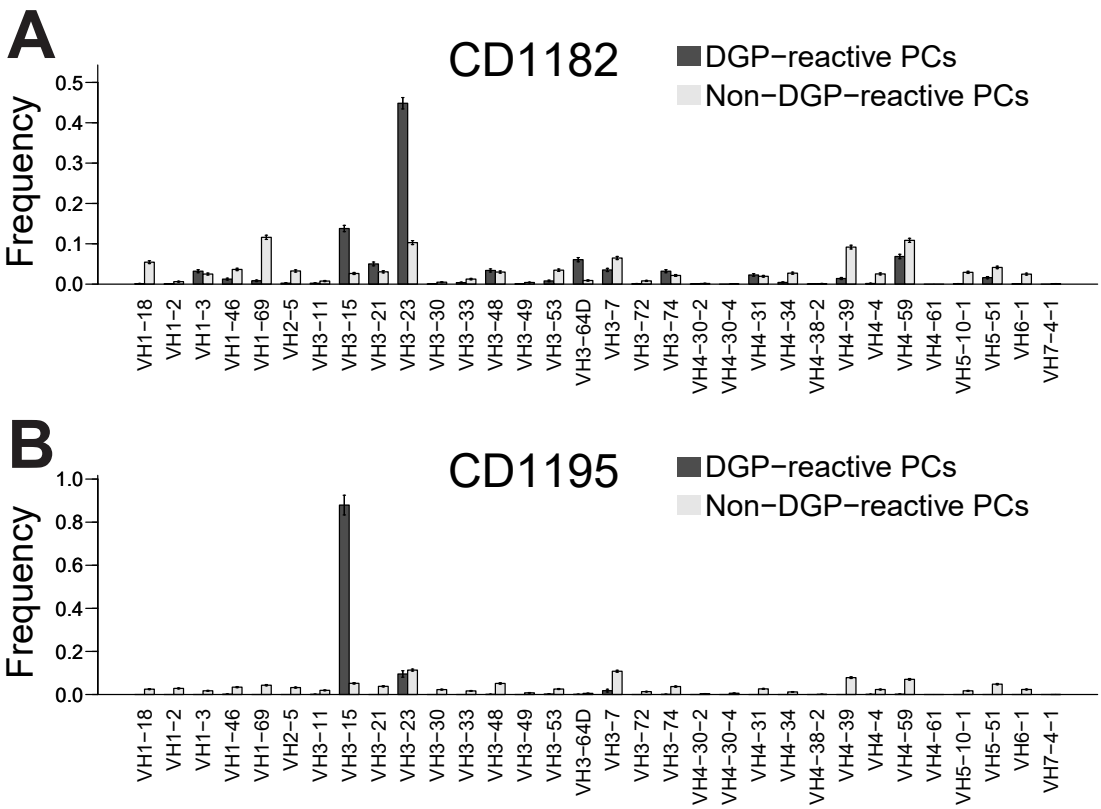
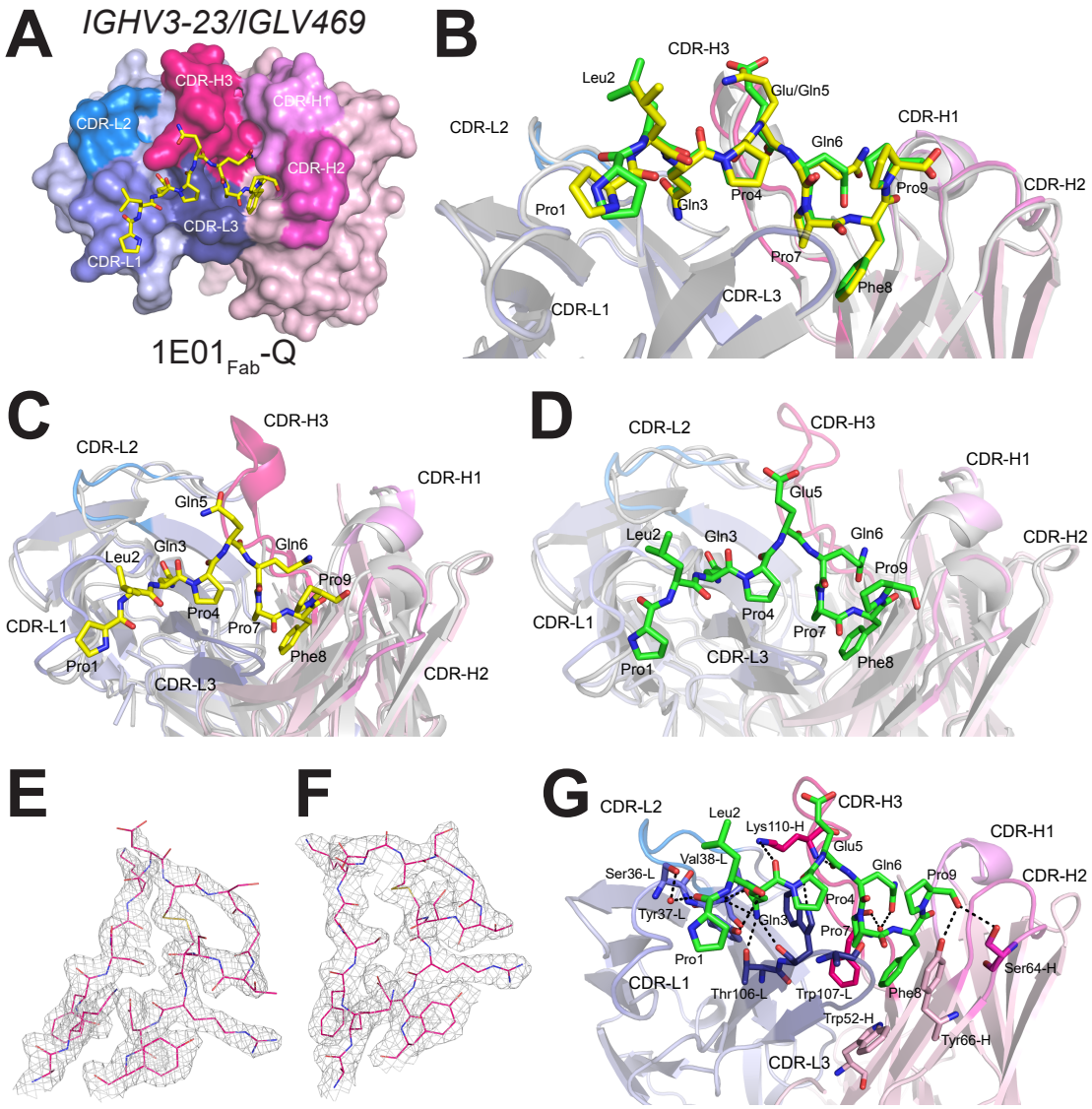
Supplemental data



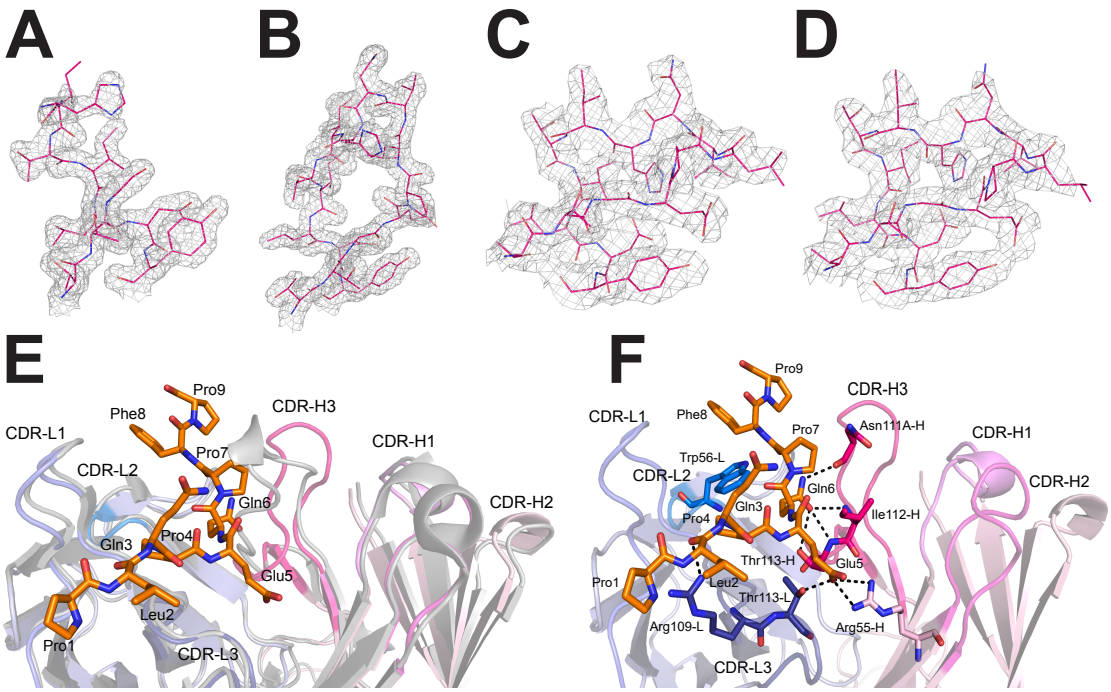
Supplementary Figure 1 *IGHV* repertoire of DGP-reactive and non-DGP-reactive PCs.

IGHV gene repertoire of DGP-reactive and non-DGP-reactive PCs from two CD patients with active disease. (**A**) A representative patient, CD1182, in whom DGP-reactive PCs predominantly used *IGHV3-23*. (**B**) *IGHV* repertoire of CD1195 for whom *IGHV3-15* dominance was observed. Bars represent the frequency of different *IGHV* gene segments ± Poisson CI with normal approximation.



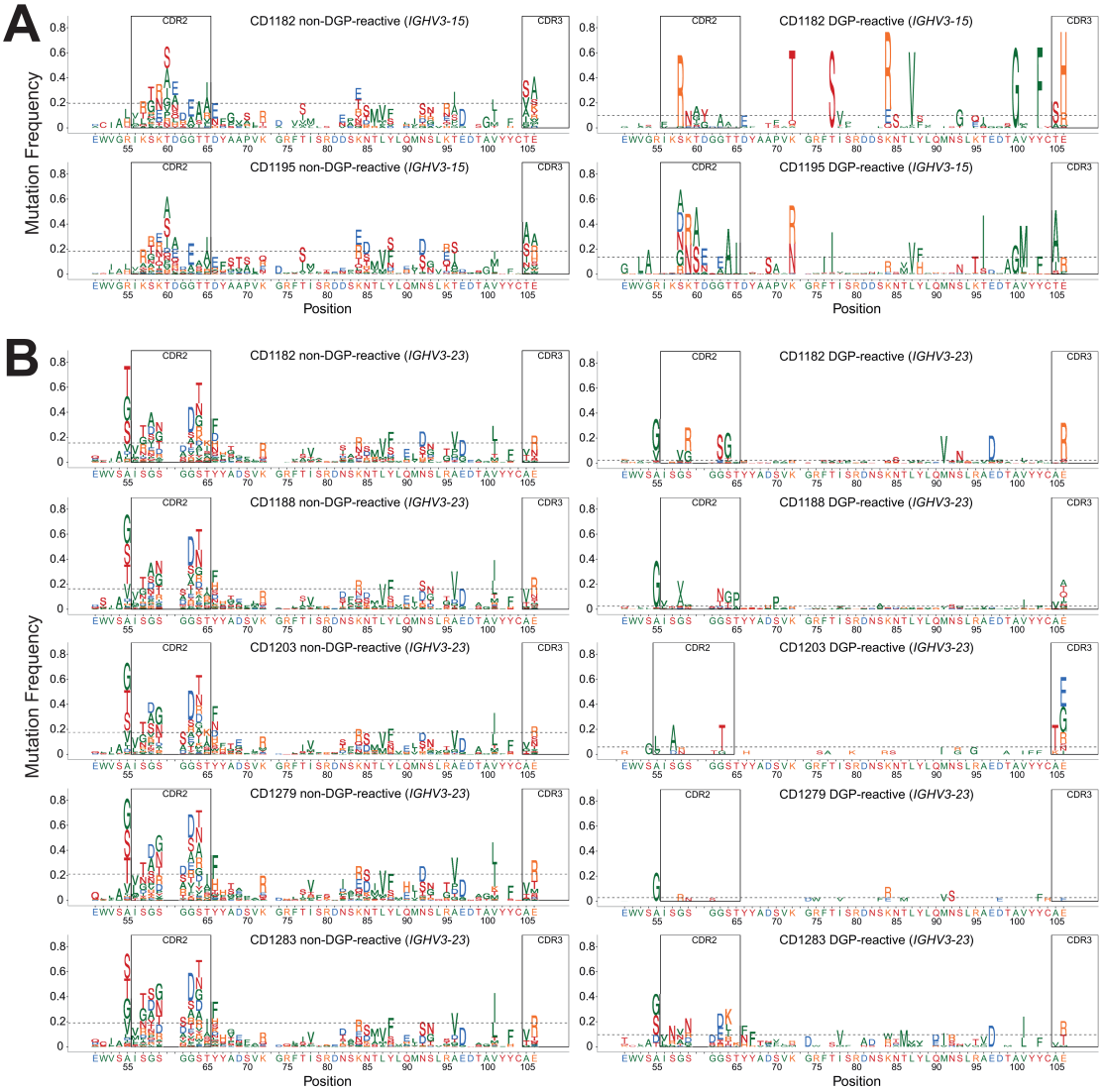
Supplementary Figure 2 Binding of native and deamidated gliadin epitope to $1E01_{Fab}$.

(**A**) Docking of the native gliadin peptide PLQPQQPFP to the hmAb 1E01. (**B**) Superimposed depiction of the native (yellow) and deamidated (green) gliadin peptides while docking to 1E01. (**C**) Superimposed depiction of $1E01_{Fab}$ alone and $1E01_{Fab}$-Q or (**D**) $1E01_{Fab}$-E. (**E** and **F**) Electron density plots for the CDR-H3 of $1E01_{Fab}$-Q (**E**) and $1E01_{Fab}$-E (**F**). (Molecules 1 in the asymmetric units are shown). (**G**) Epitope/paratope interaction in $1E01_{Fab}$-E. Interacting residues of the Fab are drawn as sticks with nitrogen atoms in blue and oxygen atoms in red. Black dotted lines represent hydrogen bonds and water molecules are is presented as red balls.



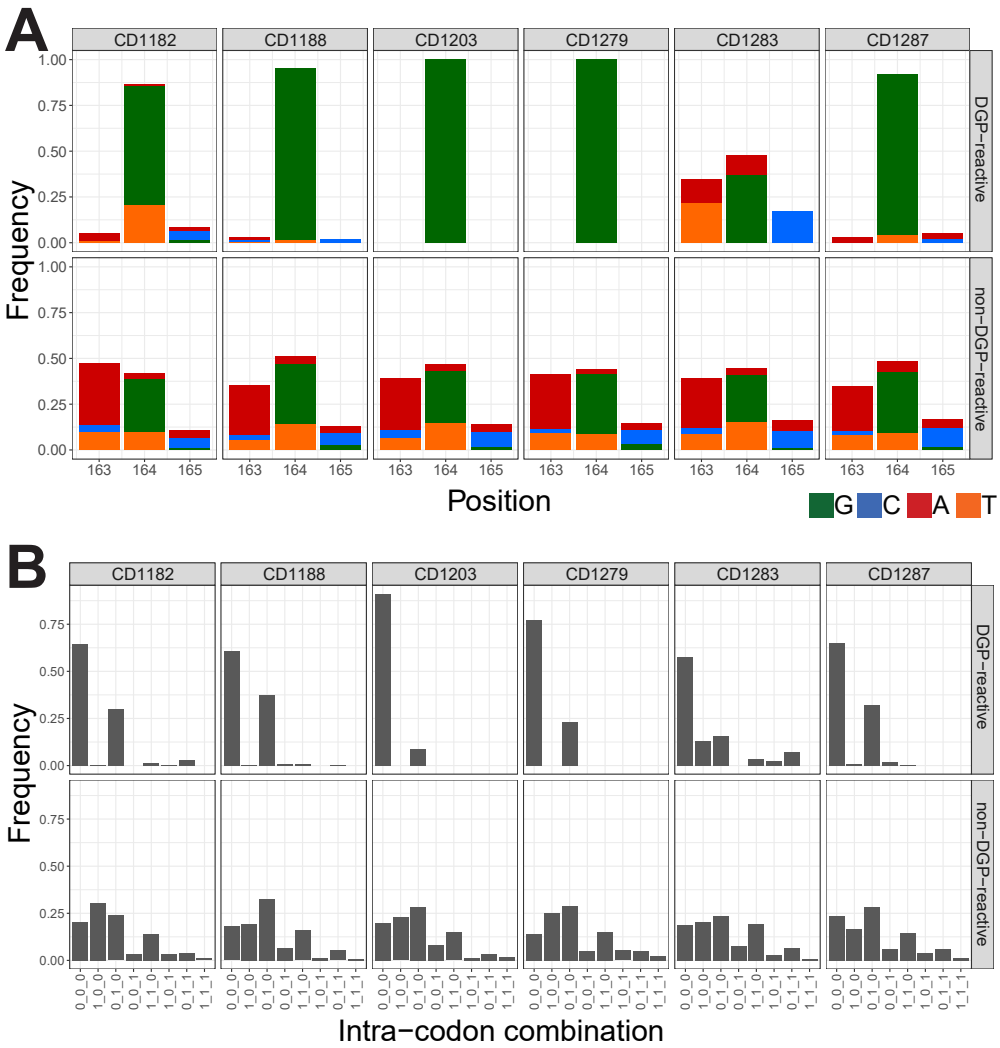
Supplementary Figure 3 Electron density and epitope/paratope interaction of 1E03.

(**A**-**D**) Electron density plots of the CDR-H3 of $1E03_{Fab}$ alone (molecules 1 and 2 of the asymmetric unit are in shown in panel **A** and **B**, respectively). Five amino acids were missing in molecule 1. Electron density plots of CDR-H3 of $1E03_{Fab}$-E (molecules 1 and 2 of the asymmetric unit are shown in panel **C** and **D**, respectively). (**E**) Superimposed depiction of $1E03_{Fab}$ alone and $1E03_{Fab}$-E. (**F**) Epitope/paratope interaction in $1E03_{Fab}$-E. Interacting residues, hydrogen bonds and color codes are as in Supplementary Figure 2G.



Supplementary Figure 4 Somatic mutations in DGP-reactive and non-DGP-reactive PCs.

Average frequency of amino acid substitution in non-DGP-reactive and DGP-reactive PCs along the (**A**) *IGHV3-15* and the (**B**) *IGHV3-23* gene segments from additional CD patients from whom thirty sequences or more were available for mutation analysis. Data from CD1287 is presented in Figures 3 and 4.



Supplementary Figure 5 Intra codon nucleotide substitution patterns at position 55.

(**A**) Nucleotide substitutions at codon 55 (consisting of nucleotides 163, 164 and 165) of *IGHV3-23* in DGP-reactive and non-DGP-reactive PCs. (**B**) Distribution of combinations of nucleotide substitutions for codon 55 of *IGHV3-23* in DGP-reactive and non-DGP-reactive PCs. Eight possible combinations with the following patterns are possible: [0 0 0] no substitution; [1 0 0], [0 1 0] and [0 0 1] single substitution at positions 1, 2 or 3, respectively; [1 1 0], [1 0 1] and [0 1 1] correspond with two substitutions at positions 1 and 2, 1 and 3, or 2 and 3: [1 1 1] substitution in all three nucleotides. The differences in substitution pattern between DGP-reactive and non-DGP-reactive PCs were significant, $p=1.46x10^{-14}$.

Supplementary Table 1 Number of unique sequences

Patient	Non-DGP-specific PCs	DGP-specific PCs
CD1182	3001	691
CD1188	7614	858
CD1190	20100	93
CD1195	11287	1613
CD1203	4118	56
CD1210	6000	256
CD1218	9480	43
CD1279	7343	41
CD1283	6073	209
CD1287	13579	853

Supplementary Table 2 Primers for induction of site-directed mutagenesis

Primer name	**Sequence**
1E03_*IGHV3-15*_R55H	CTGGAGTGGGTTGGCCATATTAAAACCAACACTG
1E03_*IGKV4-1*_T113A	ACTGTCAGCAATATTATAGAGCTCCCCCTCTCACGTT
1E01_*IGHV3-23*_Ala_55	GCTGGAGTGGGTCTCAGCTATTAGTGGTAGTGGTGG
1E01_*IGHV3-23*_Ser_55	GGCTGGAGTGGGTCTCATCCATTAGTGGTAGTGGTG
1E01_*IGHV3-23*_Thr_55	GGCTGGAGTGGGTCTCAACCATTAGTGGTAGTGGTG
1E01_*IGHV3-23*_S64N	ATTAGTGGTAGTGGTGGTAATACATACTACGCAGACTC
1E01_*IGHV3-23*_S64R	AGTGGTAGTGGTGGTAGGACATACTACGCAGACTC
1E01_*IGHV3-23*_Y66F	AGTGGTGGTAGTACATTCTACGCAGACTCCGTG
1E01_*IGHV3-23*_Y66D	TTAGTGGTAGTGGTGGTAGTACAGACTACGCAGACT

Supplementary Table 3 Crystallization conditions, data collection and crystal structure features

Protein	PDB code	Crystallization condition	Data collection	Search model	No. of molecules in asymmetric unit	Chains of the units
$1E01_{Fab}$	5IHZ	20 %w/v Polyethylene Glycol 3350,0.200 M Potassium sulphate	Diamond I03	4Q9Q	4	(A B) (C D) (E F) (H L)
$1E01_{Fab}$-E	5IFJ	0.2M Ammonium sulfate, 0.1M MES, pH=6.5, 20% PEG8000	Diamond I03	5IHZ	4	(A B C) (D E F) (G H I) (J K L)
$1E01_{Fab}$-Q	5IG7	0.2 M Ammonium sulfate 0.1 M Tris 7.5 20 % w/v PEG 5000 MME	Diamond I24	5IHZ	4	(A B C) (D E F) (G H I) (J K L)
$1E03_{Fab}$	5IK3	0.2M Ammonium sulfate, 30% PEK8000	Diamond I03	5IJK	2	(A B) (C D)
$1E03_{Fab}$-E	51JK	2.256M (NH4)2SO4, 0.1M citrate, pH=5.0	ESRF ID29	5IHZ heavy chain, 5IT2 light chain	2	(A C X) (B D Y)