

Appendix 1: Genotype frequencies in controls and cases (persistent islet autoimmunity including T1D)

| SNP | Genotype | DR3/DR4 heterozygotes | | | Other HLA genotypes | | |
|-------------|----------|-----------------------|-------|-------------------------|---------------------|-------|-------------------------|
| | | Controls | Cases | OR (95% CI) | Controls | Cases | OR (95% CI) |
| CTLA4-318 | CT/TT | 12.0 | 22.5 | 2.13 (0.77-5.89) | 18.7 | 17.7 | 0.94 (0.42-2.07) |
| CTLA4 ex.1 | AG/GG | 61.3 | 62.5 | 1.05 (0.48-2.32) | 65.9 | 61.3 | 0.82 (0.44-1.54) |
| INS HphI | AT/TT | 54.7 | 32.5 | 0.40 (0.18-0.89) | 45.5 | 43.5 | 0.92 (0.50-1.71) |
| IL4R -3223 | CT/TT | 48.0 | 42.5 | 0.80 (0.37-1.73) | 44.7 | 62.9 | 2.10 (1.12-3.92) |
| IL4R -1914 | CT/TT | 64.0 | 72.5 | 1.48 (0.64-3.43) | 71.5 | 56.5 | 0.52 (0.27-0.97) |
| IL4R 50 | AG/GG | 73.3 | 65.0 | 0.68 (0.29-1.54) | 67.5 | 82.3 | 2.23 (1.05-4.74) |
| IL4R 142 | CT/TT | 17.3 | 15.0 | 0.84 (0.29-2.41) | 21.1 | 19.4 | 0.89 (0.42-1.92) |
| IL4R 375 | AC/CC | 22.7 | 22.5 | 0.99 (0.40-2.48) | 21.1 | 27.4 | 1.41 (0.69-2.86) |
| IL4R 389 | GT/TT | 22.7 | 22.5 | 0.99 (0.40-2.48) | 21.1 | 27.4 | 1.41 (0.69-2.86) |
| IL4R 406 | TC/CC | 21.3 | 22.5 | 1.07 (0.42-2.70) | 21.1 | 24.2 | 1.19 (0.58-2.46) |
| IL4R 478 | TC/CC | 30.7 | 32.5 | 1.09 (0.48-2.48) | 32.5 | 35.5 | 1.14 (0.60-2.17) |
| IL4R 551 | AG/GG | 34.7 | 40.0 | 1.25 (0.57-2.77) | 43.9 | 45.2 | 1.05 (0.57-1.94) |
| IL4R 761 | TC/CC | 1.3 | 2.5 | N/A | 1.6 | 0.0 | N/A |
| IL4 -524 | CT/TT | 37.3 | 22.5 | 0.49 (0.20-1.17) | 30.1 | 40.3 | 1.57 (0.83-2.97) |
| IL13 -1512 | AC/CC | 29.3 | 40.0 | 1.61 (0.72-3.59) | 30.9 | 32.3 | 1.06 (0.55-2.05) |
| IL13 -1112 | CT/TT | 33.3 | 40.0 | 1.33 (0.60-2.95) | 31.7 | 32.3 | 1.02 (0.53-1.97) |
| IL13 intr.3 | CT/TT | 42.7 | 35.0 | 0.72 (0.33-1.60) | 35.8 | 33.9 | 0.92 (0.48-1.75) |
| IL13 110 | GA/AA | 41.3 | 35.0 | 0.76 (0.34-1.69) | 35.0 | 32.3 | 0.89 (0.46-1.69) |

Genotype frequencies are shown after stratification for HLA-DR3/4 status. Since several cells had values < 5 in the homozygote variant, both heterozygotes and homozygotes variant have been combined for analysis. ORs refer to the combined variant group. Statistically significant OR values (P < 0.05) are indicated in bold.

Appendix 2: Pairwise linkage disequilibrium between IL4 and IL13 SNPs

| | IL4 -524 | IL13 -1512 | IL13 -1112 | IL13 int3 | IL13 110 |
|-------------------|-----------------|-------------------|-------------------|------------------|-----------------|
| IL4 -524 | | 0.15* | 0.20* | 0.53** | 0.43** |
| IL13 -1512 | 0.02 | | 0.96** | 0.57** | 0.58** |
| IL13 -1112 | 0.03 | 0.13 | | 0.48** | 0.47** |
| IL13 int3 | 0.07 | 0.07 | 0.07 | | 1.00** |
| IL13 110 | 0.06 | 0.08 | 0.07 | 0.16 | |

Upper right triangle: absolute D' (standardized LD, $D' = D/D_{max}$)

Lower left triangle: D. Values refer to the reference allele.

Statistically significant LD values are indicated with * $P < 0.05$ and ** $P < 0.0001$

Appendix 3: Pairwise linkage disequilibrium between IL4R SNPs

| | -3223 | -1914 | 50 | 142 | 375 | 389 | 406 | 478 | 551 | 761 |
|--------------|--------------|--------------|-----------|------------|------------|------------|------------|------------|------------|------------|
| -3223 | | 0.04 | 0.90** | 0.98** | 0.29 | 0.29 | 0.27 | 0.48* | 0.56* | 0.45 |
| -1914 | - 0.005 | | 0.09 | 0.04 | 0.12 | 0.12 | 0.15 | 0.16 | 0.24* | 0.23 |
| 50 | 0.13 | - 0.02 | | 1.00** | 0.12 | 0.12 | 0.10 | 0.35* | 0.07 | 0.18 |
| 142 | - 0.03 | - 0.002 | 0.06 | | 1.00* | 1.00* | 1.00* | 0.40** | 0.32* | 0.33 |
| 375 | - 0.01 | 0.01 | 0.01 | - 0.01 | | 1.00** | 1.00** | 0.98** | 1.00** | 1.00 |
| 389 | - 0.01 | 0.01 | 0.01 | - 0.01 | 0.10 | | 1.00** | 0.98** | 1.00** | 1.00 |
| 406 | - 0.01 | 0.01 | 0.01 | - 0.01 | 0.10 | 0.10 | | 1.00** | 1.00** | 1.00 |
| 478 | - 0.02 | 0.01 | 0.03 | 0.03 | 0.09 | 0.09 | 0.09 | | 0.96** | 0.86* |
| 551 | - 0.04 | 0.03 | 0.01 | 0.03 | 0.09 | 0.09 | 0.09 | 0.13 | | 0.16 |
| 761 | - 0.001 | - 0.001 | 0.001 | 0.002 | - 0.001 | - 0.001 | - 0.001 | 0.01 | - 0.000 | |

Upper right triangle: absolute D' (standardized LD, $D' = D/D_{max}$)

Lower left triangle: D. Values refer to the reference allele.

Statistically significant LD values are indicated with * $P < 0.05$ and ** $P < 0.0001$