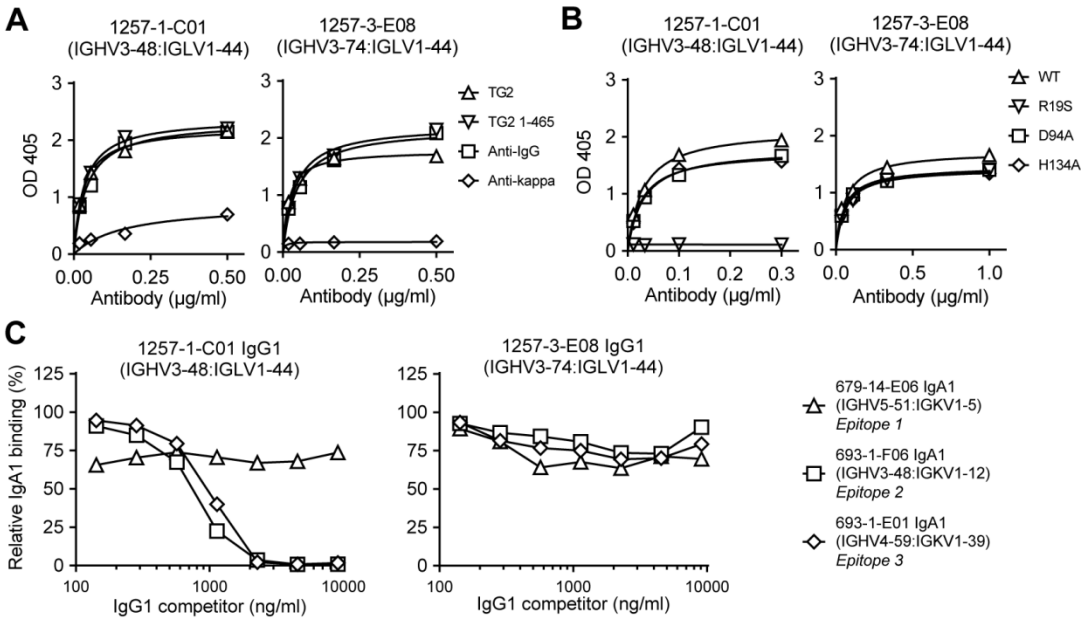



**FIGURE S1. Binding properties of lambda-containing anti-TG2 mAbs in ELISA.**

(**A)** Saturation binding curves showing binding of two anti-TG2 mAbs using lambda light chains to different coated antigens. As expected, the mAbs show good binding to both TG2 and polyclonal rabbit anti-human IgG but not to polyclonal rabbit anti-human kappa. **(B)** Effect of different TG2 point mutations on binding of lambda-containing mAbs. We have previously identified point mutations that selectively disrupt epitope 1 (H134A), Epitope 2 (R19S) or epitope 3 (D94A) (1, 2). **(C)** Competitive ELISA showing the ability of lambda-containing IgG1 mAbs to compete with three kappa-containing IgA1 mAbs for binding to TG2. The kappa-containing mAbs have previously been assigned to epitope 1, 2 or 3 as indicated.

1. Iversen, R., S. Mysling, K. Hnida, T. J. Jorgensen, and L. M. Sollid. 2014. Activity-regulating structural changes and autoantibody epitopes in transglutaminase 2 assessed by hydrogen/deuterium exchange. *Proc. Natl. Acad. Sci. USA* 111: 17146-17151.

2. Chen, X., K. Hnida, M. A. Graewert, J. T. Andersen, R. Iversen, A. Tuukkanen, D. Svergun, and L. M. Sollid. 2015. Structural basis for antigen recognition by transglutaminase 2-specific autoantibodies in celiac disease. *J. Biol. Chem.* 290: 21365-21375.

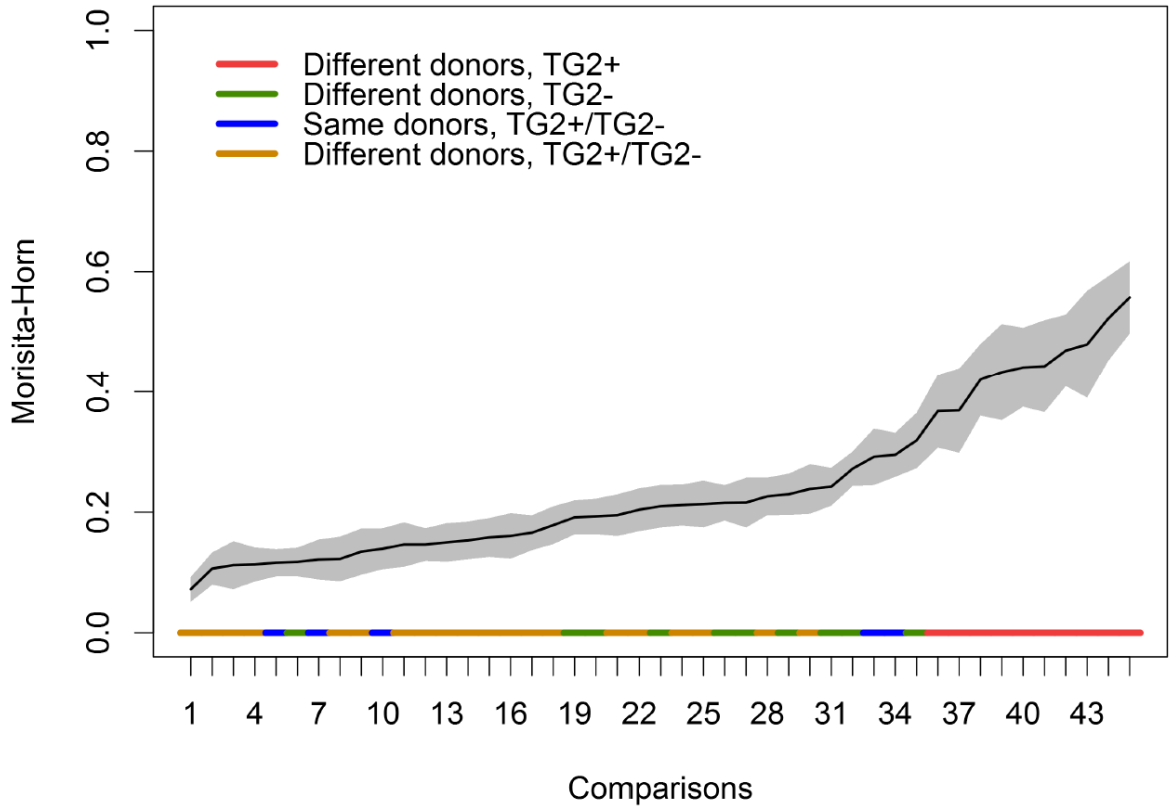
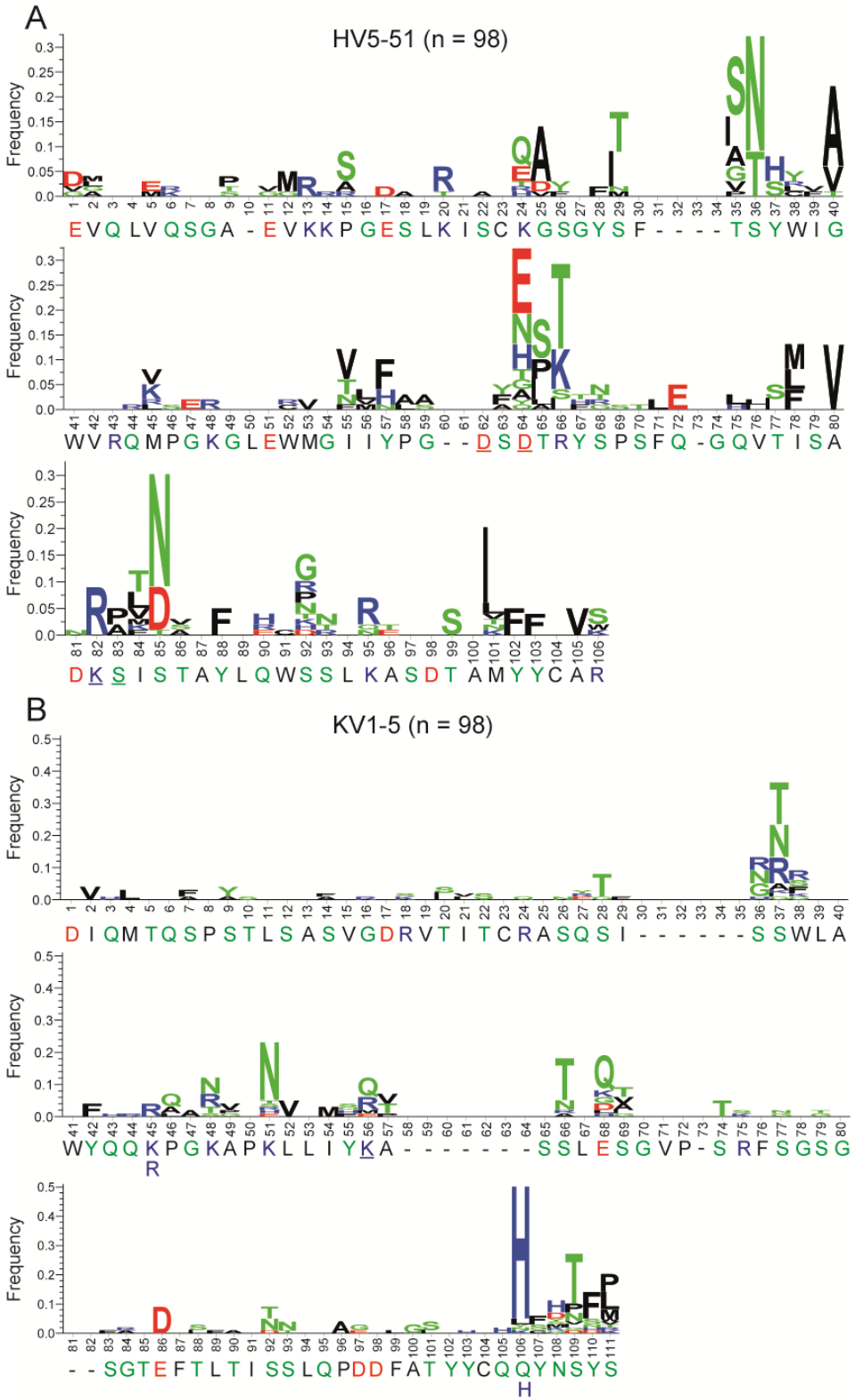



**FIGURE S2. Morisita-Horn index plot showing BCR diversity amongst TG2+ and TG2- PC populations in different patients.**

TG2+ and TG2- PC derived VH and VL sequences from five CD patients were compared in a pairwise manner and ordered according to their increasing similarities. The paired *IGHV* and *IGKV/IGHLV* gene information (counted once per clonotype) was used to assign BCR identity. The comparisons of TG2+ samples from two different patients are underlined in red, the comparisons of TG2- samples from two different patients are underlined in green, the comparisons of TG2+ and TG- samples from the same patients are underlined in blue, and the comparisons of a TG2+ sample with a TG2- sample taken from two different patients are underlined in brown. The standard error for all comparisons is indicated in gray, calculated using 1000 rounds of bootstrapping

**FIGURE S3. Frequency of AA changes**.




Graphs show the frequency of AA changes (Y-axis) at different positions (IMGT numbering shown on X-axis) along the length of *IGHV5-51* **(A)** and *IGKV1-5* **(B)**. Height of each letter (AA code) corresponds to relative frequencies, and AA residues with similar physicochemical

properties are depicted in same colors. Number of unique *IGHV5-51* and *IGKV1-5* sequences (paired to each other) subjected to this analysis, is denoted by 'n'. Letters below the numbers on X-axis show the corresponding germline AA residues. Gaps are marked by dash (-). According to IMGT numbering, positions 27-38, 56-65 and 105 correspond to CDR1, CDR2 and the beginning of CDR3, respectively. Underlined AA residues correspond to ones that were predicted to be engaged in binding between TG2 and Fab fragment of 679-14-E06 (1). The second tier of letters below X-axis shows the AA changes observed for 679-14-E06 Fab fragment (1).

1. Chen, X., K. Hnida, M. A. Graewert, J. T. Andersen, R. Iversen, A. Tuukkanen, D. Svergun, and L. M. Sollid. 2015. Structural basis for antigen recognition by transglutaminase 2-specific autoantibodies in celiac disease. *J Biol Chem* 290: 21365-21375.

**Table SI.** Primer sequences

| Name | Sequence (5'-3') |
|---|---|
| **Primers used for cDNA synthesis** | |
| Bio-STRT-T30VN | Bio-TTAAGCAGTGGTATCAACGCAGAGTCGACTTTTTTTTTTTTTTTTTTTTTTTTTTTVN |
| CaCH1 | TGGGAAGTTTCTGGCGGTCACG |
| **Primers used for 1st PCR** | |
| STRT For 2 | AAGCAGTGGTATCAACGCAGAGTGCAG |
| CaCH1-2 | GTCCGCTTTCGCTCCAGGTCACACT |
| IgK GSP1 Rev | CGATTGGAGGGCGTTATCCAC |
| IgLC Rev | CACCAGTGTGGCCTTGTTGGCTTG |
| **Primers used for 2nd PCR** | |
| R2-STRT For | GGCATTCCTGCTGAACCGCTCTTCCGATCTNNNNNNAAGCAGTGGTATCAACGCAGAGTGCAGTGCT |
| IGHJ Rev | ACACTCTTTCCCTACACGACGCTCTTCCGATCTNNNNNN**(barcode)**CTTACCTGAGGAGACGGTGACC |
| IGKC GSP2 Rev | ACACTCTTTCCCTACACGACGCTCTTCCGATCTNNNNNN**(barcode)**TCAGATGGCGGGAAGATGAAGAC |
| IGLC GSP2 Rev | ACACTCTTTCCCTACACGACGCTCTTCCGATCTNNNNNN**(barcode)**GAGGAGGGYGGGAACAGAGTGAC |
| **Primers (containing Illumina MiSeq adapter sequences) used for 3rd PCR** | |
| R1 | AATGATACGGCGACCACCGAGATCTACACTCTTTCCCTACACGACGCTCTTCCGATC |
| R2 | CAAGCAGAAGACGGCATACGAGATCGGTCTCGGCATTCCTGCTGAACCGCTC |