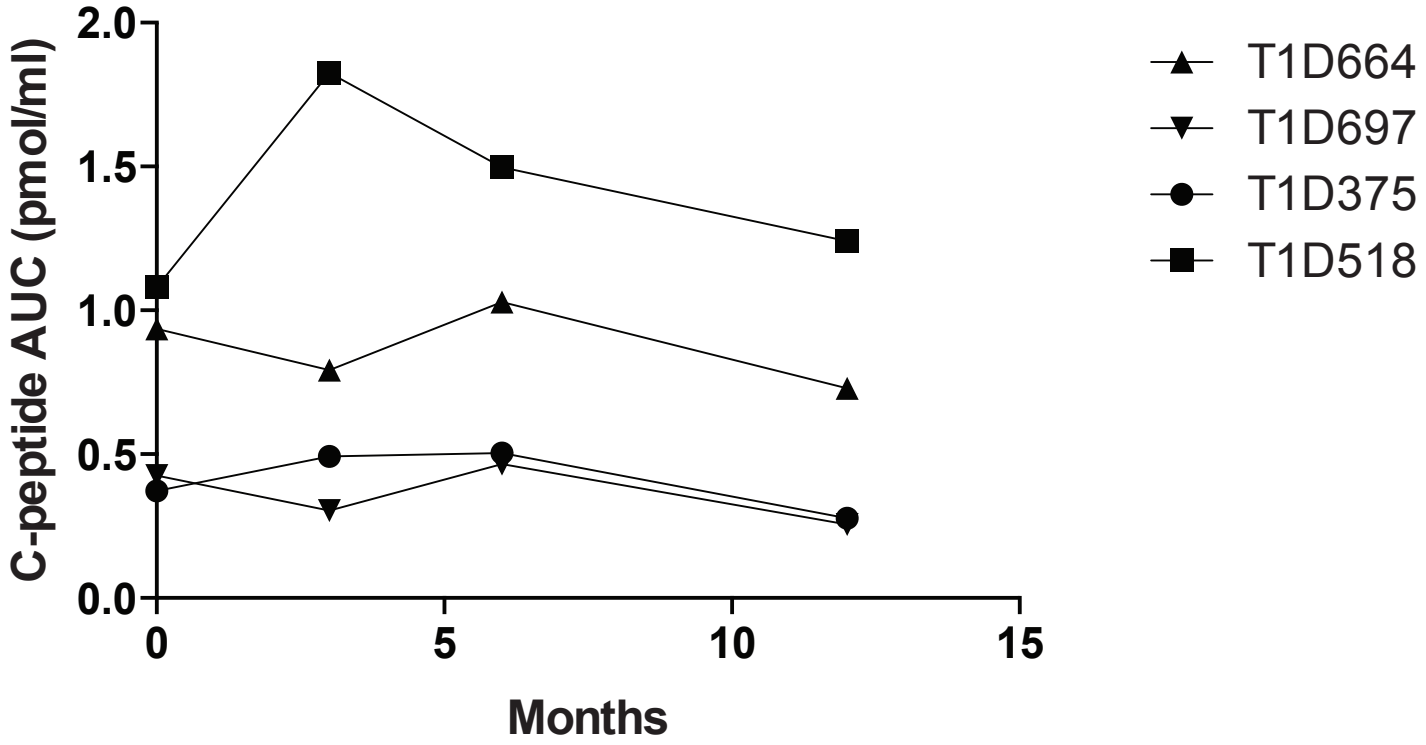
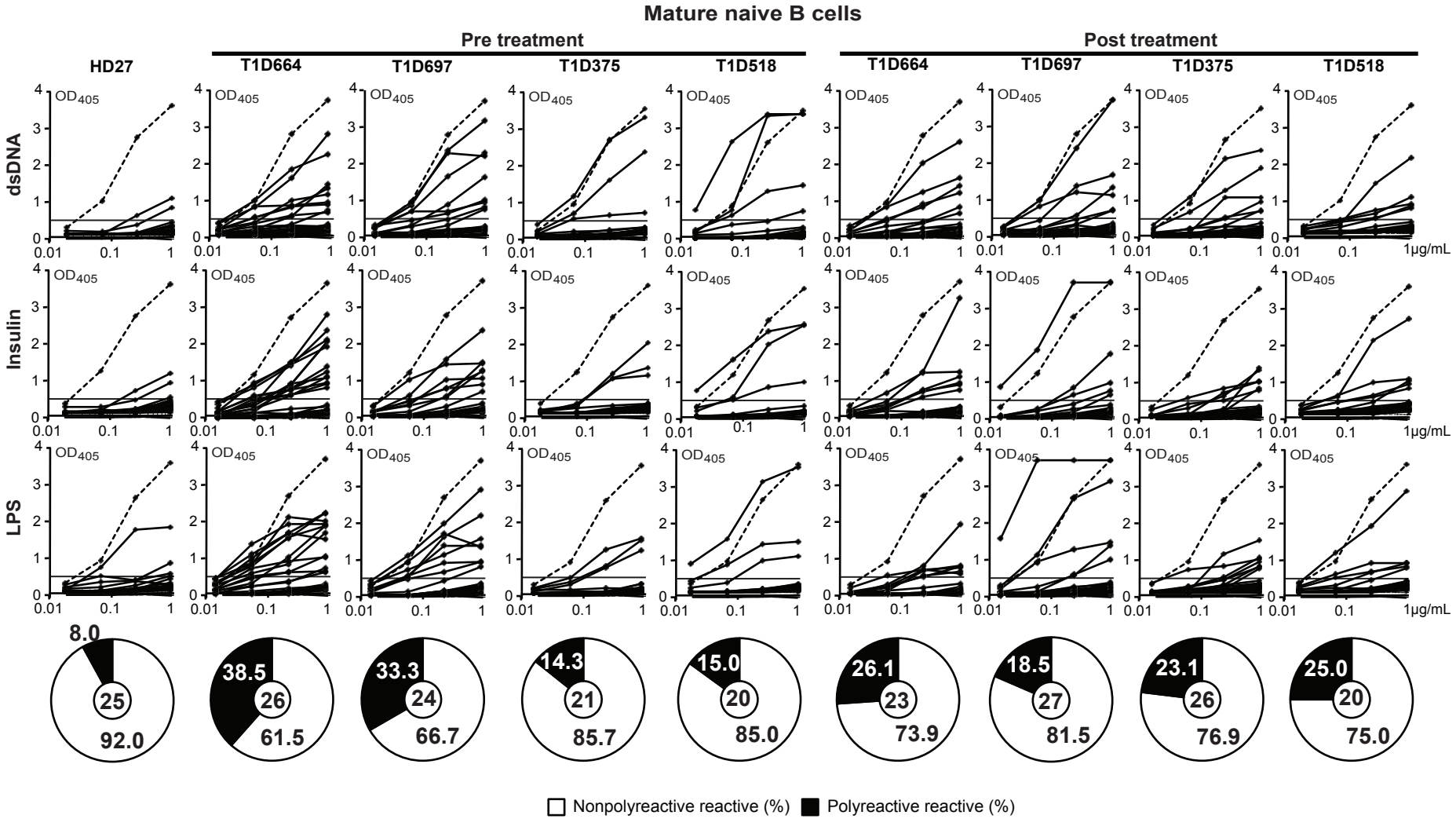
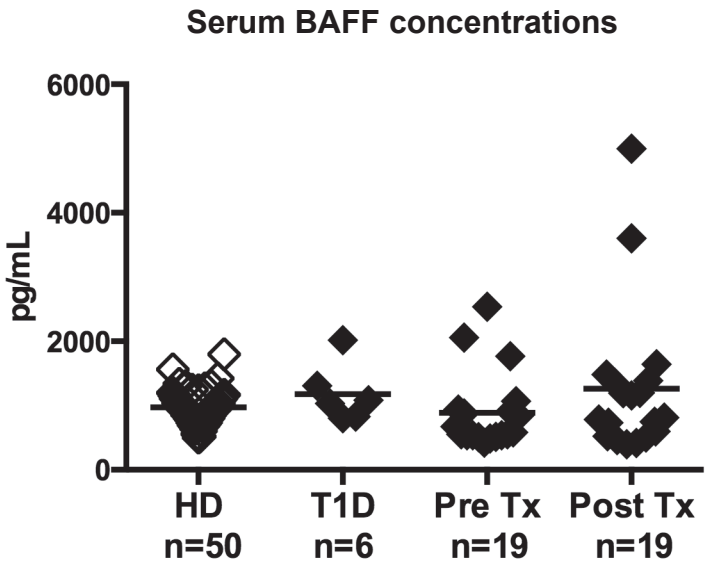


Supplemental Figure 1. C-peptide responses in four analyzed participants from the clinical trial. The C-peptide area under the curve during a four hour mixed meal tolerance test are shown for each subject at baseline, 13, 26, and 52 weeks. These participants were designated as “responders” because the value at 13 weeks showed a decline from the baseline of < 9.7%.



Supplemental Figure 2. Expression of polyreactive antibodies from mature naïve B cells isolated and cloned from a healthy donor and patients with T1D before and after Rituximab treatment. Antibodies cloned from mature naïve B cells of a healthy donor and T1D patients before and after Rituximab treatment were tested by ELISA for insulin (INS), lipopolysaccharide (LPS), and double-stranded DNA (dsDNA). Dotted lines represent the ED38-positive control and solid lines represent binding for each clone recombinant antibody. Horizontal lines define the cutoff OD405nm for positive reactivity. Polyreactivity requires surpassing the OD405nm threshold for all three antigens. Frequency of polyreactivity (filled area) clones is summarized in the pie charts, with the total number of clones tested indicated in the centers. T1D patients 664 and 697 have decreased frequency of polyreactive clones following Rituximab treatment while patients 375 and 518 resulted in increased frequency of polyreactive clones following anti B-cell therapy.



Supplemental Figure 3. T1D patients display similar serum BAFF concentrations before and 52 weeks after anti B-cell therapy. Serum BAFF concentrations (pg/mL) in healthy donors (open diamonds, n=50), previously studied T1D patients (black diamonds, n=6) and T1D patients enrolled by TRIALNET before and 52 weeks after Rituximab treatment (black diamonds, n=19) were measured by ELISA. Each diamond represents an individual, and the average is shown with a bar.

Supplemental Table 1. Additional clinical characteristics of research subjects

	Baseline*		12 weeks		26 weeks		39 weeks		52 weeks	
Random ID	**Hb1Ac**	**CPEP AUC (ng/mL)**	**Hb1Ac**	**CPEP AUC (ng/mL)**	**Hb1Ac**	**CPEP AUC (ng/mL)**	**Hb1Ac**	**CPEP AUC (ng/mL)**	**Hb1Ac**	**CPEP AUC (ng/mL)**
9024375	8.8	272.4	6.2	177.45	5.2	181.8	5.9	ND	6	209.475
9047518	8.6	783.075	5.4	657.525	5.8	539.25	6.2	ND	6.9	882.3
9002664	5.8	624.975	5	285.45	5.2	370.65	5.4	ND	5.6	362.025
9012697	7.6	294.975	8.1	109.725	7.2	167.4	6.4	ND	6.1	207.975
9006916	6.6	355.2	5.4	70.9125	5.6	201.975	5.8	ND	6.3	212.4
9009337	9.4	390.9	6.8	213.975	7.6	160.875	8.1	ND	7.9	260.625
9020804	5	1153.65	4.8	517.5	4.8	512.1	5.1	ND	5	765.825
9023002	7.1	916.05	6.2	627.3	7.6	498.6	ND	ND	5.8	892.725
9030498	7.8	712.575	5	362.325	5.1	424.425	5.9	ND	5.5	842.175
9039198	6.6	303.825	5.8	247.275	6.7	222.825	7	ND	8.8	235.35
9042028	6	1163.475	5.2	453.675	5.6	566.7	5.7	ND	6.1	820.125
9066896	6.5	487.725	5.9	238.125	6	235.875	5.6	ND	6	321.375
9077401	8	533.4	6.1	317.7	5.9	276.45	6.2	ND	6.6	418.275
9024930	11.9	789.15	6.4	556.05	6.3	736.125	6.5	ND	7.8	961.35
9045644	7.3	327.75	6.4	166.2	6.5	165.45	6.7	ND	6.9	300.375
9036566	6.2	555.15	6.1	316.275	6.2	319.875	7	ND	6.9	739.2
9079264	8.7	623.025	4.9	207	5.3	413.325	5.7	ND	5.3	495.3
9080594	6.9	805.425	5.2	554.475	5.3	329.25	5.8	ND	5.5	761.625
9049192	8.8	278.175	6.1	170.025	6.6	144.675	6.7	ND	6.5	209.7

*Hb1Ac collected at screen

Hb1Ac range: Baseline 5-11.9 (mean 7.56), 12 weeks 5-8.1 (mean 5.84), 26 weeks 4.8-7.2 (mean 6.03), 39 weeks 5.4-8.1 (mean 6.2), 52 weeks 5-8.8 (mean 6.39); CPEP AUC range: baseline 272.4-1163.475ng/mL (mean 598.47ng/mL), 12 weeks 70.91-657.53ng/mL (mean 328.89ng/mL), 26 weeks 144.68-736.13ng/mL (mean 340.4ng/mL), 39 weeks ND, 52 weeks 207.98-961.35ng/mL (mean 520.96ng/mL); patients highlighted were tested for reactivity

ND, Not done

Supplemental Table 2. Repertoire and reactivity of antibodies from mature naive B cells of T1D patient 664 pre treatment

Ig	HEAVY						LIGHT				REACTIVITY		
	VH	D	RF	JH	CDR3(aa)	Length	Vκ	Jκ	CDR3(aa)	Length	Poly	HEp-2	Staining
preTx mnT1D664 52	3-30-3	2-15	3	4	EGGVVVATFDY	11	1-12	4	QQANSFPLT	9	-	-	-
preTx mnT1D664 54	1-69	3-3	3	6	GLSGPFAGVVKKGAYYYYYMDV	22	1-5	1	QQYNSYPRT	9	+	+	-
preTx mnT1D664 59#	3-11	1-7	2	2	KWNWYFDL	8	2-29	3	MQSIQLPLFT	10			
preTx mnT1D664 64	1-3	3-9	2	4	VGYDILTGYYTFDY	14	3-20	1	QQYGSSPWT	9	-	+	-
preTx mnT1D664 68	1-69	3-22	2	1	ETREYYYDSSGYYFGYFQH	19	4-1	3	QQYYSTPFG	9	-	-	-
preTx mnT1D664 69#	1-69	3-22	2	4	KGGGGNYYDSSGYYDY	16	1-13	3	QQFNSYLLFT	10			
preTx mnT1D664 70	3-7	2-15	2	4	DLFAGYCSGGSCYSFFFRGFDY	22	3-20	2	QQYGSSPRMYT	11	+	-	-
preTx mnT1D664 72	3-33	2-2	2	4	SGYCSSTSCYHFDY	14	3-20	3	QQYGSSFT	8	-	+	-
preTx mnT1D664 73#	4-31	/	/	6	DRGRSGSHTSYYYYMDV	17	1-39	2	QQSYSTPYT	9			
preTx mnT1D664 75#	1-69	4-17	3	6	TPPMATVTTNAYYGMDV	16	1-12	4	QQANSFPVT	9			
preTx mnT1D664 76	4-39	3-10	1	4	RGLLWFPTEPYYFDY	15	3-20	4	QQYGSSPLT	9	+	-	c
preTx mnT1D664 79#	3-21	/	/	4	DLGPVRI	7	3-20	2	QQYGSSPRYT	10			
preTx mnT1D664 80	1-46	2-21	2	3	ACGGDCFAFDI	11	3-20	1	QQYGSSLWT	9	-	-	-
preTx mnT1D664 82	4-59	5-5	2	6	DRGYSYGLYYYYYMDV	16	1-33	3	QQYDNLHIFT	10	-	-	-
preTx mnT1D664 83	3-33	3-3	1	4	EAQRFLEWLFPPTTAPIDY	19	1-12	4	QQANSFPT	8	+	+	c
preTx mnT1D664 84	1-69	3-22	2	4	GYKYYYDSSGYQYFDY	16	1-5	2	QQYNSYT	7	-	-	-
preTx mnT1D664 88	1-69	3-22	2	3	DGGGSDGSGYDAFDI	15	4-1	4	QQYYSTPLT	9	-	-	-
preTx mnT1D664 90	1-46	4-17	3	4	DSADDTVTEYYFDY	14	3-11	4	QQRSNWPPLT	10	-	-	-
preTx mnT1D664 91	4-34	6-6	2	4	EPSSSYLDY	9	1-8	4	QQYYSYPLT	9	-	+	-
preTx mnT1D664 92	3-23	/	/	6	TGYYYYGMDV	10	1-16	2	QQYNSYPLYT	10	+	+	-
preTx mnT1D664 94	4-31	2-2	3	5	AAATVWDNWFDP	12	3-15	2	QQYNNWPPFYT	11	+	+	-
preTx mnT1D664 95#	5-a	6-13	2	4	LGPLYSSSWGYFDY	14	1-5	1	QQYNSYSQT	9			
preTx mnT1D664 96#	1-69	2-2	3	6	AGFLPAAIYYYGMDV	15	4-1	1	QQYYSTTWT	9			
preTx mnT1D664 57	1-2	3-10	1	5	ETGPGEDGNNWFDP	14							
	VH	D	RF	JH	CDR3(aa)	Length	Vλ	Jλ	CDR3(aa)	Length	Poly	HEp-2	Staining
preTx mnT1D664 53	4-59	3-22	2	4	GDYDSSGYYNDY	12	3-21	3	QVWDSSSPL	9	-	-	-
preTx mnT1D664 55	4-34	2-15	2	5	APRRPYCSGGSCYSDPRMGNWFDP	24	2-14	1	SSYTSSSTKV	10	+	+	c
preTx mnT1D664 56	3-33	3-3	2	6	EGSRDFWSGYWGSDYYGMDV	20	2-14	3	SSYTSSSTPVV	11	+	+	-
preTx mnT1D664 58	1-69	/	/	6	GSRWPGMDV	9	2-8	1	SSYAGSNTL	9	+	-	-
preTx mnT1D664 60#	1-46	3-22	2	4	GYYYDSSGYFGNY	13	3-10	3	YSTDSSGNHRGV	12			
preTx mnT1D664 61	3-48	/	/	6	LDPNYYYYGMDV	12	5-37	2	MIWPSNAKV	9	-	-	-
preTx mnT1D664 67	3-23	5-5	2	4	DTVGYSYGATFDY	13	1-51	2	GTWDSSLSAVV	11	-	-	-
preTx mnT1D664 71	4-30-4	/	/	4	AWGVYFDY	8	1-47	3	AAWDDSLSGRGV	12	-	-	-
preTx mnT1D664 77	1-69	1-26	2	4	EAAGVAGSYESYY	13	1-47	2	AAWDDSLSGVV	11	-	-	-
preTx mnT1D664 83#					see kappa		1-40	1	QSYDSSLSVSYV	12			
preTx mnT1D664 86	4-4	5-12	3	6	DIVRFGHYYYGMDV	14	1-47	2	AAWDDSLSGYVV	12	+	+	A
preTx mnT1D664 93	4-39	3-22	2	4	SNSSGYYY	8	3-25	1	QSADSSGTYV	10	-	-	-

RF, reading frame; #, antibody failed to be expressed

-, non-reactive; +, reactive

c, diffuse cytoplasmic staining; A, actin staining; G, golgi staining; M, mitochondrial staining; N, nuclear staining

Supplemental Table 3. Repertoire and reactivity of antibodies from mature naive B cells of T1D patient 697 pre treatment

Ig	HEAVY						LIGHT				REACTIVITY		
	VH	D	RF	JH	CDR3(aa)	Length	Vκ	Jκ	CDR3(aa)	Length	Poly	HEp-2	Staining
preTx mnT1D697 1	4-34	3-3	2	1	SPYYDFWSGYYKYFQH	16	3-15	2	QQYNNWRT	8	+	+	-
preTx mnT1D697 2	3-23	3-10	2	4	GLWYYYGSGVVFDY	14	3-20	1	QQYGSSPWT	9	+	+	-
preTx mnT1D697 3#	4-34	3-22	2	4	GSLAFYDSSGYNY	13	1-33	5	QQYDNLPIT	9			
preTx mnT1D697 4	3-23	3-22	2	4	EAWDSSGYYFDY	12	4-1	2	QQYYSTQYT	9	-	-	-
preTx mnT1D697 5	3-30	3-3	1	5	DVLRFLEWFPQRNWFDP	17	1-39	2	QQSYSTPRYT	10	+	+	-
preTx mnT1D697 10	4-49	5-5	3	6	DGVVTDPYYYYYGMDV	16	3-15	2	QQYNNWYT	8	-	-	-
preTx mnT1D697 11	4-59	6-6	2	2	VNEYSSLGSYWYFDL	15	1-39	1	QQSYSTLWT	9	-	-	-
preTx mnT1D697 17	3-9	1-26	2	4	DINPKTGSYSHQLDY	16	1-6	1	LQDYNYRT	8	-	+	-
preTx mnT1D697 20	1-69	2-2	3	6	EGQQSVPAALGGLAYYYYYMDV	22	1-39	2	QQSYSTPPIT	10	+	-	-
preTx mnT1D697 33	3-15	/	/	3	FPHYAFDI	8	2-20	2	MQGTHWPPYT	10	+	+	-
preTx mnT1D697 34	4-59	5-24	2	4	DDPVLDSFDY	10	3-11	5	QQRSNWPPIT	10	-	-	-
preTx mnT1D697 44#	1-2	5-5	2	4	DIAGYSLD	8	3-20	3	QQYGSSPVT	9			
preTx mnT1D697 46	3-53	/	/	4	PLYGTGD	7	3-20	1	QQYGSSPWT	9	-	-	-
preTx mnT1D697 47	3-30	5-12	3	6	DFDIVATGYYYYYGMDV	17	2-28	3	MQALQTAFT	9	-	-	-
preTx mnT1D697 48	1-2	/	/	6	ASVPFEGMDV	10	2-28	2	MQALQTRYT	9	-	-	-
preTx mnT1D697 14	3-30	1-26	1	4	GGWELSSIDY	10							
preTx mnT1D697 29	4-34	/	/	3	DADPA	5							
preTx mnT1D697 8							1-39	4	QQSYSTPLT	9			
preTx mnT1D697 16							4-1	2	QQYYSTPYT	9			
preTx mnT1D697 21							3-11	5	QQRSNWPRTIT	11			
	VH	D	RF	JH	CDR3(aa)	Length	Vλ	Jλ	CDR3(aa)	Length	Poly	HEp-2	Staining
preTx mnT1D697 6	4-59	6-13	2	2	DTSSSWHGSYFDL	13	3-21	3	QVWDSSSDHRV	11	-	+	-
preTx mnT1D697 9	5-51	5-5	3	4	QDTAMVTIDY	10	2-14	1	SSYTSSSTLV	10	-	-	-
preTx mnT1D697 13	1-18	4-17	2	4	SDYGDHTWRRYAASGY	16	3-25	3	QSADSSGTSWV	11	+	+	-
preTx mnT1D697 14	3-30	1-26	1	4	GGWELSSIDY	10	3-27	3	YSAADNNWV	9	-	+	N
preTx mnT1D697 22	3-30	6-6	2	4	SEYSSSSAVDY	11	3-1	2	QAWDSSTAV	9	-	+	-
preTx mnT1D697 24	3-23	2-21	2	4	DVCGGDCYSPFFDY	14	1-47	3	AAWDDSLSGPV	11	-	+	c
preTx mnT1D697 25	1-69	2-15	2	4	AEHCSGGSCYSTPYYFDY	18	2-11	3	CSYAGSYTWV	10	+	-	-
preTx mnT1D697 27	5-51	3-22	2	4	LVSSSGYYYGY	11	1-40	2	QSYDSSFVV	9	-	+	-
preTx mnT1D697 28#	5-51	/	/	5	MVDRDWFDP	9	3-25	3	QSADSSGTFWV	11			
preTx mnT1D697 35	4-59	3-3	2	3	TLTYYDFWSGSSNAFDI	17	2-23	2	CSYAGSSTPVV	11	+	-	-
preTx mnT1D697 39	3-33	3-16	2	2	DQDYGSNPTDWYFDL	15	1-36	3	AWDDSLNGPV	10	-	-	-
preTx mnT1D697 45	3-30	5-5	2	4	DHYSYGSDY	9	3-25	3	QSADSSGTWV	10	-	+	-

RF, reading frame; #, antibody failed to be expressed

-, non-reactive; +, reactive

c, diffuse cytoplasmic staining; A, actin staining; G, golgi staining; M, mitochondrial staining; N, nuclear staining

Supplemental Table 4. Repertoire and reactivity of antibodies from mature naive B cells of T1D patient 375 pre treatment

Ig	HEAVY						LIGHT				REACTIVITY		
	VH	D	RF	JH	CDR3 (aa)	Length	Vκ	Jκ	CDR3 (aa)	Length	Poly	HEp-2	Staining
preTx mnT1D375 60	3-33	6-19	3	4	EGPFGGVAGKTTLYYFDY	18	3-20	3	QQYGSSLFT	9	-	-	-
preTx mnT1D375 63	3-49	3-10	2	4	SLTGPYYYGSGSYR	14	4-1	4	QQYYSTPLT	9	-	-	-
preTx mnT1D375 66	3-48	6-19	2	3	TYSSGWFDAFDI	12	1-39	4	QQSYSTPRT	9	-	-	-
preTx mnT1D375 68	3-53	2-15	2	3	DSYCSGGSCPNAFDI	15	1-39	1	QQSYSTPRRT	10	-	-	-
preTx mnT1D375 69	3-23	3-10	3	4	RGITMVRGVIKEY	13	2-28	1	MQALQTRT	8	+	+	c
preTx mnT1D375 74	3-30	5-12	2	5	SGYSGYDFRNWFDP	14	3-20	3	QQYGSSYT	8	-	+	-
preTx mnT1D375 75	3-30	3-10	2	4	DSNGSGSSSWMYYFDY	16	3-20	1	QQTGSWT	7	-	-	-
preTx mnT1D375 76	3-23	4-17	3	4	APYRGVTTGG	10	3-15	2	QQYNNWPCS	9	+	+	-
preTx mnT1D375 79	4-30-2	4-17	2	3	VGYGDYSDAFDI	12	1-39	3	QQSYSTPF	8	-	+	-
preTx mnT1D375 82	4-59	3-10	2	3	AAYGSGSYYNVGLGADAFD	19	1-5	2	QQYNSYPCS	9	-	-	-
preTx mnT1D375 83	3-7	3-3	2	4	TYDFWSGYLDY	11	3-15	1	QQYNNWRT	8	-	-	-
preTx mnT1D375 85	4-59	4-4	2	5	GRSNDYSNFWFDP	13	2-28	2	MQALQTPYT	9	-	-	-
preTx mnT1D375 87	7-4-1	2-15	2	5	SSAYCSGGSCYSILSAYNWFDP	22	1-27	3	QKYNSAPFT	9	+	+	-
preTx mnT1D375 89	3-33	/	/	4	GMGY	4	1-16	4	QQYNSYPLT	9	-	+	N
preTx mnT1D375 96	3-30	/	/	4	WGDAQEATLDY	11	3-11	2	QQRSNWPVCS	10	-	-	-
	VH	D	RF	JH	CDR3 (aa)	Length	Vλ	Jλ	CDR3 (aa)	Length	Poly	HEp-2	Staining
preTx mnT1D375 49	5-a	3-22	2	5	QGENYYDSSGFDP	13	2-23	1	CSYAGSSTLYV	11	-	-	-
preTx mnT1D375 61	3-23	5-12	2	3	DRYSGYDSHAFDI	13	3-21	3	QVWDSSSDHPV	11	-	-	-
preTx mnT1D375 64	3-73	2-21	2	4	GDCSIAKTDY	10	1-47	3	AAWDDSLSGRV	11	-	+	N
preTx mnT1D375 73	4-39	3-10	3	4	TFPMVRGVNPCL	12	1-47	3	AAWDDTLSGWV	11	-	+	c
preTx mnT1D375 81	3-23	/	/	4	DVLSGRVPLNYFDY	14	3-25	2	QSADSSGTYVV	11	-	+	-
preTx mnT1D375 84	4-39	4-17	2	5	HDYGDYTEGSNWFDP	15	1-44	1	AAWDDSLKYV	10	-	-	-
preTx mnT1D375 85#					see kappa		3-1	2	QAWDSSTVV	9			

RF, reading frame; #, antibody failed to be expressed

-, non-reactive; +, reactive

c, diffuse cytoplasmic staining; A, actin staining; G, golgi staining; M, mitochondrial staining; N, nuclear staining

Supplemental Table 5. Repertoire and reactivity of antibodies from mature naive B cells of T1D patient 518 pre treatment

Ig	HEAVY						LIGHT				REACTIVITY		
	VH	D	RF	JH	CDR3 (aa)	Length	Vκ	Jκ	CDR3(aa)	Length	Poly	HEp-2	Staining
preTx mnT1D518 49	4-30-4	4-4	2	4	EDYDYSLIY	9	1-39	3	QQSYSTPFT	9	-	-	-
preTx mnT1D518 54	3-7	2-2	2	6	EDWYCSSTSCYTVYYYMDV	19	3-20	2	QQYGSSPPYT	10	-	+	-
preTx mnT1D518 58	3-21	3-10	3	4	DFRRVRGVIGY	11	3-15	1	QQYNNWPQT	9	+	+	N
preTx mnT1D518 61	3-30	3-10	2	4	DIGYYGSGSYYPDY	14	3-11	4	QQRSNWQVT	9	-	-	-
preTx mnT1D518 64	3-30	2-15	3	4	FSVVGRDY	8	3-11	4	QQRSNWPGLT	10	-	+	N
preTx mnT1D518 65	4-34	2-2	3	4	GPRFYKVPAAFRRYYFDY	18	3-15	1	QQYNNWPWT	9	+	+	c
preTx mnT1D518 71	4-34	/	/	3	GRAFDI	6	3-11	1	QQRSNWPT	8	-	+	-
preTx mnT1D518 72	4-59	4-17	1	3	DLLSNVGGDYVSGFDI	16	1-39	1	QQSYSTLRT	9	-	-	-
preTx mnT1D518 73	4-34	6-13	3	5	GKVSPPPIAAAGTSSWFDP	19	3-20	4	QQYGSSLLT	9	-	-	-
preTx mnT1D518 75	3-43	6-13	2	4	DIGDSSSYYYFDY	13	1-39	2	QQSYSTPRYT	10	-	-	-
preTx mnT1D518 84	3-33	6-19	3	2	DHAIAVAGLWYFDL	14	3-15	4	QQYNNWPFLT	10	-	+	-
preTx mnT1D518 86	3-23	1-26	3	4	EGIVGATPAPNFFDY	15	1-16	4	QQYNSYPLT	9	-	-	-
preTx mnT1D518 95	1-69	4-17	3	2	VGRAGGMTTVTTKYFDL	17	3-20	3	QQYGSSLT	8	+	+	c
	VH	D	RF	JH	CDR3 (aa)	Length	Vλ	Jλ	CDR3(aa)	Length	Poly	HEp-2	Staining
preTx mnT1D518 57	4-39	5-12	2	4	EPDSGYDPIHYFDY	14	3-21	3	QVWDSSSDHRV	11	-	-	-
preTx mnT1D518 63	4-34	3-10	2	5	GLYGSGSLLYRWFDP	15	3-21	2	QVWDSSSDHVV	11	-	-	-
preTx mnT1D518 76	1-18	6-19	3	5	VVAGTEGWFDP	11	3-1	3	QAWDSSTYVV	10	-	-	-
preTx mnT1D518 78	4-59	5-24	2	5	ERGNGYNLWFDP	12	1-51	2	GTWDSSLSAVV	11	-	-	-
preTx mnT1D518 83	5-51	5-24	2	3	RGDRDGYNYAFDI	13	2-23	3	CSYAGSSTV	9	-	-	-
preTx mnT1D518 87	3-30-3	6-13	1	4	DLEQQLVRYYFDY	13	3-1	3	QAWDSSTHVV	10	-	-	-
preTx mnT1D518 89	4-39	6-6	3	3	QGIAARSVDAFDI	13	2-11	2	CSYAGSYTWV	10	-	-	-

RF, reading frame; #, antibody failed to be expressed

-, non-reactive; +, reactive

c, diffuse cytoplasmic staining; A, actin staining; G, golgi staining; M, mitochondrial staining; N, nuclear staining

Supplemental Table 6. Repertoire and reactivity of antibodies from mature naive B cells of T1D patient 664 post treatment

Ig	HEAVY						LIGHT				REACTIVITY		
	VH	D	RF	JH	CDR3(aa)	Length	Vκ	Jκ	CDR3(aa)	Length	Poly	HEp-2	Staining
postTx mnT1D664 3	4-59	4-17	2	5	AAGDYVPWRPVDWFDP	16	4-1	1	QQYYSTPWT	9	-	-	-
postTx mnT1D664 6	1-46	6-19	2	6	MRSGWYEYYYYGMDV	15	1-16	2	QQYNSYPYT	9	+	+	c
postTx mnT1D664 9#	1-18	3-3	2	6	VDGTNLNYDFWSWVGNYYGMDV	22	1-39	2	QQSYSTLCT	9			
postTx mnT1D664 10#	3-30	2-8	2	6	DLGYCTNGVCYRYMDV	16	3-20	5	QQYGSSPPEVT	11			
postTx mnT1D664 11	3-21	/	/	5	DPFSLDSPESLFGVGDARPS	20	3-20	1	QQYGSSPTWT	10	-	-	-
postTx mnT1D664 13	4-39	3-3	3	4	LYVTIFGLRGDYFDY	15	4-1	2	QQYYSTPYMYT	11	+	-	-
postTx mnT1D664 17#	1-69	5-12	3	6	EPPVDIVATINYGMDV	16	1-39	2	QQSYSTPRT	9			
postTx mnT1D664 18	3-33	3-3	1	6	DLVRFLEWLNPVYDGMDV	18	1-6	2	LQDYNYPHT	9	+	-	-
postTx mnT1D664 23	4-34	6-13	2	3	GLRYSSSWLWGVAFDI	16	1-39	2	QQSYSTPQT	9	-	+	-
postTx mnT1D664 25	3-30	3-22	2	1	DYYDSSGYYYGHFQH	15	3-11	1	QQRSNWRWA	9	-	-	-
postTx mnT1D664 26	3-33	1-20	3	5	DPGTLVGDWFDP	12	3-11	3	QQRSNWPPIFT	11	-	-	-
postTx mnT1D664 29	3-7	3-10	1	2	VLIWFGHRWYFDL	13	1-8	3	QQYYSYPIT	9	+	-	-
postTx mnT1D664 31	4-59	3-22	2	4	EIAYYYDY	8	2-24	2	MQATQFPYT	9	-	-	-
postTx mnT1D664 33	1-18	4-4	2	4	DAPGNYGLRPVLDY	14	3-20	3	QQYGSSPRFT	10	-	-	-
postTx mnT1D664 34	3-23	3-22	2	4	DSYYYDSSGKY	11	2-24	1	MQATQFPWT	9	-	-	-
postTx mnT1D664 40#	7-4-1	3-22	2	5	DWDYYDSSVGP	11	1-5	2	QQYNSYSGYT	10			
postTx mnT1D664 41	3-73	3-22	2	5	QLGYDSSGYGNWFDP	15	4-1	4	QQYYSTPLT	9	-	-	-
postTx mnT1D664 42	3-33	4-23	3	4	GGTSMTTVGVYYFDY	15	1-12	1	QQANSFPQT	9	-	+	-
postTx mnT1D664 43	4-31	3-10	2	3	VRSRGWSNLTAFDI	14	1-39	1	QQSYSTPWT	9	+	+	N
postTx mnT1D664 44	3-11	4-17	2	2	SSHYYGEPYWYFDL	13	1-39	3	QQSYSTPFT	9	-	-	-
postTx mnT1D664 45	1-69	3-10	3	4	ANITMVRGVIMPFDY	15	3-20	1	QQYGSSPWT	9	+	+	-
postTx mnT1D664 48#	1-24	2-2	1	5	IQYQLLSGNWFDP	13	3-11	4	QQRSNWPPLT	10			
postTx mnT1D664 19	3-30	3-16	1	3	VVRLGELSLYRAFDI	15							
postTx mnT1D664 22	1-18	6-19	3	3	GQEGVAVAGNDAFDI	15							
postTx mnT1D664 24							2-28	4	MQALQTLT	8			
postTx mnT1D664 38							3-20	5	QQYGSSPPIT	10			
	VH	D	RF	JH	CDR3(aa)	Length	Vλ	Jλ	CDR3(aa)	Length	Poly	HEp-2	Staining
postTx mnT1D664 1	4-30	2-8	2	5	GGYCTNGVCYSWWFDP	16	1-47	3	AAWDDSLSGREV	12	-	-	c
postTx mnT1D664 2	3-21	6-25	2	6	TDIISDYGMDV	11	2-11	2	CSYAGSYT	8	-	-	-
postTx mnT1D664 7	3-30	6-19	2	4	DGFSGWYGVY	10	3-10	1	YSTDSSGNHSGV	12	-	+	N
postTx mnT1D664 14	3-33	6-6	3	4	DGVAAARLDY	10	3-25	2	QSADSSGTYVV	11	-	-	-
postTx mnT1D664 28	3-7	/	/	4	TLQTKNPGKY	10	3-10	3	YSTDSSGNHGV	11	-	+	-
postTx mnT1D664 37#	3-23	3-3	3	3	DFVGVVIPHDAFDI	14	3-9	1	QVWDSSTAFYV	11			
postTx mnT1D664 41#					see kappa		1-40	2	QSYDSSLSGPVV	12			
postTx mnT1D664 42#					see kappa		2-23	1	CSYAGSSTYV	10			
postTx mnT1D664 44#					see kappa		2-8	3	SSYAGSNKKV	10			
postTx mnT1D664 46	4-59	6-6	2	4	VGYGSSWDFDY	11	1-40	2	QSYDSSLSVVV	11	-	-	-

RF, reading frame; #, antibody failed to be expressed

-, non-reactive; +, reactive

c, diffuse cytoplasmic staining; A, actin staining; G, golgi staining; M, mitochondrial staining; N, nuclear staining

Supplemental Table 7. Repertoire and reactivity of antibodies from mature naive B cells of T1D patient 697 post treatment

Ig	HEAVY						LIGHT				REACTIVITY		
	VH	D	RF	JH	CDR3(aa)	Length	Vκ	Jκ	CDR3(aa)	Length	Poly	HEp-2	Staining
postTx mnT1D697 49#	1-18	3-10	2	5	DWYGSGSYYTDNWFDP	16	1-8	1	QQYYSYPRT	10			
postTx mnT1D697 51#	3-15	1-26	2	6	NLPDSGSYSWPHYYYYGMDV	20	1-5	1	QQYNSYSPS	9			
postTx mnT1D697 53#	3-23	2-2	3	3	EIVVVPAVHWGPDAFDI	17	1-8	2	QQYYSYPYT	9			
postTx mnT1D697 54	3-23	6-19	2	4	DRGYSSGWYADY	12	1-39	2	QQSYSTLMYT	10	-	-	N
postTx mnT1D697 55	1-8	3-10	2	4	APFLYGSPDLDY	12	2-28	4	MQALQTLT	8	-	-	-
postTx mnT1D697 56	3-23	6-19	2	4	DSEDSSGWYGY	11	3-20	2	QQYGSSPYT	9	-	-	-
postTx mnT1D697 59	1-46	3-3	3	5	DPFKVLAIFGVVPPTNWFDP	20	3-20	2	QQYGSSPGGYT	11	+	+	-
postTx mnT1D697 60	3-33	6-19	2	3	DPPPYSSGPGTGNDAFDI	18	2-28	4	MQALQTPLT	9	-	-	-
postTx mnT1D697 67	3-15	3-10	2	4	DPLTYYYGSGSYSGFRY	17	3-15	1	QQYNNWGSWT	10	-	+	-
postTx mnT1D697 68	3-11	3-10	1	5	DRKILWFGELFDGDP	15	3-20	1	QQYGSSPGT	9	+	-	-
postTx mnT1D697 71	3-23	3-3	3	5	GSGGVVVNWFDP	12	4-1	4	QQYYSTPPT	9	-	+	c
postTx mnT1D697 72#	3-49	1-26	2	3	GGSYFRDYAFDI	12	4-1	2	QQYYSTPLT	9			
postTx mnT1D697 76	4-31	2-15	2	6	LYCSGGSCYSGYYYYGMDV	19	3-11	3	QQRSNWFT	8	-	+	-
postTx mnT1D697 78#	1-18	6-19	2	6	EGYSSGWYGIKHPYYYYGMDV	21	1-33	2	QQYDNLPET	9			
postTx mnT1D697 81#	3-66	3-10	2	5	DYYGSGKTRGDNWFDP	16	1-39	1	QQSYSTPPT	9			
postTx mnT1D697 82	4-39	6-19	3	5	NFFWGIAVAGTFWGQRKNWFDP	22	1-39	2	QQSYSTPRT	9	+	+	c
postTx mnT1D697 83	4-4	2-2	2	2	SGYCSSTSCYRGYWYFDL	18	3-20	4	QQYGSSPPLT	10	+	-	-
postTx mnT1D697 84	3-33	3-22	2	5	NTYYYDSSGYQNWFDP	16	1-39	2	QQSYSTLMYT	10	-	-	-
postTx mnT1D697 85	4-59	/	/	6	QARAMDV	7	3-20	5	QQYGSSPIT	9	-	-	-
postTx mnT1D697 86	3-7	3-10	2	4	DKDYYGSEFDY	11	3-15	4	QQYNNWPLT	9	-	-	-
postTx mnT1D697 88	3-23	6-19	3	4	DRRIAVAFMSPYFDY	15	3-11	1	QQRSNWPWT	9	+	-	-
postTx mnT1D697 91	1-46	3-9	2	5	DAPGYYDILTGMGWFDP	17	3-20	1	QQYGSSPPTWT	11	-	-	-
postTx mnT1D697 92	4-34	2-15	2	4	RYCSGGSCPIDY	12	1-39	3	QQSYSTPFT	9	-	+	-
postTx mnT1D697 95	3-33	/	/	4	DSRYFDY	7	1-17	3	LQHNSYPFT	9	-	+	-
postTx mnT1D697 57	3-23	/	/	4	GKRHFDY	7							
postTx mnT1D697 62							3-20	1	QQYGKSPWT	10			
postTx mnT1D697 93							3-15	1	QQYNNWPQT	9			
postTx mnT1D697 96							1-5	1	QQYNSYSLT	9			
	VH	D	RF	JH	CDR3(aa)	Length	Vλ	Jλ	CDR3(aa)	Length	Poly	HEp-2	Staining
postTx mnT1D697 52#	3-15	3-22	2	3	DLALYDSSGYYSGSAFDI	18	3-21	2	QVWDSSSDHPV	11			
postTx mnT1D697 58	4-59	6-13	2	4	LSKDSSWYGY	10	2-14	2	SSYTSSSTLV	10	-	-	-
postTx mnT1D697 64	3-21	3-22	2	4	DFGHYDSSGDVNY	13	1-44	3	AAWDDSLNGFWV	12	-	-	-
postTx mnT1D697 65	1-8	6-19	2	4	LLGNSGWYDY	10	1-44	1	AAWDDSRMVS	10	-	-	-
postTx mnT1D697 73	1-18	5-5	3	4	DQAMVSGEIDY	11	2-14	2	SSYTSSSTLYVV	12	-	-	-
postTx mnT1D697 75	1-18	3-22	2	5	LDYYDSRWFDP	11	1-44	2	AAWDDSLNGPV	11	-	+	-
postTx mnT1D697 79	3-72	3-16	3	6	WIVSYYYMDV	10	3-21	3	QVWDSSSDHPV	11	-	-	-
postTx mnT1D697 80	3-33	6-13	3	4	DDGIAAAGPLHFDY	14	3-21	3	QVWDSSSDHPV	11	-	-	-
postTx mnT1D697 89	4-39	6-19	2	4	RDSSGLDY	8	2-14	3	SSYTSSSTWV	10	-	-	-
postTx mnT1D697 90	3-23	3-22	2	6	DNGPAQNYDSSGYYYYGMDV	20	3-1	3	QAWDSSTPWV	10	-	-	-
postTx mnT1D697 61							2-11	3	CSYAGSYTWV	10			

RF, reading frame; #, antibody failed to be expressed

-, non-reactive; +, reactive

c, diffuse cytoplasmic staining; A, actin staining; G, golgi staining; M, mitochondrial staining; N, nuclear staining

Supplemental Table 8. Repertoire and reactivity of antibodies from mature naive B cells of T1D patient 375 post treatment

Ig	HEAVY						LIGHT				REACTIVITY		
	VH	D	RF	JH	CDR3(aa)	Length	Vκ	Jκ	CDR3(aa)	Length	Poly	HEp-2	Staining
postTx mnT1D375 02	3-23	3-22	2	4	PPRGYYEPAQN	11	1-5	1	QQYNSYSST	9	-	+	c
postTx mnT1D375 07	4-59	5-24	2	4	SYGYNLYYFDY	11	3-11	5	QQRSNWPPPIT	11	-	+	-
postTx mnT1D375 08	1-2	6-13	3	2	GGGIAAAIIPLHWYFDL	17	1-5	3	QQYNSYSPFT	10	+	+	-
postTx mnT1D375 09	3-23	3-3	2	4	FTGFYDFWSGYEGELFDY	18	1-27	1	QKYNSAPWT	9	-	-	-
postTx mnT1D375 11	4-4	1-20	2	4	DDWNESIDY	9	1-8	1	QQYYSYPRT	9	-	+	c
postTx mnT1D375 16	4-59	3-22	2	2	ENYYDSSGYRYFDL	14	3-11	5	QQRSNWIT	8	-	-	-
postTx mnT1D375 17	3-30-3	3-10	2	4	DTWPTYGSGSYSIFDY	16	1-39	3	QQSYSTRFT	9	-	-	-
postTx mnT1D375 18	3-33	4-4	2	6	DGGRGDYSYYYYGMDV	16	1-27	3	QKYNSAPFT	9	-	-	-
postTx mnT1D375 19	3-7	3-10		6	GVIVAVYYYYGMDV	14	3-15	1	QQYNNWWT	8	+	-	N
postTx mnT1D375 29	7-4-1	5-12	2	3	DCCYEPHAFDI	11	1-39	1	QQSYSTRT	8	-	-	-
postTx mnT1D375 37	3-66	7-27	3	4	GGLGNWGADY	10	1-5	3	QQYNSYSPLFT	11	-	-	-
		3-16	2										
postTx mnT1D375 38	4-30-2	2-15	2	2	GGGKGSYWYFDL	12	3-15	1	QQYNNWPRT	9	+	+	N
postTx mnT1D375 39	3-23	4-17	2	3	GSYGDYAA	8	1-5	1	QQYNSYPWT	9	-	+	c
postTx mnT1D375 40	1-3	6-13	3	4	GTGIAAAAPPHFDY	14	2-28	4	MQALQTPFT	9	-	+	-
postTx mnT1D375 41	3-30	6-13	2	5	VSFSSSWYWFDP	12	1-9	4	QQLNSYPLT	9	+	+	c
postTx mnT1D375 42	3-53	3-3	2	4	EVVYVGSGYSY	11	1-39	2	QQSYSTPYT	9	-	-	-
	VH	D	RF	JH	CDR3 (aa)	Length	Vλ	Jλ	CDR3 (aa)	Length	Poly	HEp-2	Staining
postTx mnT1D375 03	4-31	3-22	2	3	AQPYYYDSIAFDI	13	3-21	1	QVWDSSSDLNYV	12	+	-	-
postTx mnT1D375 05	4-39	6-13	2	5	QSSSRNWFDP	10	1-51	2	GTWDSSLSAVV	11	-	+	-
postTx mnT1D375 10	4-31	4-17	2	6	VGYGDPRIHYYYYMDV	16	1-40	3	QSYDSSLSGFWV	12	-	+	-
postTx mnT1D375 22	3-30-3	2-8	2	4	DRGGGPMVSFDY	12	2-11	2	CSYAGSYTFGVV	12	-	-	-
postTx mnT1D375 24	4-39	2-15	2	3	HCSGGSCGLDDAFDI	15	1-44	1	AAWDDSLNGYV	11	-	-	-
postTx mnT1D375 25	3-15	5-12	2	4	LWGYEVGDY	9	3-25	1	QSADSSGTYLYV	12	-	+	-
postTx mnT1D375 26	4-59	4-17	3	6	DRGTVTTYYYYYGMDV	16	1-40	2	QSYDSSLSVYVV	12	-	-	-
postTx mnT1D375 32	1-2	3-3	2	3	TQKWFPPLFDAFDI	14	1-40	2	QSYDSSLSGYVV	12	+	+	-
postTx mnT1D375 44	4-49	3-16	2	4	AGRVDYYDFDY	11	2-14	2	SSYTSSSTPVV	11	-	-	-
postTx mnT1D375 45	5-a	3-22	2	4	RYYYDSSGYYDY	12	2-23	2	CSYAGSSTSVV	11	-	+	-

RF, reading frame; #, antibody failed to be expressed

-, non-reactive; +, reactive

c, diffuse cytoplasmic staining; A, actin staining; G, golgi staining; M, mitochondria l staining; N, nuclear staining

Supplemental Table 9. Repertoire and reactivity of antibodies from mature naive B cells of T1D patient 518 post treatment

Ig	HEAVY						LIGHT				REACTIVITY		
	VH	D	RF	JH	CDR3(aa)	Length	Vκ	Jκ	CDR3(aa)	Length	Poly	HEp-2	Staining
postTx mnT1D518 03	3-30	6-19	3	4	GGIAVDIRGYFDY	13	1-5	1	QQYNSYWT	8	-	-	c
postTx mnT1D518 06	4-59	2-8	2	6	LMVYASSPYPADMHLNYYYYGMDV	24	3-20	4	QQYGSSPIT	9	-	+	-
postTx mnT1D518 07	4-4	5-5	2	4	VSAMDEGRYYFDY	13	3-11	4	QQRSNWPPLT	10	-	-	-
postTx mnT1D518 08	1-18	6-13	2	6	DRGVAAAGDYYYYYGMDV	18	3-15	3	QQYNNWPLT	9	-	-	-
postTx mnT1D518 09	3-23	3-9	3	4	DPTIFCPVDY	10	1-39	4	QQSYSTPSLT	10	+	+	-
postTx mnT1D518 11	1-2	6-13	3	2	GGGIAAAIIPLHWYFDL	17	4-1	4	QQYYSTPLT	9	-	-	-
postTx mnT1D518 19	1-69	/	/	5	ASQGGGIDWFDP	12	1-39	1	QQSYSTPWT	9	+	-	-
postTx mnT1D518 20	3-23	1-26	1	4	LGGRELQDY	9	3-11	4	QQRSNWPLT	9	-	+	c
postTx mnT1D518 25	3-30-3	3-22	2	4	DSNWGAHFDY	10	3-20	1	QQYGSSLWT	9	-	+	-
postTx mnT1D518 26	3-23	1-26	1	4	TKWELLGSDYLFDY	14	1-33	5	QQYDNLPL	8	-	-	-
postTx mnT1D518 28	3-30	3-22	2	4	DPRFYYDSSGYYLFDY	16	3-20	4	QQYGSSPH	8	-	-	-
postTx mnT1D518 30	1-69	5-5	2	4	ARGYSYGQNDY	11	3-11	5	QQRSNWPPIT	10	+	-	-
postTx mnT1D518 34	3-23	2-2	3	5	DLIVVVPAAIIRGWFDP	17	3-11	1	QQRSNWPRT	9	+	+	c
postTx mnT1D518 37	4-61	4-23	3	4	STVVIDY	7	3-20	4	QQYGSSPRQLT	11	-	+	-
postTx mnT1D518 42	3-23	3-9	2	6	DQYYDILTGYSYYYYGMDV	19	2-28	1	MQALQTPGT	9	-	-	-
postTx mnT1D518 43	4-34	/	/	5	DDWFDP	6	4-1	1	QQYYSTPRT	9	-	+	-
	VH	D	RF	JH	CDR3(aa)	Length	Vλ	Jλ	CDR3(aa)	Length	Poly	HEp-2	Staining
postTx mnT1D518 10	1-58	1-26	2	6	DPVGAVYYYYGMDV	14	1-44	3	AAWDDSLNGWV	11	+	-	-
postTx mnT1D518 13	3-23	/	/	3	GTATGAFDI	9	1-40	1	QSYDSSLSGYV	11	-	-	-
postTx mnT1D518 23	4-59	3-22	2	3	DRLRESSLTYYYDSSGYYNDAFDI	24	1-51	1	GTWDSSLSAGV	11	-	-	-
postTx mnT1D518 31	3-23	3-22	2	4	MGLLFYYYFDY	11	1-51	1	GTWDSSLSAGV	11	-	-	-

RF, reading frame; #, antibody failed to be expressed

-, non-reactive; +, reactive

c, diffuse cytoplasmic staining; A, actin staining; G, golgi staining; M, mitochondrial staining; N, nuclear staining

Appendix 1: Type 1 Diabetes TrialNet Study Group

Steering Committee: J.S. Skyler (University of Miami, Chair), M. Anderson (University of California, San Francisco), P. Antinozzi (Wake Forest University), M. Atkinson (University of Florida), M. Battaglia (San Raffaele University), D. Becker (University of Pittsburgh), P. Bingley (University of Bristol), E. Bosi (San Raffaele University), J. Buckner (Benaroya Research Institute), P. Colman (Walter & Eliza Hall Institute of Medical Research), L. DiMeglio (Indiana University), S. Gitelman, (University of California, San Francisco), R. Goland (Columbia University), P. Gottlieb (Barbara Davis Center for Childhood Diabetes), C. Greenbaum (Benaroya Research Institute), K. Herold (Yale University), R. Insel (Juvenile Diabetes Research Foundation), T. Kay (St Vincent's Institute of Medical Research), M. Knip (University of Helsinki), J. Krischer (University of South Florida), A. Lernmark (Skane University), J.B. Marks (University of Miami), A. Moran (University of Minnesota), J. Palmer (University of Washington), M. Peakman (King's College), L. Philipson (University of Chicago), A. Pugliese (University of Miami), P. Raskin (University of Texas Southwestern), M. Redondo (Baylor University), H. Rodriguez (University of South Florida), B. Roep (Leiden University Medical Center), W. Russell (Vanderbilt University), L. Spain (National Institute of Diabetes and Digestive and Kidney Diseases [NIDDK]), D.A. Schatz (University of Florida), J. Sosenko (University of Miami), D. Wherrett (University of Toronto), D. Wilson (Stanford University), W. Winter (University of Florida), A. Ziegler (Forschergruppe Diabetes); Previous Members: C. Benoist (Joslin Diabetes Center), J. Blum (Indiana University), K. Bourcier, P. Chase (Barbara Davis Center for Childhood Diabetes), M. Clare-Salzler (University of Florida), R. Clynes (Columbia University), G. Eisenbarth (Barbara Davis Center for Childhood Diabetes), C. G. Fathman (Stanford University), G. Grave (National Institute of Child Health and Human Development), B. Hering (University of Minnesota), F. Kaufman (Children's Hospital Los Angeles), E. Leschek (NIDDK), J. Mahon (University of Western Ontario), K. Nanto-Salonen (University of Turku), G. Nepom (Benaroya Research Institute), T. Orban (Joslin Diabetes Center), R. Parkman (Children's Hospital Los Angeles), M. Pescovitz (Indiana University), J. Peyman (National Institute of Allergy and Infectious Disease), M. Roncarolo (San Raffaele University), P. Savage (NIDDK), O. Simell (University of Turku), R. Sherwin (Yale University), M. Siegelman (University of Texas Southwestern), A. Steck (Barbara Davis Center for Childhood Diabetes), J. Thomas (Vanderbilt University), M. Trucco (University of Pittsburgh), J. Wagner (University of Minnesota).

Executive Committee: Jay S. Skyler, Katarzyna Bourcier, Carla J. Greenbaum, Richard Insel, Jeffrey P. Krischer, Ellen Leschek, Lisa Rafkin, Lisa Spain. Past Members: Catherine Cowie, Mary Foulkes, Heidi Krause- Steinrauf, John M. Lachin, Saul Malozowski, John Peyman, John Ridge, Peter Savage, Stephanie J. Zafonte.

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Appendix 2

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