DAISY longitudinal T-cell responses to hybrid insulin peptides

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## Background

The aim of this analysis is to evaluate T-cell responses to hybrid insulin peptides over time in the prediabetic period. The analysis includes data from 25 Aab+ participants and 38 HLA-DR-DQ matched Aab- participants.

## Methods

Table 1: Aab+ and AAb- participants were compared using t-tests for continuous variables and Fisher’s exact test for categorical variables.

Figure 1b: Linear mixed models with a random intercept to account for correlation of measures within a participant were used to compare responses in Aab+ and Aab- participants. Response levels were natural log transformed prior to analysis.

Figure 1c, Figure 1d, Supplemental Figure 3: Paired t-tests were used to test whether the specified peptide responses differed.

Figure 2a-b: Linear mixed models with random intercepts and random slopes were used to test whether Aab+ and Aab- participants have different trajectories in their IFNy/IL10 ratios over time. Ratios were natural log transformed prior to analysis.

Figure 3 and Supplemental Figure 5: Linear mixed models with a random intercept to account for correlation of measures within a participant were used to compare responses in Aab+ participants who progressed to T1D and those who did not progress to T1D, and in Aab- participants who seroconverted to those who did not seroconvert. Response levels were natural log transformed prior to analysis.

Supplemental Figure 6: A t-test was used to compare the duration since seroconversion in Aab+ participants who progressed to T1D and those who did not progress.

Figure 4 and Supplemental Figure 7: Linear mixed models with a random intercept to account for correlation of measures within a participant were used to test the association between peptide responses and clinical variables. Response levels were natural log transformed prior to analysis. Similar models with a quadratic relationship between the variables were also tested.

## Results

Table 1

|  | level | Aab- | Aab+ | p | test |
| --- | --- | --- | --- | --- | --- |
| n |  | 38 | 25 |  |  |
| Age.at.Visit..years. (mean (SD)) |  | 18.70 (3.58) | 18.07 (3.76) | 0.506 |  |
| Sex (%) | Female | 20 (52.6) | 14 ( 56.0) | 1.000 | exact |
|  | Male | 18 (47.4) | 11 ( 44.0) |  |  |
| Race (%) | African American | 3 ( 7.9) | 0 ( 0.0) | 0.270 | exact |
|  | Caucasian | 35 (92.1) | 25 (100.0) |  |  |
| Ethnicity (%) | Hispanic or Latino | 7 (18.4) | 6 ( 24.0) | 0.752 | exact |
|  | Non-Hispanic or Latino | 31 (81.6) | 19 ( 76.0) |  |  |
| numvisit (mean (SD)) |  | 4.03 (0.79) | 4.00 (1.00) | 0.908 |  |
| fup (mean (SD)) |  | 21.60 (4.07) | 19.34 (6.04) | 0.081 |  |
| ab\_at\_enrollment (%) | 0 | 37 (97.4) | 0 ( 0.0) | <0.001 | exact |
|  | 1 | 1 ( 2.6) | 12 ( 48.0) |  |  |
|  | 2 | 0 ( 0.0) | 8 ( 32.0) |  |  |
|  | 3 | 0 ( 0.0) | 5 ( 20.0) |  |  |

The Fisher’s exact test for HLA genotype is shown below.

##   
## Fisher's Exact Test for Count Data  
##   
## data: HLA  
## p-value = 0.503  
## alternative hypothesis: two.sided

The tables below are the results of the mixed models for Figure 1b. For each peptide, there are two tables. The first table contains the least-squares mean (on the log scale) of the peptide in each group. The second table provides the p-value for the group comparison.

## [1] "IFN.y.No.Antigen"  
## group emmean SE df lower.CL upper.CL  
## Aab- -0.827 0.566 62 -1.96 0.305  
## Aab+ -0.255 0.701 61 -1.66 1.147  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## (Aab-) - (Aab+) -0.572 0.901 61 -0.634 0.5282  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IFN.y.Pediarix"  
## group emmean SE df lower.CL upper.CL  
## Aab- 6.11 0.0923 62 5.93 6.30  
## Aab+ 6.04 0.1144 61 5.81 6.26  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## (Aab-) - (Aab+) 0.0749 0.147 61 0.510 0.6121  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IFN.y.B.9.23..Native."  
## group emmean SE df lower.CL upper.CL  
## Aab- -0.853 0.46 62 -1.773 0.0658  
## Aab+ 0.221 0.57 61 -0.918 1.3607  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## (Aab-) - (Aab+) -1.07 0.732 61 -1.468 0.1473  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IFN.y.B.9.23..B22E."  
## group emmean SE df lower.CL upper.CL  
## Aab- 1.17 0.379 62 0.417 1.93  
## Aab+ 2.18 0.469 61 1.239 3.11  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## (Aab-) - (Aab+) -1 0.603 61 -1.662 0.1016  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IFN.y.C.Peptide.Neuropeptide.Y"  
## group emmean SE df lower.CL upper.CL  
## Aab- 0.633 0.364 62 -0.0956 1.36  
## Aab+ 0.543 0.452 61 -0.3606 1.45  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## (Aab-) - (Aab+) 0.0898 0.58 61 0.155 0.8775  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IFN.y.C.Peptide.IAPP..1"  
## group emmean SE df lower.CL upper.CL  
## Aab- 0.83 0.283 62 0.265 1.40  
## Aab+ 1.17 0.353 61 0.463 1.88  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## (Aab-) - (Aab+) -0.339 0.453 61 -0.748 0.4571  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IFN.y.C.Peptide.IAPP.2"  
## group emmean SE df lower.CL upper.CL  
## Aab- 1.65 0.416 62 0.8192 2.48  
## Aab+ 1.07 0.518 61 0.0388 2.11  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## (Aab-) - (Aab+) 0.578 0.664 61 0.870 0.3879  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IFN.y.C.Peptide.A.chain"  
## group emmean SE df lower.CL upper.CL  
## Aab- 2.99 0.319 62 2.35 3.63  
## Aab+ 3.19 0.394 61 2.40 3.97  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## (Aab-) - (Aab+) -0.195 0.507 61 -0.384 0.7021  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IFN.y.C.Peptide.10.24"  
## group emmean SE df lower.CL upper.CL  
## Aab- 0.364 0.463 62 -0.561 1.29  
## Aab+ 0.559 0.572 61 -0.586 1.70  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## (Aab-) - (Aab+) -0.194 0.736 61 -0.264 0.7926  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IL.10.No.Antigen"  
## group emmean SE df lower.CL upper.CL  
## Aab- 1.90 0.191 62 1.52 2.29  
## Aab+ 1.37 0.236 61 0.90 1.84  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## (Aab-) - (Aab+) 0.533 0.303 61 1.760 0.0835  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IL.10.Pediarix"  
## group emmean SE df lower.CL upper.CL  
## Aab- 5.48 0.128 62 5.23 5.74  
## Aab+ 5.36 0.158 61 5.04 5.68  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## (Aab-) - (Aab+) 0.12 0.203 61 0.593 0.5550  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IL.10.B.9.23..Native."  
## group emmean SE df lower.CL upper.CL  
## Aab- 0.1434 0.369 62 -0.595 0.882  
## Aab+ 0.0522 0.457 61 -0.861 0.966  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## (Aab-) - (Aab+) 0.0912 0.587 61 0.155 0.8771  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IL.10.B.9.23..B22E."  
## group emmean SE df lower.CL upper.CL  
## Aab- 1.88 0.303 62 1.27 2.48  
## Aab+ 1.76 0.376 61 1.01 2.51  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## (Aab-) - (Aab+) 0.113 0.483 61 0.234 0.8159  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IL.10.C.Peptide.Neuropeptide.Y"  
## group emmean SE df lower.CL upper.CL  
## Aab- 0.544 0.333 62 -0.123 1.21  
## Aab+ 0.307 0.415 61 -0.522 1.14  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## (Aab-) - (Aab+) 0.237 0.532 61 0.445 0.6580  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IL.10.C.Peptide.IAPP..1"  
## group emmean SE df lower.CL upper.CL  
## Aab- 0.0981 0.386 62 -0.674 0.871  
## Aab+ -0.1475 0.484 61 -1.116 0.821  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## (Aab-) - (Aab+) 0.246 0.619 61 0.397 0.6931  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IL.10.C.Peptide.IAPP.2"  
## group emmean SE df lower.CL upper.CL  
## Aab- 2.61 0.233 62 2.14 3.08  
## Aab+ 1.65 0.290 61 1.07 2.23  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## (Aab-) - (Aab+) 0.962 0.372 61 2.586 0.0121  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IL.10.C.Peptide.A.chain"  
## group emmean SE df lower.CL upper.CL  
## Aab- 3.22 0.136 62 2.95 3.50  
## Aab+ 3.22 0.167 61 2.89 3.56  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## (Aab-) - (Aab+) 0.00112 0.215 61 0.005 0.9958  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IL.10.C.Peptide.10.24"  
## group emmean SE df lower.CL upper.CL  
## Aab- 1.94 0.200 62 1.54 2.34  
## Aab+ 1.92 0.247 61 1.43 2.42  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## (Aab-) - (Aab+) 0.0131 0.318 61 0.041 0.9672  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IFN.y.IL.10.Pediarix"  
## group emmean SE df lower.CL upper.CL  
## Aab- 0.632 0.110 62 0.4124 0.852  
## Aab+ 0.361 0.137 61 0.0871 0.634  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## (Aab-) - (Aab+) 0.272 0.176 61 1.547 0.1270  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IFN.y.IL.10.B.9.23..Native."  
## group emmean SE df lower.CL upper.CL  
## Aab- -0.4718 0.117 62 -0.706 -0.238  
## Aab+ 0.0409 0.145 61 -0.249 0.331  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## (Aab-) - (Aab+) -0.513 0.186 61 -2.751 0.0078  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IFN.y.IL.10.B.9.23..B22E."  
## group emmean SE df lower.CL upper.CL  
## Aab- -0.0917 0.121 62 -0.334 0.151  
## Aab+ 0.0929 0.150 61 -0.208 0.393  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## (Aab-) - (Aab+) -0.185 0.193 61 -0.955 0.3433  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IFN.y.IL.10.C.Peptide.Neuropeptide.Y"  
## group emmean SE df lower.CL upper.CL  
## Aab- -0.2253 0.117 62 -0.460 0.00907  
## Aab+ -0.0336 0.145 61 -0.324 0.25697  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## (Aab-) - (Aab+) -0.192 0.187 61 -1.027 0.3087  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IFN.y.IL.10.C.Peptide.IAPP..1"  
## group emmean SE df lower.CL upper.CL  
## Aab- -0.147 0.108 62 -0.364 0.0698  
## Aab+ 0.117 0.135 61 -0.154 0.3870  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## (Aab-) - (Aab+) -0.264 0.173 61 -1.522 0.1333  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IFN.y.IL.10.C.Peptide.IAPP.2"  
## group emmean SE df lower.CL upper.CL  
## Aab- -0.204 0.143 62 -0.489 0.0813  
## Aab+ -0.266 0.177 61 -0.621 0.0886  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## (Aab-) - (Aab+) 0.0623 0.228 61 0.273 0.7855  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IFN.y.IL.10.C.Peptide.A.chain"  
## group emmean SE df lower.CL upper.CL  
## Aab- 0.310 0.117 62 0.0750 0.544  
## Aab+ 0.225 0.145 61 -0.0639 0.515  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## (Aab-) - (Aab+) 0.0841 0.186 61 0.451 0.6533  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IFN.y.IL.10.C.Peptide.10.24"  
## group emmean SE df lower.CL upper.CL  
## Aab- -0.537 0.161 62 -0.858 -0.216  
## Aab+ -0.614 0.199 61 -1.011 -0.217  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## (Aab-) - (Aab+) 0.0768 0.255 61 0.301 0.7647  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.

The tables below are the results of the paired t-tests for Figure 1c, 1d, and Supplemental Figure 3. The p-values test whether the peptide responses are different, stratified by group.

Figure 1c. Testing whether there is a difference between IFN.y.B.9.23..Native. and IFN.y.B.9.23..B22E.., among Ab+ patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab+", ]$IFN.y.B.9.23..Native. - dat[dat$group == "Aab+", ]$IFN.y.B.9.23..B22E.  
## t = -5.5594, df = 99, p-value = 2.297e-07  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -31.95529 -15.14471  
## sample estimates:  
## mean of x   
## -23.55

Figure 1c. Testing whether there is a difference between IFN.y.C.Peptide.10.24 and IFN.y.C.Peptide.IAPP.2, among Ab+ patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab+", ]$IFN.y.C.Peptide.10.24 - dat[dat$group == "Aab+", ]$IFN.y.C.Peptide.IAPP.2  
## t = -2.4179, df = 90, p-value = 0.01763  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -15.294005 -1.497204  
## sample estimates:  
## mean of x   
## -8.395604

Figure 1c. Testing whether there is a difference between IFN.y.C.Peptide.10.24 and IFN.y.C.Peptide.Neuropeptide.Y., among Ab+ patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab+", ]$IFN.y.C.Peptide.10.24 - dat[dat$group == "Aab+", ]$IFN.y.C.Peptide.Neuropeptide.Y  
## t = 1.9245, df = 95, p-value = 0.05729  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -0.1381342 8.8881342  
## sample estimates:  
## mean of x   
## 4.375

Figure 1c. Testing whether there is a difference between IFN.y.C.Peptide.10.24 and IFN.y.C.Peptide.IAPP.1., among Ab+ patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab+", ]$IFN.y.C.Peptide.10.24 - dat[dat$group == "Aab+", ]$IFN.y.C.Peptide.IAPP..1  
## t = 1.4489, df = 91, p-value = 0.1508  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -1.270054 8.117881  
## sample estimates:  
## mean of x   
## 3.423913

Figure 1c. Testing whether there is a difference between IFN.y.C.Peptide.10.24 and IFN.y.C.Peptide.A.chain., among Ab+ patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab+", ]$IFN.y.C.Peptide.10.24 - dat[dat$group == "Aab+", ]$IFN.y.C.Peptide.A.chain  
## t = -8.5931, df = 98, p-value = 1.355e-13  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -69.35521 -43.33165  
## sample estimates:  
## mean of x   
## -56.34343

Figure 1d. Testing whether there is a difference between IL.10.B.9.23..Native. and IL.10.B.9.23..B22E., among Ab+ patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab+", ]$IL.10.B.9.23..Native. - dat[dat$group == "Aab+", ]$IL.10.B.9.23..B22E.  
## t = -7.213, df = 99, p-value = 1.115e-10  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -20.04437 -11.39563  
## sample estimates:  
## mean of x   
## -15.72

Figure 1d. Testing whether there is a difference between IL.10.C.Peptide.10.24 and IL.10.C.Peptide.IAPP.2, among Ab+ patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab+", ]$IL.10.C.Peptide.10.24 - dat[dat$group == "Aab+", ]$IL.10.C.Peptide.IAPP.2  
## t = -3.5535, df = 90, p-value = 0.0006077  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -12.917990 -3.653439  
## sample estimates:  
## mean of x   
## -8.285714

Figure 1d. Testing whether there is a difference between IL.10.C.Peptide.10.24 and IL.10.C.Peptide.Neuropeptide.Y, among Ab+ patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab+", ]$IL.10.C.Peptide.10.24 - dat[dat$group == "Aab+", ]$IL.10.C.Peptide.Neuropeptide.Y  
## t = 6.0872, df = 95, p-value = 2.417e-08  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## 4.288854 8.440313  
## sample estimates:  
## mean of x   
## 6.364583

Figure 1d. Testing whether there is a difference between IL.10.C.Peptide.10.24 and IL.10.C.Peptide.IAPP.1, among Ab+ patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab+", ]$IL.10.C.Peptide.10.24 - dat[dat$group == "Aab+", ]$IL.10.C.Peptide.IAPP..1  
## t = 5.8147, df = 91, p-value = 8.911e-08  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## 4.093460 8.341323  
## sample estimates:  
## mean of x   
## 6.217391

Figure 1d. Testing whether there is a difference between IL.10.C.Peptide.10.24 and IL.10.C.Peptide.A.chain, among Ab+ patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab+", ]$IL.10.C.Peptide.10.24 - dat[dat$group == "Aab+", ]$IL.10.C.Peptide.A.chain  
## t = -7.3882, df = 98, p-value = 4.999e-11  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -35.73863 -20.60481  
## sample estimates:  
## mean of x   
## -28.17172

Supp. Figure 3. Testing whether there is a difference between IFN.y.No.Antigen and IFN.y.Pediarix., among Ab+ patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab+", ]$IFN.y.No.Antigen - dat[dat$group == "Aab+", ]$IFN.y.Pediarix  
## t = -18.317, df = 99, p-value < 2.2e-16  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -629.8969 -506.7631  
## sample estimates:  
## mean of x   
## -568.33

Supp. Figure 3. Testing whether there is a difference between IFN.y.No.Antigen and IFN.y.B.9.23..Native., among Ab+ patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab+", ]$IFN.y.No.Antigen - dat[dat$group == "Aab+", ]$IFN.y.B.9.23..Native.  
## t = 1.1671, df = 99, p-value = 0.246  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -0.7141583 2.7541583  
## sample estimates:  
## mean of x   
## 1.02

Supp. Figure 3. Testing whether there is a difference between IFN.y.No.Antigen and IFN.y.B.9.23..B22E., among Ab+ patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab+", ]$IFN.y.No.Antigen - dat[dat$group == "Aab+", ]$IFN.y.B.9.23..B22E.  
## t = -5.3585, df = 99, p-value = 5.476e-07  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -30.87265 -14.18735  
## sample estimates:  
## mean of x   
## -22.53

Supp. Figure 3. Testing whether there is a difference between IFN.y.No.Antigen and IFN.y.C.Peptide.IAPP.2, among Ab+ patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab+", ]$IFN.y.No.Antigen - dat[dat$group == "Aab+", ]$IFN.y.C.Peptide.IAPP.2  
## t = -4.494, df = 91, p-value = 2.051e-05  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -17.272763 -6.683759  
## sample estimates:  
## mean of x   
## -11.97826

Supp. Figure 3. Testing whether there is a difference between IFN.y.No.Antigen and IFN.y.C.Peptide.Neuropeptide.Y, among Ab+ patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab+", ]$IFN.y.No.Antigen - dat[dat$group == "Aab+", ]$IFN.y.C.Peptide.Neuropeptide.Y  
## t = 0.97749, df = 96, p-value = 0.3308  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -0.6375461 1.8746595  
## sample estimates:  
## mean of x   
## 0.6185567

Supp. Figure 3. Testing whether there is a difference between IFN.y.No.Antigen and IFN.y.C.Peptide.IAPP..1, among Ab+ patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab+", ]$IFN.y.No.Antigen - dat[dat$group == "Aab+", ]$IFN.y.C.Peptide.IAPP..1  
## t = -0.28349, df = 92, p-value = 0.7774  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -1.721690 1.291583  
## sample estimates:  
## mean of x   
## -0.2150538

Supp. Figure 3. Testing whether there is a difference between IFN.y.No.Antigen and IFN.y.C.Peptide.A.chain., among Ab+ patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab+", ]$IFN.y.No.Antigen - dat[dat$group == "Aab+", ]$IFN.y.C.Peptide.A.chain  
## t = -9.0742, df = 98, p-value = 1.235e-14  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -73.10927 -46.87052  
## sample estimates:  
## mean of x   
## -59.9899

Supp. Figure 3. Testing whether there is a difference between IFN.y.No.Antigen and IFN.y.C.Peptide.10.24, among Ab+ patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab+", ]$IFN.y.No.Antigen - dat[dat$group == "Aab+", ]$IFN.y.C.Peptide.10.24  
## t = -1.6862, df = 98, p-value = 0.09494  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -7.9379764 0.6450471  
## sample estimates:  
## mean of x   
## -3.646465

Supp. Figure 3. Testing whether there is a difference between IL.10.No.Antigen and IL.10.Pediarix, among Ab+ patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab+", ]$IL.10.No.Antigen - dat[dat$group == "Aab+", ]$IL.10.Pediarix  
## t = -13.796, df = 99, p-value < 2.2e-16  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -384.8853 -288.0947  
## sample estimates:  
## mean of x   
## -336.49

Supp. Figure 3. Testing whether there is a difference between IL.10.No.Antigen and IL.10.B.9.23..Native., among Ab+ patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab+", ]$IL.10.No.Antigen - dat[dat$group == "Aab+", ]$IL.10.B.9.23..Native.  
## t = 4.9639, df = 99, p-value = 2.881e-06  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## 1.740781 4.059219  
## sample estimates:  
## mean of x   
## 2.9

Supp. Figure 3. Testing whether there is a difference between IL.10.No.Antigen and IL.10.B.9.23..B22E., among Ab+ patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab+", ]$IL.10.No.Antigen - dat[dat$group == "Aab+", ]$IL.10.B.9.23..B22E.  
## t = -5.8952, df = 99, p-value = 5.201e-08  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -17.135007 -8.504993  
## sample estimates:  
## mean of x   
## -12.82

Supp. Figure 3. Testing whether there is a difference between IL.10.No.Antigen and IL.10.C.Peptide.IAPP.2, among Ab+ patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab+", ]$IL.10.No.Antigen - dat[dat$group == "Aab+", ]$IL.10.C.Peptide.IAPP.2  
## t = -5.5871, df = 91, p-value = 2.382e-07  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -17.636594 -8.385145  
## sample estimates:  
## mean of x   
## -13.01087

Supp. Figure 3. Testing whether there is a difference between IL.10.No.Antigen and IL.10.C.Peptide.Neuropeptide.Y, among Ab+ patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab+", ]$IL.10.No.Antigen - dat[dat$group == "Aab+", ]$IL.10.C.Peptide.Neuropeptide.Y  
## t = 2.917, df = 96, p-value = 0.004401  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## 0.5863013 3.0838018  
## sample estimates:  
## mean of x   
## 1.835052

Supp. Figure 3. Testing whether there is a difference between IL.10.No.Antigen and IL.10.C.Peptide.IAPP..1, among Ab+ patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab+", ]$IL.10.No.Antigen - dat[dat$group == "Aab+", ]$IL.10.C.Peptide.IAPP..1  
## t = 2.1465, df = 92, p-value = 0.03447  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## 0.09883177 2.54632952  
## sample estimates:  
## mean of x   
## 1.322581

Supp. Figure 3. Testing whether there is a difference between IL.10.No.Antigen and IL.10.C.Peptide.A.chain, among Ab+ patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab+", ]$IL.10.No.Antigen - dat[dat$group == "Aab+", ]$IL.10.C.Peptide.A.chain  
## t = -8.2713, df = 98, p-value = 6.668e-13  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -40.41647 -24.77545  
## sample estimates:  
## mean of x   
## -32.59596

Supp. Figure 3. Testing whether there is a difference between IL.10.No.Antigen and IL.10.C.Peptide.10.24, among Ab+ patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab+", ]$IL.10.No.Antigen - dat[dat$group == "Aab+", ]$IL.10.C.Peptide.10.24  
## t = -4.5379, df = 98, p-value = 1.614e-05  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -6.359016 -2.489469  
## sample estimates:  
## mean of x   
## -4.424242

Figure 1c. Testing whether there is a difference between IFN.y.B.9.23..Native. and IFN.y.B.9.23..B22E.., among Ab- patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab-", ]$IFN.y.B.9.23..Native. - dat[dat$group == "Aab-", ]$IFN.y.B.9.23..B22E.  
## t = -6.3673, df = 152, p-value = 2.161e-09  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -35.98576 -18.94235  
## sample estimates:  
## mean of x   
## -27.46405

Figure 1c. Testing whether there is a difference between IFN.y.C.Peptide.10.24 and IFN.y.C.Peptide.IAPP.2, among Ab- patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab-", ]$IFN.y.C.Peptide.10.24 - dat[dat$group == "Aab-", ]$IFN.y.C.Peptide.IAPP.2  
## t = -6.1022, df = 141, p-value = 9.558e-09  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -28.10173 -14.34897  
## sample estimates:  
## mean of x   
## -21.22535

Figure 1c. Testing whether there is a difference between IFN.y.C.Peptide.10.24 and IFN.y.C.Peptide.Neuropeptide.Y., among Ab- patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab-", ]$IFN.y.C.Peptide.10.24 - dat[dat$group == "Aab-", ]$IFN.y.C.Peptide.Neuropeptide.Y  
## t = 5.0364, df = 149, p-value = 1.353e-06  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## 1.916134 4.390533  
## sample estimates:  
## mean of x   
## 3.153333

Figure 1c. Testing whether there is a difference between IFN.y.C.Peptide.10.24 and IFN.y.C.Peptide.IAPP.1., among Ab- patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab-", ]$IFN.y.C.Peptide.10.24 - dat[dat$group == "Aab-", ]$IFN.y.C.Peptide.IAPP..1  
## t = 4.5256, df = 145, p-value = 1.245e-05  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## 1.697524 4.329873  
## sample estimates:  
## mean of x   
## 3.013699

Figure 1c. Testing whether there is a difference between IFN.y.C.Peptide.10.24 and IFN.y.C.Peptide.A.chain., among Ab- patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab-", ]$IFN.y.C.Peptide.10.24 - dat[dat$group == "Aab-", ]$IFN.y.C.Peptide.A.chain  
## t = -10.314, df = 149, p-value < 2.2e-16  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -82.02107 -55.64560  
## sample estimates:  
## mean of x   
## -68.83333

Figure 1d. Testing whether there is a difference between IL.10.B.9.23..Native. and IL.10.B.9.23..B22E., among Ab- patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab-", ]$IL.10.B.9.23..Native. - dat[dat$group == "Aab-", ]$IL.10.B.9.23..B22E.  
## t = -5.9822, df = 152, p-value = 1.515e-08  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -15.537096 -7.822382  
## sample estimates:  
## mean of x   
## -11.67974

Figure 1d. Testing whether there is a difference between IL.10.C.Peptide.10.24 and IL.10.C.Peptide.IAPP.2, among Ab- patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab-", ]$IL.10.C.Peptide.10.24 - dat[dat$group == "Aab-", ]$IL.10.C.Peptide.IAPP.2  
## t = -4.8314, df = 141, p-value = 3.493e-06  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -18.498002 -7.755519  
## sample estimates:  
## mean of x   
## -13.12676

Figure 1d. Testing whether there is a difference between IL.10.C.Peptide.10.24 and IL.10.C.Peptide.Neuropeptide.Y, among Ab- patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab-", ]$IL.10.C.Peptide.10.24 - dat[dat$group == "Aab-", ]$IL.10.C.Peptide.Neuropeptide.Y  
## t = 3.6103, df = 149, p-value = 0.0004171  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## 2.405223 8.221444  
## sample estimates:  
## mean of x   
## 5.313333

Figure 1d. Testing whether there is a difference between IL.10.C.Peptide.10.24 and IL.10.C.Peptide.IAPP.1, among Ab- patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab-", ]$IL.10.C.Peptide.10.24 - dat[dat$group == "Aab-", ]$IL.10.C.Peptide.IAPP..1  
## t = 3.6507, df = 145, p-value = 0.0003644  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## 2.519202 8.467099  
## sample estimates:  
## mean of x   
## 5.493151

Figure 1d. Testing whether there is a difference between IL.10.C.Peptide.10.24 and IL.10.C.Peptide.A.chain, among Ab- patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab-", ]$IL.10.C.Peptide.10.24 - dat[dat$group == "Aab-", ]$IL.10.C.Peptide.A.chain  
## t = -8.7896, df = 149, p-value = 3.366e-15  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -37.78141 -23.91193  
## sample estimates:  
## mean of x   
## -30.84667

Supp. Figure 3. Testing whether there is a difference between IFN.y.No.Antigen and IFN.y.Pediarix., among Ab- patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab-", ]$IFN.y.No.Antigen - dat[dat$group == "Aab-", ]$IFN.y.Pediarix  
## t = -24.697, df = 152, p-value < 2.2e-16  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -621.0621 -529.0556  
## sample estimates:  
## mean of x   
## -575.0588

Supp. Figure 3. Testing whether there is a difference between IFN.y.No.Antigen and IFN.y.B.9.23..Native., among Ab- patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab-", ]$IFN.y.No.Antigen - dat[dat$group == "Aab-", ]$IFN.y.B.9.23..Native.  
## t = 2.467, df = 152, p-value = 0.01474  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## 0.2928456 2.6483309  
## sample estimates:  
## mean of x   
## 1.470588

Supp. Figure 3. Testing whether there is a difference between IFN.y.No.Antigen and IFN.y.B.9.23..B22E., among Ab- patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab-", ]$IFN.y.No.Antigen - dat[dat$group == "Aab-", ]$IFN.y.B.9.23..B22E.  
## t = -6.0688, df = 152, p-value = 9.841e-09  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -34.45569 -17.53124  
## sample estimates:  
## mean of x   
## -25.99346

Supp. Figure 3. Testing whether there is a difference between IFN.y.No.Antigen and IFN.y.C.Peptide.IAPP.2, among Ab- patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab-", ]$IFN.y.No.Antigen - dat[dat$group == "Aab-", ]$IFN.y.C.Peptide.IAPP.2  
## t = -6.9398, df = 141, p-value = 1.313e-10  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -31.32542 -17.43514  
## sample estimates:  
## mean of x   
## -24.38028

Supp. Figure 3. Testing whether there is a difference between IFN.y.No.Antigen and IFN.y.C.Peptide.Neuropeptide.Y, among Ab- patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab-", ]$IFN.y.No.Antigen - dat[dat$group == "Aab-", ]$IFN.y.C.Peptide.Neuropeptide.Y  
## t = 0.10156, df = 149, p-value = 0.9192  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -1.107377 1.227377  
## sample estimates:  
## mean of x   
## 0.06

Supp. Figure 3. Testing whether there is a difference between IFN.y.No.Antigen and IFN.y.C.Peptide.IAPP..1, among Ab- patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab-", ]$IFN.y.No.Antigen - dat[dat$group == "Aab-", ]$IFN.y.C.Peptide.IAPP..1  
## t = -0.27889, df = 145, p-value = 0.7807  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -1.550902 1.167340  
## sample estimates:  
## mean of x   
## -0.1917808

Supp. Figure 3. Testing whether there is a difference between IFN.y.No.Antigen and IFN.y.C.Peptide.A.chain., among Ab- patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab-", ]$IFN.y.No.Antigen - dat[dat$group == "Aab-", ]$IFN.y.C.Peptide.A.chain  
## t = -10.964, df = 149, p-value < 2.2e-16  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -84.95231 -59.00769  
## sample estimates:  
## mean of x   
## -71.98

Supp. Figure 3. Testing whether there is a difference between IFN.y.No.Antigen and IFN.y.C.Peptide.10.24, among Ab- patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab-", ]$IFN.y.No.Antigen - dat[dat$group == "Aab-", ]$IFN.y.C.Peptide.10.24  
## t = -3.7758, df = 150, p-value = 0.0002293  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -4.771704 -1.493197  
## sample estimates:  
## mean of x   
## -3.13245

Supp. Figure 3. Testing whether there is a difference between IL.10.No.Antigen and IL.10.Pediarix, among Ab- patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab-", ]$IL.10.No.Antigen - dat[dat$group == "Aab-", ]$IL.10.Pediarix  
## t = -15.946, df = 152, p-value < 2.2e-16  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -379.7228 -296.0027  
## sample estimates:  
## mean of x   
## -337.8627

Supp. Figure 3. Testing whether there is a difference between IL.10.No.Antigen and IL.10.B.9.23..Native., among Ab- patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab-", ]$IL.10.No.Antigen - dat[dat$group == "Aab-", ]$IL.10.B.9.23..Native.  
## t = 2.444, df = 152, p-value = 0.01567  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## 0.7477029 7.0562187  
## sample estimates:  
## mean of x   
## 3.901961

Supp. Figure 3. Testing whether there is a difference between IL.10.No.Antigen and IL.10.B.9.23..B22E., among Ab- patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab-", ]$IL.10.No.Antigen - dat[dat$group == "Aab-", ]$IL.10.B.9.23..B22E.  
## t = -3.4954, df = 152, p-value = 0.0006206  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -12.17402 -3.38154  
## sample estimates:  
## mean of x   
## -7.777778

Supp. Figure 3. Testing whether there is a difference between IL.10.No.Antigen and IL.10.C.Peptide.IAPP.2, among Ab- patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab-", ]$IL.10.No.Antigen - dat[dat$group == "Aab-", ]$IL.10.C.Peptide.IAPP.2  
## t = -4.9124, df = 141, p-value = 2.459e-06  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -18.142745 -7.730494  
## sample estimates:  
## mean of x   
## -12.93662

Supp. Figure 3. Testing whether there is a difference between IL.10.No.Antigen and IL.10.C.Peptide.Neuropeptide.Y, among Ab- patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab-", ]$IL.10.No.Antigen - dat[dat$group == "Aab-", ]$IL.10.C.Peptide.Neuropeptide.Y  
## t = 3.1652, df = 149, p-value = 0.001879  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## 1.90864 8.25136  
## sample estimates:  
## mean of x   
## 5.08

Supp. Figure 3. Testing whether there is a difference between IL.10.No.Antigen and IL.10.C.Peptide.IAPP..1, among Ab- patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab-", ]$IL.10.No.Antigen - dat[dat$group == "Aab-", ]$IL.10.C.Peptide.IAPP..1  
## t = 3.0113, df = 145, p-value = 0.003069  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## 1.892473 9.121226  
## sample estimates:  
## mean of x   
## 5.506849

Supp. Figure 3. Testing whether there is a difference between IL.10.No.Antigen and IL.10.C.Peptide.A.chain, among Ab- patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab-", ]$IL.10.No.Antigen - dat[dat$group == "Aab-", ]$IL.10.C.Peptide.A.chain  
## t = -8.9976, df = 149, p-value = 9.907e-16  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -37.93005 -24.26995  
## sample estimates:  
## mean of x   
## -31.1

Supp. Figure 3. Testing whether there is a difference between IL.10.No.Antigen and IL.10.C.Peptide.10.24, among Ab- patients.

##   
## One Sample t-test  
##   
## data: dat[dat$group == "Aab-", ]$IL.10.No.Antigen - dat[dat$group == "Aab-", ]$IL.10.C.Peptide.10.24  
## t = -0.11245, df = 150, p-value = 0.9106  
## alternative hypothesis: true mean is not equal to 0  
## 95 percent confidence interval:  
## -4.919601 4.389800  
## sample estimates:  
## mean of x   
## -0.2649007

The tables below are the results of the mixed models for Figure 2. The p-values test whether Aab+ and Aab- participants have different trajectories in their peptide responses over time..

Figure 2. Testing whether Aab+ and Aab- participants have different trajectories of IFN.y.IL.10.Pediarix over time.

|  | Chisq | Df | Pr(>Chisq) |
| --- | --- | --- | --- |
| Visit..months.:group | 4.070115 | 2 | 0.1306729 |

Figure 2. Testing whether Aab+ and Aab- participants have different trajectories of IFN.y.IL.10.B.9.23..Native. over time.

|  | Chisq | Df | Pr(>Chisq) |
| --- | --- | --- | --- |
| Visit..months.:group | 8.637044 | 2 | 0.0133196 |

Figure 2. Testing whether Aab+ and Aab- participants have different trajectories of IFN.y.IL.10.B.9.23..B22E. over time.

|  | Chisq | Df | Pr(>Chisq) |
| --- | --- | --- | --- |
| Visit..months.:group | 0.5981626 | 2 | 0.7414991 |

Figure 2. Testing whether Aab+ and Aab- participants have different trajectories of IFN.y.IL.10.C.Peptide.Neuropeptide.Y over time.

|  | Chisq | Df | Pr(>Chisq) |
| --- | --- | --- | --- |
| Visit..months.:group | 1.62485 | 2 | 0.4437805 |

Figure 2. Testing whether Aab+ and Aab- participants have different trajectories of IFN.y.IL.10.C.Peptide.IAPP..1 over time.

|  | Chisq | Df | Pr(>Chisq) |
| --- | --- | --- | --- |
| Visit..months.:group | 2.924368 | 2 | 0.2317297 |

Figure 2. Testing whether Aab+ and Aab- participants have different trajectories of IFN.y.IL.10.C.Peptide.IAPP.2 over time.

|  | Chisq | Df | Pr(>Chisq) |
| --- | --- | --- | --- |
| Visit..months.:group | 1.477585 | 2 | 0.4776905 |

Figure 2. Testing whether Aab+ and Aab- participants have different trajectories of IFN.y.IL.10.C.Peptide.A.chain over time.

|  | Chisq | Df | Pr(>Chisq) |
| --- | --- | --- | --- |
| Visit..months.:group | 5.467822 | 2 | 0.0649647 |

Figure 2. Testing whether Aab+ and Aab- participants have different trajectories of IFN.y.IL.10.C.Peptide.10.24 over time.

|  | Chisq | Df | Pr(>Chisq) |
| --- | --- | --- | --- |
| Visit..months.:group | 0.8820017 | 2 | 0.6433922 |

The tables below are the results of the mixed models for Figure 3 and Supplemental Figure 5, for the comparison of Aab+ who progressed to T1D to Aab+ who did not progress. For each peptide, there are two tables. The first table contains the least-squares mean (on the log scale) of the peptide in each group. The second table provides the p-value for the group comparison.

## [1] "IFN.y.IL.10.Pediarix"  
## Developed.T1D emmean SE df lower.CL upper.CL  
## 0 0.400 0.208 24 -0.0292 0.83  
## 1 0.166 0.457 23 -0.7801 1.11  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## Developed.T1D0 - Developed.T1D1 0.235 0.502 23 0.467 0.6448  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IFN.y.IL.10.B.9.23..Native."  
## Developed.T1D emmean SE df lower.CL upper.CL  
## 0 -0.0263 0.183 24 -0.405 0.352  
## 1 0.3075 0.383 23 -0.485 1.100  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## Developed.T1D0 - Developed.T1D1 -0.334 0.425 23 -0.786 0.4400  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IFN.y.IL.10.B.9.23..B22E."  
## Developed.T1D emmean SE df lower.CL upper.CL  
## 0 0.0453 0.213 24 -0.393 0.484  
## 1 0.3232 0.452 23 -0.612 1.258  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## Developed.T1D0 - Developed.T1D1 -0.278 0.499 23 -0.556 0.5834  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IFN.y.IL.10.C.Peptide.Neuropeptide.Y"  
## Developed.T1D emmean SE df lower.CL upper.CL  
## 0 0.00789 0.180 24 -0.364 0.380  
## 1 -0.24765 0.373 23 -1.020 0.525  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## Developed.T1D0 - Developed.T1D1 0.256 0.415 23 0.616 0.5437  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IFN.y.IL.10.C.Peptide.IAPP..1"  
## Developed.T1D emmean SE df lower.CL upper.CL  
## 0 0.0993 0.151 24 -0.213 0.412  
## 1 0.2010 0.313 23 -0.447 0.849  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## Developed.T1D0 - Developed.T1D1 -0.102 0.348 23 -0.292 0.7726  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IFN.y.IL.10.C.Peptide.IAPP.2"  
## Developed.T1D emmean SE df lower.CL upper.CL  
## 0 -0.432 0.234 24 -0.915 0.0504  
## 1 0.417 0.508 23 -0.634 1.4678  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## Developed.T1D0 - Developed.T1D1 -0.849 0.559 23 -1.518 0.1426  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IFN.y.IL.10.C.Peptide.A.chain"  
## Developed.T1D emmean SE df lower.CL upper.CL  
## 0 0.269 0.174 24 -0.0908 0.628  
## 1 0.069 0.382 23 -0.7211 0.859  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## Developed.T1D0 - Developed.T1D1 0.2 0.42 23 0.475 0.6390  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IFN.y.IL.10.C.Peptide.10.24"  
## Developed.T1D emmean SE df lower.CL upper.CL  
## 0 -0.521 0.289 24 -1.12 0.0756  
## 1 -1.064 0.608 23 -2.32 0.1933  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## Developed.T1D0 - Developed.T1D1 0.543 0.673 23 0.806 0.4284  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.

The tables below are the results of the mixed models for Figure 3 and Supplemental Figure 5, for the comparison of Aab- who seroconverted to Aab- who did not seroconvert. For each peptide, there are two tables. The first table contains the least-squares mean (on the log scale) of the peptide in each group. The second table provides the p-value for the group comparison.

## [1] "IFN.y.IL.10.Pediarix"  
## Converted.to.pos emmean SE df lower.CL upper.CL  
## 0 0.630 0.0792 37 0.4696 0.79  
## 1 0.622 0.2713 36 0.0721 1.17  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## Converted.to.pos0 - Converted.to.pos1 0.00782 0.283 36 0.028 0.9781  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IFN.y.IL.10.B.9.23..Native."  
## Converted.to.pos emmean SE df lower.CL upper.CL  
## 0 -0.472 0.113 37 -0.7 -0.244  
## 1 -0.418 0.386 36 -1.2 0.365  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## Converted.to.pos0 - Converted.to.pos1 -0.0544 0.402 36 -0.135 0.8931  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IFN.y.IL.10.B.9.23..B22E."  
## Converted.to.pos emmean SE df lower.CL upper.CL  
## 0 -0.118 0.0964 37 -0.314 0.0769  
## 1 0.277 0.3305 36 -0.393 0.9473  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## Converted.to.pos0 - Converted.to.pos1 -0.396 0.344 36 -1.149 0.2581  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IFN.y.IL.10.C.Peptide.Neuropeptide.Y"  
## Converted.to.pos emmean SE df lower.CL upper.CL  
## 0 -0.262 0.108 37 -0.482 -0.0431  
## 1 0.291 0.396 36 -0.511 1.0939  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## Converted.to.pos0 - Converted.to.pos1 -0.554 0.41 36 -1.350 0.1854  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IFN.y.IL.10.C.Peptide.IAPP..1"  
## Converted.to.pos emmean SE df lower.CL upper.CL  
## 0 -0.167 0.115 37 -0.399 0.066  
## 1 0.177 0.453 36 -0.742 1.095  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## Converted.to.pos0 - Converted.to.pos1 -0.343 0.467 36 -0.735 0.4673  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IFN.y.IL.10.C.Peptide.IAPP.2"  
## Converted.to.pos emmean SE df lower.CL upper.CL  
## 0 -0.255 0.122 37 -0.503 -0.00669  
## 1 0.537 0.482 36 -0.441 1.51487  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## Converted.to.pos0 - Converted.to.pos1 -0.791 0.498 36 -1.591 0.1205  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IFN.y.IL.10.C.Peptide.A.chain"  
## Converted.to.pos emmean SE df lower.CL upper.CL  
## 0 0.261 0.113 37 0.0322 0.49  
## 1 0.827 0.400 36 0.0162 1.64  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## Converted.to.pos0 - Converted.to.pos1 -0.566 0.415 36 -1.362 0.1817  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.   
## [1] "IFN.y.IL.10.C.Peptide.10.24"  
## Converted.to.pos emmean SE df lower.CL upper.CL  
## 0 -0.525 0.127 37 -0.783 -0.268  
## 1 -0.664 0.452 36 -1.581 0.252  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log(mu + 0) (not the response) scale.   
## Confidence level used: 0.95   
## contrast estimate SE df t.ratio p.value  
## Converted.to.pos0 - Converted.to.pos1 0.139 0.469 36 0.297 0.7685  
##   
## Degrees-of-freedom method: containment   
## Results are given on the log (not the response) scale.

The table below shows the comparison of duration since seroconversion in Aab+ who developed T1D (N=5) and Aab+ who did not develop T1D (N=20).

|  | level | 0 | 1 | p | test |
| --- | --- | --- | --- | --- | --- |
| n |  | 20 | 5 |  |  |
| Duration.from.Sero.Conversion..years. (mean (SD)) |  | 8.91 (6.21) | 11.00 (3.93) | 0.484 |  |

The tables below show the results of the mixed models testing the association between the response to peptides and clinical variables.

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.Pediarix and IAA.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | 0.2423576 | 0.4932679 | 25 | 0.4913306 | 0.6274785 |
| IAA..nl…0.011. | 5.3551970 | 18.7756642 | 25 | 0.2852201 | 0.7778252 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.B.9.23..Native. and IAA.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | -0.3643523 | 0.2625942 | 26 | -1.387511 | 0.1770647 |
| IAA..nl…0.011. | 10.3772196 | 9.6404488 | 26 | 1.076425 | 0.2916244 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.B.9.23..B22E. and IAA.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | -0.3795579 | 0.541727 | 26 | -0.7006443 | 0.4897482 |
| IAA..nl…0.011. | 22.9217947 | 19.029739 | 26 | 1.2045249 | 0.2392374 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.C.Peptide.10.24 and IAA.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | -0.0782447 | 0.3895211 | 25 | -0.2008740 | 0.8424224 |
| IAA..nl…0.011. | -9.9063480 | 9.9364665 | 25 | -0.9969689 | 0.3283321 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.C.Peptide.IAPP.2 and IAA.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | -0.7336111 | 0.7913602 | 20 | -0.9270255 | 0.3649660 |
| IAA..nl…0.011. | 13.0488555 | 28.5967401 | 20 | 0.4563057 | 0.6530866 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.C.Peptide.Neuropeptide.Y and IAA.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | 0.2023097 | 0.3808295 | 23 | 0.5312344 | 0.6003497 |
| IAA..nl…0.011. | -8.5135790 | 11.5088485 | 23 | -0.7397420 | 0.4669406 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.C.Peptide.IAPP..1 and IAA.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | -0.0672166 | 0.292952 | 19 | -0.2294458 | 0.8209744 |
| IAA..nl…0.011. | 8.1392725 | 10.408238 | 19 | 0.7820029 | 0.4438497 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.C.Peptide.A.chain and IAA.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | 0.4192115 | 0.5893248 | 25 | 0.7113420 | 0.4834573 |
| IAA..nl…0.011. | 0.7073634 | 20.9546315 | 25 | 0.0337569 | 0.9733391 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.Pediarix and glucose AUC.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | -0.0302783 | 1.8261147 | 16 | -0.0165807 | 0.9869761 |
| Gluc.AUC..mg.dl.min. | 0.0025144 | 0.0131901 | 16 | 0.1906274 | 0.8512153 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.B.9.23..Native. and glucose AUC.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | 1.9220683 | 0.9023384 | 16 | 2.130097 | 0.0490324 |
| Gluc.AUC..mg.dl.min. | -0.0140975 | 0.0063423 | 16 | -2.222783 | 0.0409916 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.B.9.23..B22E. and glucose AUC.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | -0.2895442 | 1.9895965 | 16 | -0.1455291 | 0.8861108 |
| Gluc.AUC..mg.dl.min. | 0.0013756 | 0.0142977 | 16 | 0.0962134 | 0.9245459 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.C.Peptide.10.24 and glucose AUC.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | 2.5441150 | 1.7992629 | 15 | 1.413976 | 0.1777878 |
| Gluc.AUC..mg.dl.min. | -0.0259368 | 0.0129251 | 15 | -2.006705 | 0.0631555 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.C.Peptide.IAPP.2 and glucose AUC.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | -2.7520326 | 2.1067705 | 14 | -1.306280 | 0.2125119 |
| Gluc.AUC..mg.dl.min. | 0.0184481 | 0.0152457 | 14 | 1.210052 | 0.2462945 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.C.Peptide.Neuropeptide.Y and glucose AUC.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | 1.1344117 | 0.7682804 | 14 | 1.476559 | 0.1619314 |
| Gluc.AUC..mg.dl.min. | -0.0085101 | 0.0054715 | 14 | -1.555331 | 0.1421780 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.C.Peptide.IAPP..1 and glucose AUC.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | 0.1249487 | 0.7747776 | 14 | 0.1612704 | 0.8741846 |
| Gluc.AUC..mg.dl.min. | -0.0015646 | 0.0054969 | 14 | -0.2846294 | 0.7800950 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.C.Peptide.A.chain and IAA.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | 0.2293463 | 1.842358 | 15 | 0.1244852 | 0.9025841 |
| Gluc.AUC..mg.dl.min. | -0.0010769 | 0.013275 | 15 | -0.0811188 | 0.9364199 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.Pediarix and HbA1c.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | 0.0138319 | 1.7670617 | 79 | 0.0078276 | 0.9937742 |
| A1C…. | 0.0740822 | 0.3390192 | 79 | 0.2185192 | 0.8275881 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.B.9.23..Native. and HbA1c.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | -1.581627 | 2.0912945 | 80 | -0.7562908 | 0.4516963 |
| A1C…. | 0.268788 | 0.3996089 | 80 | 0.6726278 | 0.5031224 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.B.9.23..B22E. and HbA1c.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | -0.6759779 | 2.1441304 | 80 | -0.3152690 | 0.7533783 |
| A1C…. | 0.1246373 | 0.4103663 | 80 | 0.3037221 | 0.7621282 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.C.Peptide.10.24 and HbA1c.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | -0.2306510 | 2.378733 | 78 | -0.0969638 | 0.9230039 |
| A1C…. | -0.0927485 | 0.454672 | 78 | -0.2039899 | 0.8388927 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.C.Peptide.IAPP.2 and HbA1c.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | -2.3966452 | 2.1342181 | 68 | -1.1229617 | 0.2654030 |
| A1C…. | 0.4017722 | 0.4073126 | 68 | 0.9863978 | 0.3274348 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.C.Peptide.Neuropeptide.Y and HbA1c.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | -1.6533091 | 1.4929545 | 75 | -1.107408 | 0.2716568 |
| A1C…. | 0.3060456 | 0.2847147 | 75 | 1.074920 | 0.2858564 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.C.Peptide.IAPP..1 and HbA1c.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | -1.8969959 | 1.3528453 | 69 | -1.402227 | 0.1653305 |
| A1C…. | 0.3679406 | 0.2578604 | 69 | 1.426898 | 0.1581188 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.C.Peptide.A.chain and IAA.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | -0.9608689 | 1.5328868 | 78 | -0.6268361 | 0.5325971 |
| A1C…. | 0.2395105 | 0.2938707 | 78 | 0.8150199 | 0.4175425 |

The tables below show the results of the mixed models testing the association between the response to peptides and clinical variables, allowing a quadratic relationship between the two.

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.Pediarix and IAA, allowing for a quadratic relationship.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | 0.2010775 | 0.6536606 | 24 | 0.3076176 | 0.7610270 |
| IAA..nl…0.011. | 10.0696977 | 49.8795792 | 24 | 0.2018802 | 0.8417118 |
| I(IAA..nl…0.011.^2) | -56.9720561 | 548.4907038 | 24 | -0.1038706 | 0.9181352 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.B.9.23..Native. and IAA, allowing for a quadratic relationship.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | -0.6509394 | 0.3224602 | 25 | -2.018666 | 0.0543701 |
| IAA..nl…0.011. | 39.3233356 | 24.4503096 | 25 | 1.608296 | 0.1203277 |
| I(IAA..nl…0.011.^2) | -323.9531146 | 268.5301845 | 25 | -1.206394 | 0.2389584 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.B.9.23..B22E. and IAA, allowing for a quadratic relationship.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | -0.3599852 | 0.6973463 | 25 | -0.5162216 | 0.6102358 |
| IAA..nl…0.011. | 21.0074518 | 50.1414997 | 25 | 0.4189634 | 0.6788208 |
| I(IAA..nl…0.011.^2) | 20.9120273 | 547.9400942 | 25 | 0.0381648 | 0.9698594 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.C.Peptide.10.24 and IAA, allowing for a quadratic relationship.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | 0.0834935 | 0.4534931 | 24 | 0.1841119 | 0.8554724 |
| IAA..nl…0.011. | -26.8526775 | 25.2323869 | 24 | -1.0642147 | 0.2978220 |
| I(IAA..nl…0.011.^2) | 196.8305847 | 273.7940336 | 24 | 0.7189002 | 0.4791440 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.C.Peptide.IAPP.2 and IAA, allowing for a quadratic relationship.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | -0.7135196 | 1.090105 | 19 | -0.6545418 | 0.5206082 |
| IAA..nl…0.011. | 10.9762524 | 81.134905 | 19 | 0.1352840 | 0.8938103 |
| I(IAA..nl…0.011.^2) | 23.7433303 | 867.532941 | 19 | 0.0273688 | 0.9784510 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.C.Peptide.Neuropeptide.Y and IAA, allowing for a quadratic relationship.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | 0.3354306 | 0.4713968 | 22 | 0.7115674 | 0.4842102 |
| IAA..nl…0.011. | -22.1519423 | 30.1571871 | 22 | -0.7345494 | 0.4703717 |
| I(IAA..nl…0.011.^2) | 158.1567158 | 325.3056386 | 22 | 0.4861788 | 0.6316480 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.C.Peptide.IAPP..1 and IAA, allowing for a quadratic relationship.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | -0.2693902 | 0.4110406 | 18 | -0.6553860 | 0.5205083 |
| IAA..nl…0.011. | 28.0348791 | 29.9969524 | 18 | 0.9345909 | 0.3623686 |
| I(IAA..nl…0.011.^2) | -224.5639122 | 317.1351933 | 18 | -0.7081015 | 0.4879512 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.C.Peptide.A.chain and IAA, allowing for a quadratic relationship.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | 0.5939798 | 0.7794703 | 24 | 0.7620301 | 0.4534662 |
| IAA..nl…0.011. | -17.6111208 | 56.2932478 | 24 | -0.3128461 | 0.7571000 |
| I(IAA..nl…0.011.^2) | 213.5905468 | 610.4735875 | 24 | 0.3498768 | 0.7294829 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.Pediarix and glucose AUC, allowing for a quadratic relationship.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | 2.4568368 | 6.5453311 | 15 | 0.3753572 | 0.7126495 |
| Gluc.AUC..mg.dl.min. | -0.0358415 | 0.0975491 | 15 | -0.3674196 | 0.7184384 |
| I(Gluc.AUC..mg.dl.min.^2) | 0.0001388 | 0.0003494 | 15 | 0.3970747 | 0.6969049 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.B.9.23..Native. and glucose AUC, allowing for a quadratic relationship.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | 2.1561970 | 2.5469689 | 15 | 0.8465738 | 0.4105361 |
| Gluc.AUC..mg.dl.min. | -0.0178368 | 0.0367307 | 15 | -0.4856103 | 0.6342602 |
| I(Gluc.AUC..mg.dl.min.^2) | 0.0000140 | 0.0001298 | 15 | 0.1076080 | 0.9157328 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.B.9.23..B22E. and glucose AUC, allowing for a quadratic relationship.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | 5.8779202 | 6.7632883 | 15 | 0.8690921 | 0.3984900 |
| Gluc.AUC..mg.dl.min. | -0.0938022 | 0.1004919 | 15 | -0.9334297 | 0.3653813 |
| I(Gluc.AUC..mg.dl.min.^2) | 0.0003444 | 0.0003596 | 15 | 0.9578059 | 0.3533449 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.C.Peptide.10.24 and glucose AUC, allowing for a quadratic relationship.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | -11.2645095 | 5.5545796 | 14 | -2.027968 | 0.0620359 |
| Gluc.AUC..mg.dl.min. | 0.1854231 | 0.0831235 | 14 | 2.230693 | 0.0425743 |
| I(Gluc.AUC..mg.dl.min.^2) | -0.0007618 | 0.0002981 | 14 | -2.555476 | 0.0228732 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.C.Peptide.IAPP.2 and glucose AUC, allowing for a quadratic relationship.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | 3.8013144 | 7.3398719 | 13 | 0.5178993 | 0.6132288 |
| Gluc.AUC..mg.dl.min. | -0.0840885 | 0.1109384 | 13 | -0.7579749 | 0.4619861 |
| I(Gluc.AUC..mg.dl.min.^2) | 0.0003790 | 0.0004062 | 13 | 0.9330541 | 0.3677988 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.C.Peptide.Neuropeptide.Y and glucose AUC, allowing for a quadratic relationship.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | 0.8465129 | 2.7386154 | 13 | 0.3091025 | 0.7621417 |
| Gluc.AUC..mg.dl.min. | -0.0041097 | 0.0405168 | 13 | -0.1014322 | 0.9207552 |
| I(Gluc.AUC..mg.dl.min.^2) | -0.0000158 | 0.0001443 | 13 | -0.1095999 | 0.9144005 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.C.Peptide.IAPP..1 and glucose AUC, allowing for a quadratic relationship.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | 0.5525992 | 2.7639043 | 13 | 0.1999343 | 0.8446256 |
| Gluc.AUC..mg.dl.min. | -0.0081034 | 0.0408819 | 13 | -0.1982139 | 0.8459438 |
| I(Gluc.AUC..mg.dl.min.^2) | 0.0000235 | 0.0001456 | 13 | 0.1614689 | 0.8742065 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.C.Peptide.A.chain and IAA, allowing for a quadratic relationship.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | 6.1607342 | 6.5066954 | 14 | 0.9468300 | 0.3597825 |
| Gluc.AUC..mg.dl.min. | -0.0925233 | 0.0972393 | 14 | -0.9515015 | 0.3574890 |
| I(Gluc.AUC..mg.dl.min.^2) | 0.0003305 | 0.0003486 | 14 | 0.9481960 | 0.3591108 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.Pediarix and HbA1c, allowing for a quadratic relationship.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | 5.9979645 | 7.2581230 | 78 | 0.8263796 | 0.4111095 |
| A1C…. | -2.4669622 | 2.9498366 | 78 | -0.8363047 | 0.4055383 |
| I(A1C….^2) | 0.2649886 | 0.3007062 | 78 | 0.8812208 | 0.3809057 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.B.9.23..Native. and HbA1c, allowing for a quadratic relationship.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | 11.1634492 | 7.9372044 | 79 | 1.406471 | 0.1635058 |
| A1C…. | -4.9084503 | 3.1471226 | 79 | -1.559663 | 0.1228369 |
| I(A1C….^2) | 0.5195685 | 0.3138137 | 79 | 1.655659 | 0.1017582 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.B.9.23..B22E. and HbA1c, allowing for a quadratic relationship.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | 5.7021114 | 8.4207852 | 79 | 0.6771472 | 0.5002907 |
| A1C…. | -2.4953343 | 3.3742218 | 79 | -0.7395288 | 0.4617778 |
| I(A1C….^2) | 0.2655004 | 0.3397027 | 79 | 0.7815670 | 0.4368052 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.C.Peptide.10.24 and HbA1c, allowing for a quadratic relationship.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | 4.2347403 | 9.3929283 | 77 | 0.4508435 | 0.6533694 |
| A1C…. | -1.9105538 | 3.7254626 | 77 | -0.5128367 | 0.6095337 |
| I(A1C….^2) | 0.1827428 | 0.3715447 | 77 | 0.4918460 | 0.6242275 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.C.Peptide.IAPP.2 and HbA1c, allowing for a quadratic relationship.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | 10.0759919 | 8.2335443 | 67 | 1.223773 | 0.2253240 |
| A1C…. | -4.7318311 | 3.3142927 | 67 | -1.427705 | 0.1580215 |
| I(A1C….^2) | 0.5206801 | 0.3348428 | 67 | 1.554999 | 0.1246576 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.C.Peptide.Neuropeptide.Y and HbA1c, allowing for a quadratic relationship.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | 5.5560149 | 5.9218548 | 74 | 0.9382221 | 0.3511825 |
| A1C…. | -2.5729496 | 2.3154782 | 74 | -1.1111958 | 0.2700815 |
| I(A1C….^2) | 0.2844639 | 0.2278273 | 74 | 1.2485944 | 0.2157492 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.C.Peptide.IAPP..1 and HbA1c, allowing for a quadratic relationship.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | 7.1475056 | 5.1947379 | 68 | 1.375913 | 0.1733636 |
| A1C…. | -3.3028611 | 2.0632696 | 68 | -1.600790 | 0.1140595 |
| I(A1C….^2) | 0.3680322 | 0.2059948 | 68 | 1.786609 | 0.0784580 |

Figure 4 and Supp. Figure 7. Association between IFN.y.IL.10.C.Peptide.A.chain and IAA, allowing for a quadratic relationship.

|  | Value | Std.Error | DF | t-value | p-value |
| --- | --- | --- | --- | --- | --- |
| (Intercept) | 3.5826581 | 6.1910863 | 77 | 0.5786800 | 0.5644940 |
| A1C…. | -1.6624725 | 2.5128882 | 77 | -0.6615784 | 0.5102164 |
| I(A1C….^2) | 0.1958315 | 0.2558309 | 77 | 0.7654723 | 0.4463303 |