**Supplementary Appendix**

**Figure S1:** Study Flow Chart

**Table S1:** High Risk HLA Phased DR~DQ Genotypes followed in TEDDY

**Table S2:** Celiac Disease Autoimmunity (CDA) and other characteristics of 6,628 children by HLA-DQ haplogenotype and by site

**Table S3:** Strategy for matching bone marrow registry HLA DQ haplogenotypes to those from TEDDY

**Table S4:** Cumulative % Risk (95% CI) of Celiac Disease Autoimmunity (CDA) and Celiac Disease (CD) By Site and Haplogenotype

**Table S5.** Stem Cell Donor Haplogenotype Frequencies

**Table S6.** TEDDY Study Group

**Table S1: High Risk HLA Phased DR~DQ Genotypes followed in TEDDY**

|  |  |
| --- | --- |
| **HLA DR-DQ Haplogenotypes** | **Abbreviation** |
| DR4-DQA1\*03:0X-DQB1\*03:02/DR3-DQA1\*05:01-DQB1\*02:01 | DQ2.5/DQ8.1 |
| DR4-DQA1\*03:0X-DQB1\*03:02/ DR4-DQA1\*03:0X-DQB1\*03:02 | DQ8.1/ DQ8.1 |
| DR4-DQA1\*03:0X-DQB1\*03:02/DR8-DQA1\*04:01-DQB1\*04:02 | DQ8.1/DQ4.2 |
| DR3-DQA1\*05:01-DQB1\*02:01/ DR3-DQA1\*05:01-DQB1\*02:01 | DQ2.5/ DQ2.5 |

**Table S2**: **Celiac Disease Autoimmunity (CDA) and other characteristics of 6,628 children by HLA-DQ haplogenotype and by site**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **All HLA types**  (n=6,628) | **DQ2.5 / DQ2.5**  n=1,429(22%) | **DQ2.5 / DQ8.1**  n=2,690 (41%) | **DQ8.1 / DQ8.1**  n=1,353 (20%) | **DQ8.1 / DQ4.2**  n=1,156(17%) |
| **Characteristic** | n (% of total) | n (% of above) | n (% of above) | n (% of above) | n (% of above) |
| **CDA** | 1299 (20) | 535 (37) | 513 (19) | 195 (14) | 56 (5) |
| **CD** | 529 (8) | 264 (18) | 183 (7) | 73 (5) | 9 (1) |
| **Family History**b | 317 (5) | 111 (8) | 146 (5) | 43 (3) | 17 (1) |
| **Sex ( F / M )** | 49% / 51% | 46% / 54% | 49% / 51% | 51% / 49% | 49% / 51% |
| **Site** | n (% of total) | n (% of site total) | n (% of site total) | n (% of site total) | n (% of site total) |
| **Colorado** | 1,055 (16) | 241 (23) | 403 (38) | 246 (23) | 165 (16) |
| **Georgia** | 635 (10) | 153 (24) | 283 (45) | 123 (19) | 76 (12) |
| **Washington** | 982 (15) | 266 (27) | 419 (43) | 185 (19) | 112 (11) |
| **Finland** | 1,505 (23) | 232 (15) | 527 (35) | 253 (17) | 493 (33) |
| **Germany** | 365 (6) | 82 (22) | 175 (48) | 73 (20) | 35 (10) |
| **Sweden** | 2,086 (31) | 455 (22) | 883 (42) | 473 (23) | 275 (13) |

aAbbreviations: Celiac Disease Autoimmunity, CDA; Celiac Disease, CD.

bFamily history refers to self-reported history of celiac disease.

**Table S3: Strategy for matching bone marrow registry HLA DQ haplogenotypes to those from TEDDY.** Six haplogenotype categories from the bone marrow registry were used. The table displays the known risk haplogenotypes for celiac disease in the population and the available proxy TEDDY haplogenotypes.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Bone Marrow Registry Phased DQ haplogenotype** | **Number of**  **DQ2.5**  **haplotypes (type)** | **Number of DQ8.1 haplotypes** | **TEDDY proxy haplogenotype** | **Number of DQ2.5 haplotypes (type)** | **Number of DQ8.1 haplotypes** |
| DQ2.5 / DQ2.5a | 2 (cis) | 0 | DQ2.5 / DQ2.5 | 2 (cis) | 0 |
| DQ2.5 / DQ8.1 | 1 (cis) | 1 | DQ2.5 / DQ8.1 | 1 (cis) | 1 |
| DQ2.5 / Xb | 1 (cis) | 0 | DQ2.5 / DQ8.1 | 1 (cis) | 0 |
| DQ2.2 / DQ7.5 | 1 (trans) | 0 | DQ2.5 / DQ8.1 | 1 (cis) | 0 |
| DQ8.1 / DQ8.1 | 0 | 2 | DQ8.1 / DQ8.1 | 0 | 2 |
| DQ8.1 / XA | 0 | 1 | DQ8.1 / DQ4.2 | 0 | 1 |

a This includes DQ2.5/DQ2.2 as well given the presence of two high risk B1\*02 alleles.

b X denotes haplotypes which are not DQ2.5 nor DQ8.1.

**Table S4: Cumulative % Risk (95% CI) of Celiac Disease Autoimmunity (CDA) and Celiac Disease (CD) By Site and Haplogenotype.** The table displays the cumulative risk of CD and CDA in the TEDDY study population at each site stratified by haplogenotype

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Clinic**  **Site** | **CDA or CD status by age** | **DQ2.5/DQ2.5**  **%** | **DQ2.5/DQ8.1**  **%** | **DQ8.1/DQ8.1**  **%** | **DQ8.1/DQ4.2**  **%** |
| **Colorado** | | | | | |
| CDA | 5 years | 33.9 (29.0-39.5) | 14.4 (12.3-16.9) | 10.4 (8.6-12.5) | 3.2 (2.4-4.3) |
|  | 10 years | 50.9 (43.8-59.2) | 21.6 (18.5-25.2) | 15.6 (12.9-18.8) | 4.8 (3.6-6.5) |
| CD | 5 years | 13.0 (10.3-16.3) | 4.3 (3.4-5.5) | 3.3 (2.4-4.5) | 0.5 (0.2-1.0) |
|  | 10 years | 22.6 (18.2-28.2) | 7.5 (6.0-9.5) | 5.8 (4.3-7.7) | 0.8 (0.4-1.7) |
| **Georgia** | | | | | |
| CDA | 5 years | 32.7 (26.9-39.8) | 13.9 (11.4-17.0) | 10.0 (8.0-12.6) | 3.1 (2.2-4.3) |
|  | 10 years | 49.2 (40.6-59.7) | 20.9 (17.2-25.4) | 15.1 (12.0-18.9) | 4.7 (3.4-6.4) |
| CD | 5 years | 7.8 (5.5-11.1) | 2.6 (1.8-3.7) | 2.0 (1.3-3.0) | 0.3 (0.1-0.6) |
|  | 10 years | 13.6 (9.6-19.2) | 4.5 (3.2-6.5) | 3.5 (2.3-5.2) | 0.5 (0.2-1.1)) |
| **Washington** | | | | | |
| CDA | 5 years | 25.8 (21.8-30.6) | 11.0 (9.2-13.1) | 7.9 (6.4-9.7) | 2.4 (1.8-3.3) |
|  | 10 years | 38.8 (24.8-45.8) | 16.5 (13.9-19.6) | 11.9 (9.6-14.6) | 3.7 (2.7-5.0) |
| CD | 5 years | 5.2 (3.8-7.2) | 1.7 (1.2-2.4) | 1.3 (0.9-2.0) | 0.2 (0.1-0.4) |
|  | 10 years | 9.1 (6.7-12.5) | 3.0 (2.2-4.2) | 2.3 (1.6-3.4) | 0.4 (0.2-0.7) |
| **Finland** | | | | | |
| CDA | 5 years | 40.2 (34.8-46.4) | 17.1 (14.8-19.7) | 12.3 (10.3-14.7) | 3.8 (2.9-5.0) |
|  | 10 years | 60.4 (52.5-69.6) | 25.7 (22.3-29.5) | 18.5 (15.5-22.1) | 5.7 (4.4-7.5) |
| CD | 5 years | 11.6 (9.2-14.7) | 3.9 (3.0-4.9) | 2.9 (2.2-4.0) | 0.4 (0.2-1.8) |
|  | 10 years | 20.3 (16.2-25.4) | 6.7 (5.3-8.5) | 5.1 (3.8-6.9) | 0.8 (0.4-11.5) |
| **Germany** | | | | | |
| CDA | 5 years | 33.1 (25.8-42.4) | 14.1 (11.0-18.0) | 10.1 (7.7-13.3) | 3.1 (2.2-4.2) |
|  | 10 years | 49.8 (38.9-63.7) | 21.1 (16.5-27.1) | 15.2 (11.6-20.0) | 4.7 (3.3-6.7) |
| CD | 5 years | 7.6 (4.8-11.9) | 2.5 (1.6-4.0) | 1.9 (1.2-3.2) | 0.3 (0.1-0.7) |
|  | 10 years | 13.3 (8.5-20.7) | 4.4 (2.8-6.9) | 3.4 (2.1-5.5) | 0.5 (0.2-1.1) |
| **Sweden** | | | | | |
| CDA | 5 years | 42.0 (37.3-47.2) | 17.8 (15.9-20.0) | 12.8 (10.9-15.1) | 4.0 (3.0-5.3) |
|  | 10 years | 63.1 (56.3-70.7) | 26.8 (24.0-30.0) | 19.3 (16.5-22.5) | 6.0 (4.5-7.9) |
| CD | 5 years | 16.2 (13.7-19.3) | 5.4 (4.5-6.5) | 4.1 (3.2-5.3) | 0.6 (0.3-1.2) |
|  | 10 years | 28.3 (24.2-33.2) | 9.4 (7.9-11.2) | 7.2 (5.6-9.2) | 1.1 (0.5-2.1) |

**a Brackets represent the 95% confidence interval.**

**Table S5**. **Stem Cell Donor Haplogenotype Frequencies**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | Registry HLA Haplogenotype | **DQ2.5**  **/DQ2.5a** | **DQ2.5**  **/DQ8.1** | **DQ2.5 /Xb** | **DQ8.1**  **/DQ8.1** | **DQ8.1**  **/ X** | **All 5**  **Groups** |
| **Site** | Total Registry size (n) | % | % | % | % | % | % |
| Colorado | 36,333 | 3.4 | 2.4 | 14.8 | 1.5 | 17.4 | 39.5 |
| Georgia | 82,112 | 2.8 | 1.9 | 12.9 | 1.4 | 15.4 | 34.4 |
| Washington | 63,682 | 3.1 | 2.3 | 13.9 | 1.1 | 17.1 | 37.5 |
| Finland | 4,963 | 1.8 | 1.8 | 15.3 | 1.5 | 17.1 | 37.5 |
| Germany | 2,547,137 | 2.9 | 1.9 | 14.9 | 0.9 | 15.0 | 35.6 |
| Sweden | 6,239 | 3.0 | 3.1 | 15.9 | 1.8 | 17.8 | 41.6 |

a includes sum of DQ2.5/DQ2.5 and DQ2.5/DQ2.2

b includes sum of DQ2.5/X (cis) and DQ2.2/DQ7.5 (trans)

**Table S6**. **TEDDY Study Group**

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