\mid X\}}{P\{Y=0\mid X\}}=\beta_0+X^T\beta$$

where X is a matrix of predictors. Coefficients of regression model are usually estimated by maximum likelihood.

In order to estimate coefficients of penalized logistic regression it is necessary to minimize the following function:

$$L(\beta_0,\beta,\lambda)=-l(\beta_0,\beta)+\frac{\lambda}{2}\parallel\beta\parallel_2^2,$$

where l indicates the binomial log-likelihood, and λ is a positive constant.

In order to choose the value of parameter λ, Mee Young Park and Trevor Hastie (2006) implemented the cross-validation technique. We also used this solution with a slight modification. In brief, keeping in mind that the cross validation technique is based on random division of data, we repeated the above procedure 100 times choosing 100 candidates values of parameter λ. After that, we selected a parameter λ as the mean of 100 obtained λ values during iterative procedure. Using set of candidate values $\lambda = \{0.01, 0.5, 1, 2, 3, 4\}$ we observed $\lambda \approx 2$. For CD28(AA) and IFNG(TT), using Akaike information criterion we obtained the following regression:

$$\log\frac{P\{Y=1\mid X\}}{P\{Y=0\mid X\}}=-0.20+\underset{(0.068)}{0.33}\,CD28(AA)+\underset{(0.916)}{0.02}\,IFNG(TT)+\underset{(0.021)}{0.48}\,CD28(AA):IFNG(TT)$$

In parenthesis are p-values of corresponding coefficients.

In order to analyze the influence of the source population for the three case-control sets, we performed two types of penalized logistic regression. For the first type, we have included D1, D2 and D3 as indicators of case/control sets

$$\log\frac{P\{Y=1\mid X\}}{P\{Y=0\mid X\}} = -0.19 - \underset{(0.943)}{0.01}\,D_1 - \underset{(0.851)}{0.02}\,D_2 + \underset{(0.810)}{0.03}\,D_3 + \\ + \underset{(0.070)}{0.34}\,CD28(AA) + \underset{(0.931)}{0.02}\,IFNG(TT) + \underset{(0.022)}{0.47}\,CD28(AA):IFNG(TT)$$

where *D* takes a value 1 if an individual is from the corresponding set and 0 otherwise. In parenthesis are the p-values of corresponding coefficients.

For the second type of analysis we included the indicator (variable "Race") for the last group (non-white).

$$\log\frac{P\{Y=1\mid X\}}{P\{Y=0\mid X\}} = -0.21 + \underset{(0.810)}{0.05}\,RACE + \\ + \underset{(0.070)}{0.34}\,CD28(AA) + \underset{(0.931)}{0.02}\,IFNG(TT) + \underset{(0.022)}{0.47}\,CD28(AA):IFNG(TT)$$

where *RACE* is race indicator: it takes 1 for non-white individual and 0 otherwise. Note that in the previous equation the variable *RACE* is the indicator D_3 of the third group (non-white), so the other indicator variables D_1 and D_2 from the previous regression essentially contribute only in the intercept coefficient. In parenthesis are p-values of corresponding coefficients.

Thus, we observed high p-values and very small values of coefficients for group indicators (D1, D2, D3) and race variable (RACE). This indicates the absence of influence of the population source and the absence of ethnic influence on the studied phenotype.

Supplementary Table 2. CD28 TT/IFNG AA genotype frequencies in all groups, including the additional control group

The controls consisted of 129 women and 64 men.
The additional control group consisted of 83 women and was genotyped only for CD28 and IFNG polymorphisms.

	cases	controls		additional control group
genotypes	women	women	men	women
CD28 TT/IFN AA	79 (35%)	28 (22%)	11 (17%)	16 (19%)
OTHER	150 (65%)	101 (78%)	53 (83%)	67 (81%)