Supplemental Information

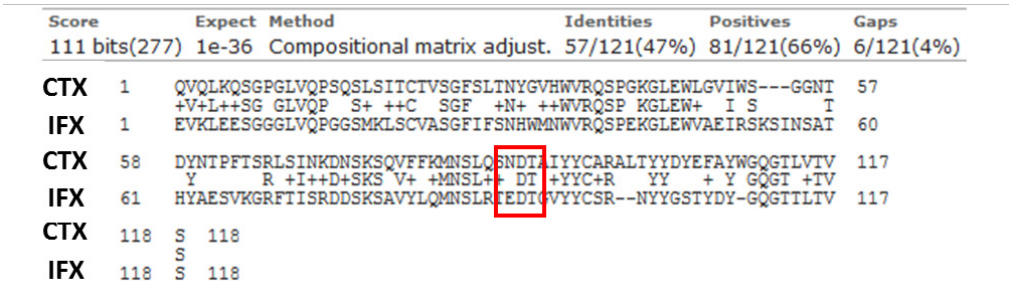
Table S1 Characteristics of ADL-treated patients. n.a., not available. m, male, f, female, gastro, serum sent from a gastroenterologist, lab, sent from a clinical lab, rheuma, sent from a rheumatologist.

ID	age	gender	source
ADL41	29	m	gastro
ADL67	31	m	lab
ADL72	/	m	lab
ADL86	61	m	rheuma
ADL89	9	f	rheuma
ADL90	26	m	gastro
ADL114	19	m	lab
ADL122	11	m	lab
ADL123	38	m	rheuma
ADL134	29	m	gastro

Table S2 Single 15-mer peptides used for ELISA analysis with sera from ADL-treated patients and untreated individuals. VH, heavy chain variable region, VL, light chain variable region, CH, heavy chain.

ID	sequence	epitope	location on ADL
A1	SGFTFDDYAMHWVRQ	1	VH
B1	AMHWVRQAPGKGLEW	1	VH
C1	RAEDTAVYYCAKVSY	2	VH
E1	ITCRASQGIRNYLAW	3	VL
A2	QPEDVATYYCQRYNR	4	VL
C2	LYSKLTVDKSRWQQG	5	CH3
F2	ACPLAFATPIMIPQS	random	-
A3	RVFDSGANEFLIEGI	random	-
B3	LKMESEPVNGGNEVA	random	-
C3	SRRGGVKVEELQDEI	random	-
E3	EQLSVWSLIADRNIN	random	-
F3	KEMDLLEMDSSDKGI	random	-
A4	CLLLSDGLFDRAAST	random	-
B4	DNVKVLIKRSLPKAL	random	-
C4	ETKVSGIVICNPRDT	random	-
E4	VWADASLFTFHYHQY	random	-
F4	YHGTPYTTEYLPLGK	random	-

VH -> CTX-specific glycosylation



Score	Expect	Method	Identities	Positives	Gaps
111 bits(277)	1e-36	Compositional matrix adjust.	57/121(47%)	81/121(66%)	6/121(4%)

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CTX   1    QVQLKQSGPGLVQPSQSLSITCTVSGFSLTNYGVHWVRQSPGKGLEWLGVIWS---GGNT  57
           +V+L++SG GLVQP  S+ ++C  SGF  +N+ ++WVRQSP KGLEW+  I S      T
IFX   1    EVKLEESGGGLVQPGGSMKLSCVASGFIFSNHWMNWVRQSPEKGLEWVAEIRSKSINSAT  60

CTX   58   DYNTPFTSRLSINKDNSKSQVFFKMNSLQSNDTAIYYCARALTYYDYEFAYWGQGTLVTV  117
            Y      R +I++D+SKS V+ +MNSL++ DT +YYC+R   YY   + Y GQGT +TV
IFX   61   HYAESVKGRFTISRDDSKSAVYLQMNSLREDTGVYYCSR--NYYGSTYDY-GQGTTLTV  117

CTX   118  S  118
           S
IFX   118  S  118
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Figure S1 Sequence alignment of cetuximab and infliximab heavy chain variable region (VH) indicates a high similarity on the amino acid level, but different glycosylation properties. 87% of the amino acids are identical and 96% show a positive correlation. For the variable part of the heavy chain, an amino acid identity of 47% is indicated and 66% positive correlation. The cetuximab-specific N-glycosylation Sequon is indicated by a red box.

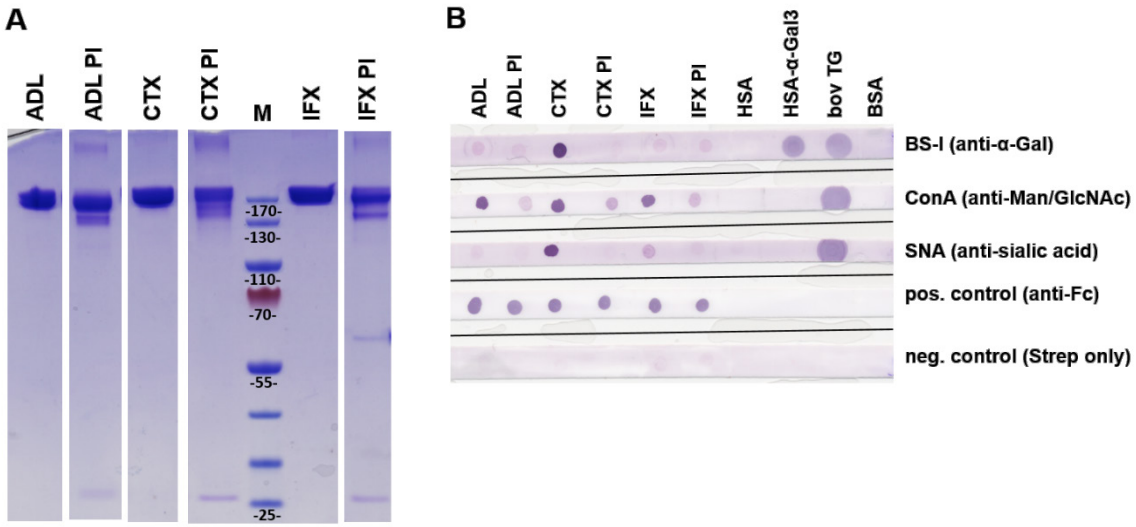

Figure S2 Analysis of ICRIP assay components. A, analysis of structural integrity of biologicals treated with periodate by SDS-PAGE. B, glycan analysis of IgE assay components by lectin binding assay. PI, periodate-treated, M, molecular weight marker, HSA, human serum albumin, bov TG, bovine thyroglobulin, BSA, bovine serum albumin.

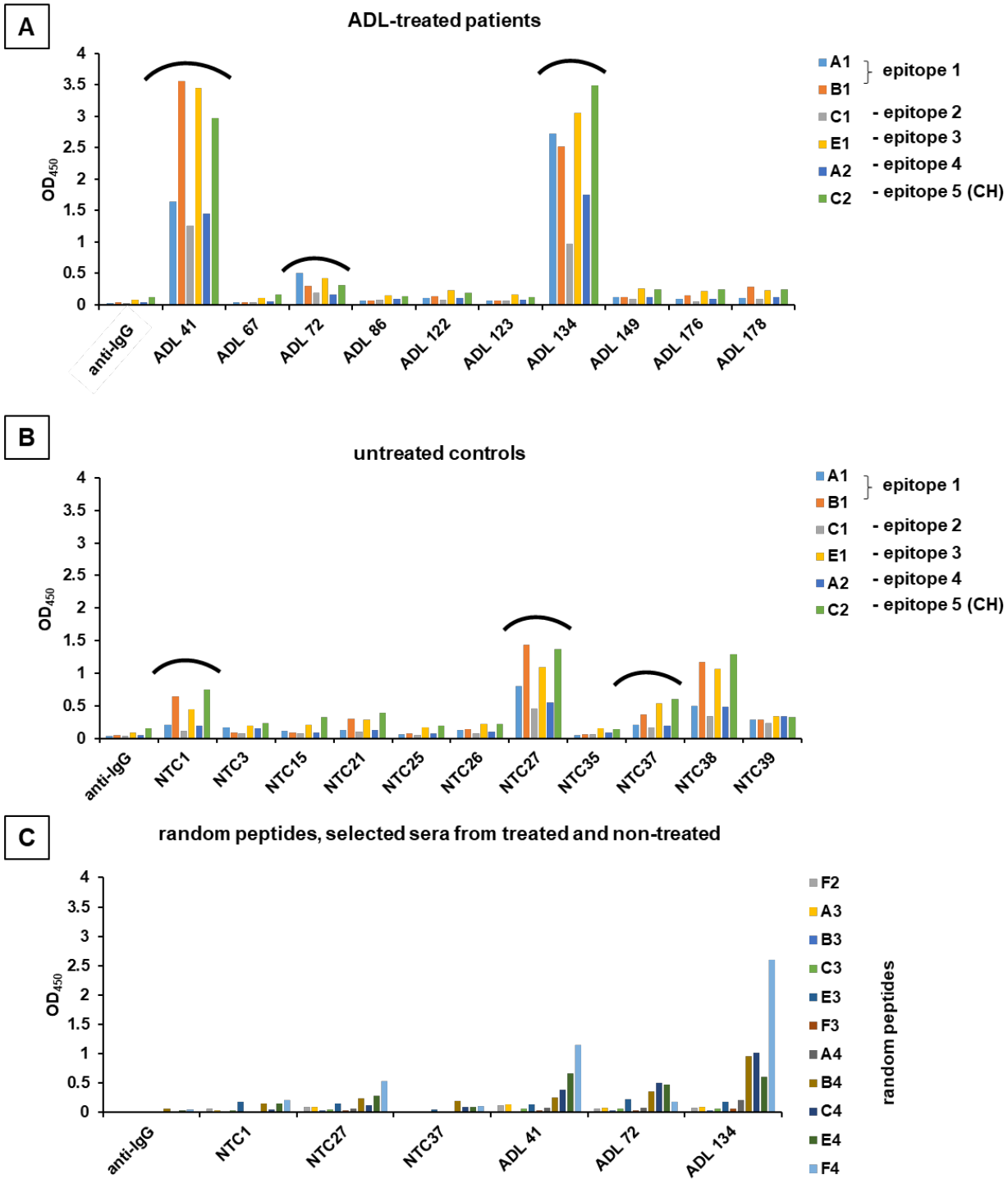

Figure S3 Peptide epitope analysis of selected single 15-mer oligopeptides from the adalimumab sequence by ELISA. Serum IgG analysis was performed with A) sera from ADL-treated patients and B) untreated control individuals. The selection of peptides was based on the microarray data shown in Fig. 3A, for sequences see Table S2. C) Selected positive sera were analyzed with random peptides in the same ELISA system in terms of cross-reactivity. Of note, sera ADL41 and ADL134, positive for mapped ADL epitopes, show relatively high signals for random peptides B4, C4, E4 and F4. The ELISA assays A) and B) were performed as two independent experiments with similar results, data from one experiment are shown. Assay C) was performed once. The threshold for a positive signal is 0.45 (see Methods).