Loss-of-function but not dominant-negative intragenic *IKZF1* deletions are associated with an adverse prognosis in adult *BCR-ABL*-negative acute lymphoblastic leukemia

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Nucleic acid preparation

DNA and RNA were prepared by TRIzol (Life Technologies, Darmstadt, Germany) or by AllPrep DNA/RNA (QIAGEN, Hilden, Germany). TRIzol DNA was purified using DNA Clean & Concentrate (Zymo Research, Freiburg, Germany). Reverse transcription was performed using between 150ng-1µg RNA, either by Ready-To-Go You-Prime First-Strand Beads (GE Healthcare Europe, Freiburg, Germany) or by Transcriptor First Strand cDNA Synthesis Kit (Roche, Mannheim, Germany).

Identification of rare genomic breakpoints

To identify genomic breakpoints in patients positive for Δ2-3 in RT-PCR ex1/4 we used the multiplex PCR by Meyer et al.[1] with all 16 primers at 150 nM and the FastStart High Fidelity PCR System kit (Roche) under the following conditions: 2 min at 94°C, 10 cycles of 10 sec at 94°C, 30 sec at 64°C, 5 min at 68°C followed by 25 cycles with additional 20 sec elongation for each cycle. Cases negative in this PCR were further investigated with a different PCR Δ2-3B (forward primer by Meyer and reverse primers I3-R1A GTCCTTTGCACTGATGACTTATTCCCATG, I3-R1B CATCTGGGTTTGGATATGTTCATGCTGAC, I3-R1C CTACCCTGTAAATACCATCCCCTAGTCC, I3-R13B CACTGACAGACAAGAAGTTAGCTGAGG, with 250 nM of each primer).

In cases with atypical RT-PCR products, breakpoints were identified using primers as specified in Supplemental Methods (Tables S4-5). For Δ2 (primer concentration 150 nM) and Δ5-7 (primer concentration 300 nM) the FastStart High Fidelity PCR System (Roche) was used as described above. PCRs Δ2-7B and Δ4-7B were used with the HotStarTaq kit (QIAGEN) at 500 nM primer concentration and the following conditions: 15 min at 95°C, followed by 35 cycles of 30 sec at 94°C, 60 sec min at 65°C and 2.5 min at 72°C.

Sequencing and bioinformatic analysis

All PCR products were purified using the GenUP PCR Cleanup Kit (Biotechrabbit, Hennigsdorf, Germany). Multiple bands were excised from agarose gel and purified using the Thermoscientific GeneJET Gel Extraction Kit (Life Technologies, Darmstadt, Germany). Products were analyzed by Sanger sequencing using routine methods at the Max Planck Genome Center, Cologne, Germany. All sequences were submitted to the EMBL nucleotide sequence database (accession numbers LN875583-LN875775) and were analyzed using RSSsite for the presence of cryptic recombination signal sequences (cRSS) near the two breakpoint locations.[2]

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[1] Meyer C, zur Stadt U, Escherich G, Hofmann J, Binato R, da Conceição Barbosa T et al. Refinement of IKZF1 recombination hotspots in pediatric BCP-ALL patients. Am J Blood Res 2013; 3: 165-173.

[2] Merelli I, Guffanti A, Fabbri M, Cocito A, Furia L, Grazini U et al. RSSsite: a reference database and prediction tool for the identification of cryptic Recombination Signal Sequences in human and murine genomes. Nucleic Acids Res 2010; 38 Suppl: W262-7.

Statistical analysis

Survival analyses were performed according to the Kaplan-Meier method. Overall survival was calculated from date of diagnosis until death or last follow-up. Disease free survival was calculated from date of first complete remission to relapse or death from any cause. Survival rates are given as probabilities of survival at 5 years, with a 95% confidence interval. The log-rank test was used to compare survival curves. Differences between 2 groups were compared by the two-tailed Fisher's test, differences between 3 or more groups by Pearson's chi square. For all analyses, $p \leq 0.05$ was considered statistically significant. Statistics were calculated using SAS 9.4 (SAS Institute Inc., Cary, NC, USA) and IBM SPSS Statistics v22 (IBM Germany, Ehningen, Germany).

Supplementary Tables

Supplementary Table 1: Results of previous studies on the prognostic effect of *IKZF1* deletions in BCR-ABL-negative adult patients (Abbreviations: pts = patients; CIR = cumulative incidence of relapse; EFS = event-free survival; RFS = relapse-free survival; OS = overall survival; HR = hazard ratio; n.s. = not significant)

study	pts	*IKZF1* deletion	value	statistic	results
Beldjord 2014	216	focal vs. wildtype	CIR	multivariate Cox model	**HR 2.65 (1.48-4.73), p=0.001**
	324	focal vs. wildtype		univariate Cox model	**HR 2.24 (1.39-3.62), p=0.001**
		complete vs. wildtype		univariate Cox model	HR 1.01 (0.91-1.11), n.s. (p=0.85)
		Δ4-7 vs. Δ2-7/Δ4-8 vs. other		Kaplan Meyer	n.s. (no p-value given)
Moorman 2012	304	any deletion vs. wildtype	EFS RFS OS	multivariate Cox model	1.26 (0.89-1.78), n.s. (p=0.196) 1.23 (0.78-1.93) , n.s. (p=0.375) 1.23 (0.86-1.76) , n.s. (p=0.263)
		any deletion vs. wildtype	EFS RFS OS	univariate Cox model	**1.54 (1.12-2.12), p=0.008** 1.48 (0.98-2.24), n.s. (p=0.63) **1.55 (1.11-2.16), p=0.010**
		other deletions vs. Ik6	EFS	univariate Cox model	**HR 2.17 (1.21-3.89), p=0.009**
Mi 2012	134	Ik6 vs. wildtype	RFS	Log-rank test	n.s. (p=0.114)
Dupuis 2012	113	any deletion vs. wildtype	PFS	Log-rank test	**0.004**
		haploinsufficient and null-mutations vs. wildtype	OS PFS	Log-rank test	**0.01** **0.003**

Supplementary Table 2: Blast count of all 482 patient samples, percentage by samples type

material	<50% blasts	50-75% blasts	>75% blasts	total
bone marrow	14 (4,3%)	36 (10,9%)	280 (84,8%)	330
peripheral blood	22 (16,7%)	34 (25,8%)	76 (57,5%)	132
bone marrow or peripheral blood	3 (15,0%)	4 (20%)	13 (65,0%)	20
total	39 (8,0%)	74 (15,4%)	369 (76,6%)	482

Supplementary Table 3: Blast count of 127 patient samples that were *IKZF1* deleted and where *IKZF1* deletions were quantified

material	<50% blasts	50-75% blasts	>75% blasts	total
bone marrow	2 (2,3%)	7 (7,9%)	79 (89,8%)	88
peripheral blood	2 (5,9%)	11 (32,3%)	21 (61,8%)	34
bone marrow or peripheral blood	2 (40%)	1 (20%)	2 (40%)	5
total	6 (4,7%)	19 (15,0%)	102 (80,3%)	127

Supplementary Table 4: Oligonucleotides used in experiments

Experiment	Name	Oligonucleotide sequence (5'-3')
PCR Δ2-7	IKZF1-F2A	ACTACAGAGACTTCAGCTCTATTCCATTTC
	IKZF1-F2B	TGATTTGGATGTGTGTGTTTCATGCGTGG
	IKZF1-F7	ACCATCAAATACAGGTCAACAGGACTGA
	IKZF1-R7	AGGGACTCTCTAGACAAAATGGCAGGA
PCR Δ2-8	IKZF1-F2A	ACTACAGAGACTTCAGCTCTATTCCATTTC
	IKZF1-F2B	TGATTTGGATGTGTGTGTTTCATGCGTGG
	IKZF1-F8	CCCACTGCACAGATGAACAGAGCA
	IKZF1-R8	CCTCCTGCTATTGCACGTCTCGGT
PCR Δ4-7	IKZF1-F4	CTTAGAAGTCTGGAGTCTGTGAAGGTC
	IKZF1-F7	ACCATCAAATACAGGTCAACAGGACTGA
	IKZF1-R7	AGGGACTCTCTAGACAAAATGGCAGGA
PCR Δ4-8	IKZF1-F4	CTTAGAAGTCTGGAGTCTGTGAAGGTC
	IKZF1-F8	CCCACTGCACAGATGAACAGAGCA
	IKZF1-R8	CCTCCTGCTATTGCACGTCTCGGT
PCR Δ2-3 (Meyer 2013)	IKZF1.I1.F1B	AGTTCACTTCTGTCAAGCGTCTGTTGCTCT
	IKZF1.I1.F2	TGGATGTGTGTGTTTCATGCGTGGTTAATA
	IKZF1.I1.F3	TCATGTGGACCATGGCTTTCTTGTATTTCT
	IKZF1.I1.F4	TGGCTGAAAATGGGTCCTAATTAGTGGAAA
	IKZF1.I3.R2	GATGGCACTGGCAGTCATTTCTCTATGTCT
	IKZF1.I3.R4	TCTAGGAAGGACTTGGGCACATTGAAGAAT
	IKZF1.I3.R5	CTGTTACTGCCTGCAGGATAGACTTCTGGA
	IKZF1.I3.R6	TCTCGGCACTTACACACACTCTCTTTAGGC
	IKZF1.I3.R7	GGTACCCCAACCCATCCTTATACATGACAC
	IKZF1.I3.R8	CTGGCACTTCTGTCAAAACCTCACATCTCT
	IKZF1.I3.R9	CTTCCGGGTCCAGGATCTCCATATAACAAT
	IKZF1.I3.R10	TTTCATATAAAATGCTGCGAACACCTTGGA
	IKZF1.I3.R11	TATTCTCTTTCACAGGACAGTTTCCCAGCA
	IKZF1.I3.R12	AATGTACACTGTTAGTCCCCACCTGACCAA
	IKZF1.I3.R13	TGACTGAGACATAATGGACAAGAGCCCAAT
	IKZF1.I3.R14	CAAGGACTCTATGACTCGGTACCACTTGGA
PCR Δ2-3B	IKZF1.I1.F1B	AGTTCACTTCTGTCAAGCGTCTGTTGCTCT
	IKZF1.I1.F2	TGGATGTGTGTGTTTCATGCGTGGTTAATA
	IKZF1.I1.F3	TCATGTGGACCATGGCTTTCTTGTATTTCT
	IKZF1.I1.F4	TGGCTGAAAATGGGTCCTAATTAGTGGAAA
	IKZF1-I3-R1A	GTCCTTTGCACTGATGACTTATTCCCATG
	IKZF1-I3-R1B	CATCTGGGTTTGGATATGTTCATGCTGAC
	IKZF1-I3-R1C	CTACCCTGTAAATACCATCCCCTAGTCC
	IKZF1-I3-R13B	CACTGACAGACAAGAAGTTAGCTGAGG
RT-PCR ex1/8	IKZF1-ex1FA	AAAGCGCGACGCACAAATCCA
	IKZF1-ex8R	CGTTGTTGATGGCTTGGTCCATCAC
RT-PCR ex1/4	IKZF1-ex1FB	CGAGGATCAGTCTTGGCCCCAA
	IKZF1-ex4R	GAATGCCTCCAACTCCCGACAAAG

qPCR Δ2-7	IKZF1-q27-F1	CATGTACATTTTTGATCTAGGTCTTAG
	IKZF1-q27-R1	GTTAAATAAAGAACCCTCAGGCAT
	IKZF1-q27-P1	FAM-TCAGGAATAAAATGCAAATCACCTTGAAGA-BBQ
qPCR Δ4-7	IKZF1-q47-F1	CAGCCCATAGGGTATAAATAATCTG
	IKZF1-q47-R1	TTAAATAAAGAACCCTCAGGCATTC
	IKZF1-q47-P1	FAM-AATTGACGGCATCCAGGGATCTCAG-BBQ1
qPCR Δ4-8	IKZF1-q48-F1	AAAATATTCTTAGAAGTCTGGAGTCTG
	IKZF1-q48-R1	CCAAGCATGTCTCGGCATAC
	IKZF1-q48-R2	GAAAAGCACTATTCCACGTAGAC
	IKZF1-q48-P1	Cy5-TGAAGGTCACACCCTCTGGTCTT-BBQ
hck internal control	hck-f	TATTAGCACCATCCATAGGAGGCTT
	hck-r	GTTAGGGAAAGTGGAGCGGAAG
	hck-p	HEX-TAACGCGTCCACCAAGGATGCGAA-BHQ1

Supplementary Table 5: Oligonucleotides used on single patients only

Experiment	**Patient**	**Name**	**Oligonucleotide sequence (5'-3')**
PCR Δ2	#119	IKZF1.I1.F1B	AGTTCACTTCTGTCAAGCGTCTGTTGCTCT
		IKZF1.I1.F2	TGGATGTGTGTGTTTCATGCGTGGTTAATA
		IKZF1.I1.F3	TCATGTGGACCATGGCTTTCTTGTATTTCT
		IKZF1.I1.F4	TGGCTGAAAATGGGTCCTAATTAGTGGAAA
		IKZF1-R2A	CCCCAGCTACCCTATCCTTTGAACAG
		IKZF1-R2B	CCAATGAAGAAATGTCGTACTTTCCGC
		IKZF1-R2C	CTTGCATCCCTTCATCACTGTCTTGG
PCR Δ2-7B	#85, #199, #291	IKZF1.I1.F1B	AGTTCACTTCTGTCAAGCGTCTGTTGCTCT
		IKZF1.I1.F2	TGGATGTGTGTGTTTCATGCGTGGTTAATA
		IKZF1.I1.F3	TCATGTGGACCATGGCTTTCTTGTATTTCT
		IKZF1.I1.F4	TGGCTGAAAATGGGTCCTAATTAGTGGAAA
		IKZF1-R7	AGGGACTCTCTAGACAAAATGGCAGGA
PCR Δ4-7B	#338	IKZF1-F4B	ACTCTGACTATACTCTCTCCTGGTATCACA
		IKZF1-F4C	CAAACTGTTCTGGGCCAATATCACCAC
		IKZF1-F4D	TTCCCAACCTCCTCCTTCATTAGTGG
		IKZF1-F4E	TTTGGTTCTGTTACAGCTCTCAGTGAC
		IKZF1-F4F	TGCAGCTAAGATTCCAGACCAGGTAT
		IKZF1-R7	AGGGACTCTCTAGACAAAATGGCAGGA
PCR Δ5-7	#424 (and #225)	IKZF1-F5A	GAGTGGCCTCCTGTATTGTTTCTTTCAGC
		IKZF1-F5B	GATTGTCTGTGCCTATCTAGTTCCCATCTG
		IKZF1-R7	AGGGACTCTCTAGACAAAATGGCAGGA

Supplementary Table 6: Characteristics of all patients

Sex	
Male	285 (59.1%)
Female	197 (40.9%)
Age	
15-25	172 (35.7%)
26-35	97 (20.1%)
36-45	78 (16.2%)
46-55	87 (18.0%)
56-65	48 (10.0%)
Immunophenotype	
pre B ALL	111 (23.0%)
common ALL	314 (65.2%)
pro B ALL	57 (11.8%)
Leukocyte	
≤30/nL	308 (64.8%)
>30/nL	167 (35.2%)
no data	7
Risk group	
Standard risk	268 (55.6%)
High risk	214 (44.4%)
CNS involvement	
No	372 (94.4%)
Yes	22 (5.6%)
No data	88
Clinical course	
CR	428 (88.8%)
ED	31 (6.4%)
Failure	23 (4.8%)
Total	482 (100%)

Supplementary Table 7: Characteristics of patients with multiple *IKZF1* mutations (high deletion load mutations are shown in dark blue, low deletion load mutations in light blue, unquantified mutations in grey)

patient	Δ4-7	Δ2-7	Δ4-8	Δ2-8	Δ2-3	number of mutations
#29	Δ4-7	Δ2-7				2
#36		Δ2-7			Δ2-3	2
#46			Δ4-8		Δ2-3	2
#58	Δ4-7				Δ2-3	2
#100	Δ4-7	Δ2-7				2
#126	Δ4-7	Δ2-7				2
#127	Δ4-7		Δ4-8			2
#133	Δ4-7	Δ2-7				2
#143			Δ4-8		Δ2-3	2
#154		Δ2-7	Δ4-8			2
#157		Δ2-7			Δ2-3	2
#160			Δ4-8	Δ2-8		2
#174	Δ4-7				Δ2-3	2
#189		Δ2-7	Δ4-8			2
#198	Δ4-7	Δ2-7				2
#199		Δ2-7			Δ2-3	2
#204		Δ2-7			Δ2-3	2
#210		Δ2-7	Δ4-8			2
#215		Δ2-7			Δ2-3	2
#243		Δ2-7	Δ4-8			2
#256		Δ2-7			Δ2-3	2
#257	Δ4-7				Δ2-3	2
#266		Δ2-7			Δ2-3	2
#276	Δ4-7	Δ2-7				2
#335	Δ4-7	Δ2-7				2
#360		Δ2-7	Δ4-8			2
#400	Δ4-7		Δ4-8			2
#414	Δ4-7	Δ2-7				2
#108	Δ4-7	Δ2-7	Δ4-8			3
#111	Δ4-7	Δ2-7	Δ4-8			3
#113	Δ4-7	Δ2-7			Δ2-3	3
#175	Δ4-7	Δ2-7	Δ4-8			3
#285	Δ4-7	Δ2-7			Δ2-3	3
#365	Δ4-7	Δ2-7	Δ4-8			3
#395	Δ4-7	Δ2-7	Δ4-8			3
#461	Δ4-7	Δ2-7		Δ2-8		3
#470	Δ4-7	Δ2-7	Δ4-8	Δ2-8		4

Supplementary Table 8: Characteristics of patients according to *IKZF1* status

	mutation	wild-type	P
Sex			
Male	72 (56.3%)	213 (60.2%)	0.4636 (Fisher)
Female	56 (43.7%)	141 (39.8%)	
Age			
15-25	49 (38.3%)	123 (34.7%)	0.3843 (X²)
26-35	26 (20.3%)	71 (20.1%)	
36-45	17 (13.3%)	61 (17.2%)	
46-55	19 (14.8%)	68 (19.2%)	
56-65	17 (13.3%)	31 (8.8%)	
Immunophenotype			
pre B ALL	19 (14.8%)	92 (26.0%)	0.0064 (X²)
common ALL	98 (76.6%)	216 (61.0%)	
pro B ALL	11 (8.6%)	46 (13.0%)	
WBC			
<30/nl	79 (62.7%)	229 (65.6%)	0.5869 (Fisher)
>30/nl	47 (37.3%)	120 (34.4%)	
Missing values	7		
Risk group			
Standard Risk	67 (52.3%)	201 (56.8%)	0.4074 (Fisher)
High Risk	61 (47.7%)	153 (43.2%)	
CNS involvement			
No	100 (94.4%)	272 (94.4%)	1.0000 (Fisher)
Yes	6 (5.6%)	16 (5.6%)	
Missing values	88		
Clinical course			
CR	114 (89.1%)	314 (88.7%)	0.9936 (X²)
ED	8 (6.2%)	23 (6.5%)	
Failure	6 (4.7%)	17 (4.8%)	

Supplementary Table 9: Characteristics of patients according to different *IKZF1* deletion types

	dominant-negative only	both forms of deletion	loss-of-function only	wild-type	P (X^2)
Sex					
Male	30 (60.0%)	16 (72.7%)	26 (46.43%)	213 (60.2%)	0.1330
Female	20 (40.0%)	6 (27.3%)	30 (53.57%)	141 (39.8%)	
Age					
15-25	22 (44.0%)	7 (31.8%)	20 (35.7%)	123 (34.7%)	0.5485
26-35	8 (16.0%)	7 (31.8%)	11 (19.6%)	71 (20.1%)	
36-45	6 (12.0%)	2 (9.1%)	9 (16.1%)	61 (17.2%)	
46-55	6 (12.0%)	2 (9.1%)	11 (19.6%)	68 (19.2%)	
56-65	8 (16.0%)	4 (18.2%)	5 (8.9%)	31 (8.8%)	
Immunophenotype					
pre-B	6 (12,0%)	5 (22.7%)	8 (14.3%)	92 (26.0%)	0.0781
Common	39 (78,0%)	15 (68.2%)	44 (78.6%)	216 (61.0%)	
pro-B	5 (10,0%)	2 (9.1%)	4 (7.1%)	46 (13.0%)	
WBC					
<30/nl	34 (68.0%)	14 (63.6%)	31 (57.4%)	229 (65.6%)	0.6518
>30/nl	16 (32.0%)	8 (36.4%)	23 (42.6%)	120 (34.4%)	
Missing values	n=7				
Risk group					
Standard Risk	29 (58.0%)	12 (54.5%)	26 (46.4%)	201 (56.8%)	0.5252
High Risk	21 (42.0%)	10 (45.5%)	30 (53.6%)	153 (43.2%)	
CNS involvement					
No	41 (95.4%)	16 (100%)	43 (91.5%)	272 (94.4%)	0.6190
Yes	2 (4.6%)	0	4 (8.5%)	16 (5.6%)	
Missing values	n=88				
Clinical course					
CR	45 (90.0%)	20 (90.9%)	49 (87.5%)	314 (88.7%)	0.9042

Supplementary Table 10: Sequence of all breakpoints with accession numbers

del	accession number	patient	proximal breakpoint	proximal sequence	insert	distal sequence	distal breakpoint
Δ2	LN875583	#119	50.312.112	GCACAGCTCCTGACCATGCATGAAGGTCCTCTGAAATCGGTAAG		CTGAACANAAAGCCTCCAAGATGAAATTAGTTTTACTGTTAAACTTCA	50.319.280
Δ2-3	LN875584	#36	50.305.636	GGCACAGCTTTCAAATGCAGCTTCCCTCTCTCTAGGGACTGCAG	GGGGGA	CATTTGCACATGTACATACACATGTACACACGTGCACACGTGGTCACT	50.359.627
Δ2-3	LN875585	#46	50.306.999	GAAATAAATTCCATGTGCATATGCACATATGCACACAGAGCGTG	AGAAGG	TATTGGGAGTAGATTTAACCATTATGTAAATTGGATTTTTTAATTTTA	50.351.221
Δ2-3	LN875586	#58	50.307.772	AAGGGCACATGTACATTTTTGATCTAGGTCTTAGAAACGTAGAG	CCCC	GAATTCGGTGTTTCAAGGCTTACACTTTGATGCCCAAGACTGCACAAG	50.366.344
Δ2-3	LN875587	#113	50.307.794	TCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCATTATAC	GGG	CGTCACTTTAACAGTCACTGAGCTGTGACTCTTGGGGGAAAGATTGTG	50.367.267
Δ2-3	LN875588	#118	50.305.920	TAAGGCCAGGTTCAATTTGGTTATGAGTCGAGGGGTGGGGGGGA	GGG	ACAGTGTGGTGTTCAGAGGCATAGGCTCTAGGCTCCCTGGCAGCACTG	50.332.955
Δ2-3	LN875589	#143	50.308.978	TTGCATGGATTGGAATAGCCATTGTGTTCTTCCGTCTTCCCTGC	CTTATGG	GGTGTTCAGAGGCATAGGCTCTAGGCTCCCTGGCAGCACTGAGAGATA	50.332.962
Δ2-3	LN875590	#157	50.308.981	CATGGATTGGAATAGCCATTGTGTTCTTCCGTCTTCCCTGCTGG	CTCCAAAG	GGTATTGGTGTCTCTCTTTCTCTCCCACTCTCCCCAGTGTTGGAATTG	50.369.485
Δ2-3	LN875591	#174	50.310.862	TAATTGTTACCAAGCCATTGATGCTTCTATTCTTCCCTTTGCCC	ACCCTGGG	GAGCTAATAGCTGTACCCTAAATGATCCTGGCTTTGAATTCTCTTATC	50.352.225
Δ2-3	LN875592	#199	50.306.409	TGAACTAAATGGTCATGTTTTCTTCCCCTTTTGTTTCACGGTGA	A	CCCACAGTGAATTACCACCTTACTAAAATATTCATGGGTATATACTAT	50.345.195
Δ2-3	LN875593	#204	50.306.408	TTGAACTAAATGGTCATGTTTTCTTCCCCTTTTGTTTCACGGTG	GGGG	CCACAGTGAATTACCACCTTACTAAAATATTCATGGGTATATACTATG	50.345.196
Δ2-3	LN875594	#215	50.307.794	TCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCATTATAC	GA	AAGTGGGAAGTGTCTTGACAGAATTCGGTGTTTCAAGGCTTACACTTT	50.366.324
Δ2-3	LN875595	#256	50.307.793	ATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCATTATA	GG	CGTCACTTTAACAGTCACTGAGCTGTGACTCTTGGGGGAAAGATTGTG	50.367.267
Δ2-3	LN875596	#257	50.307.788	TTTTGATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCA	CCCCCCCG	GTCACTGAGCTGTGACTCTTGGGGGAAAGATTGTGCGTGTGTGTGTGT	50.367.280
Δ2-3	LN875597	#266	50.305.919	TTAAGGCCAGGTTCAATTTGGTTATGAGTCGAGGGGTGGGGGGG	CCTTA	GCTATATCAGATAACATCTTGTACTAGGTTTTGGAATAGACCGGTGAG	50.334.210
Δ2-3	LN875598	#304	50.306.927	TCTCTATATATTAATGTACTTATACACACACTTC	CACC	GCTGGCTCCTAGAGTGCGAGGAGCTCTCAGTGACTGCTGTGCATACTC	50.364.747
Δ2-3	LN875599	#327	50.306.408	TTGAACTAAATGGTCATGTTTTCTTCCCCTTTTGTTTCACGGTG		CACAGTGAATTACCACCTTACTAAAATATTCATGGGTATATACTATGG	50.345.197
Δ2-3	LN875600	#351	50.307.787	TTTTTGATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGC	CCCTTCCAA	CACTGAGCTGTGACTCTTGGGGGAAAGATTGTGCGTGTGTGTGTGTGT	50.367.282
Δ2-3	LN875601	#443	50.308.968	TTTCTTTGTGTGCTTGCATGGATTGGAATAGCCATTGTGTTCTTCCG	CCTTCTCCC	CAAGGACAGAGTACTGCTTTCAGCCACCATTTGTCCAATGAGTGGCTG	50.373.025
Δ2-7	LN875602	#29 clone 1	50.307.794	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCATTATAC	C	ACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.935
Δ2-7	LN875603	#29 clone 2	50.307.785	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCA	CCC	CAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.939
Δ2-7	LN875604	#36	50.307.792	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCATTAT	TCC	AAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.933
Δ2-7	LN875605	#50	50.307.790	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCATT	CCTGGGG	ACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.935
Δ2-7	LN875606	#85	50.305.725	CCACTCACAATTTCCCACTGCGCCGCAGGCAGTATATTTCAGCT	GGGG	ACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.935
Δ2-7	LN875607	#100	50.307.773	GATCTAGGTCTTAGAAACGTAGAGT	CAGAG	ACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.935
Δ2-7	LN875608	#108	50.307.792	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCATTAT	TAC	GAAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.932
Δ2-7	LN875609	#111 clone 1	50.307.778	GATCTAGGTCTTAGAAACGTAGAGTTTCAG	GGG	GGT	50.395.968
Δ2-7	LN875610	#111 clone 2	50.307.791	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCATTA	CCCCT	GAAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.932
Δ2-7	LN875611	#112	50.307.773	GATCTAGGTCTTAGAAACGTAGAGT	GGGGAG	GTTTCTTCTTCAAGGT	50.395.955

Δ2-7	LN875612	#113	50.307.791	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCATTA	NNNNNNNNNNNN	GTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.942
Δ2-7	LN875613	#126	50.307.794	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCATTATAC	CCCTAGG	GTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.942
Δ2-7	LN875614	#130	50.307.781	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGG	CTCGAGGGG	AGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.941
Δ2-7	LN875615	#133	50.307.791	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCATTA	NNNNNNNNNNN	ATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.937
Δ2-7	LN875616	#147	50.307.785	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCA	CCCCGAG	ACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.935
Δ2-7	LN875617	#154	50.307.788	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCA	CCCCTGGGATCA	CTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.944
Δ2-7	LN875618	#157	50.307.785	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCA	GCCGT	CATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.936
Δ2-7	LN875619	#175	50.307.792	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCATTAT	TTAA	GAAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.932
Δ2-7	LN875620	#178	50.307.787	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGC	TTCCC	ACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.935
Δ2-7	LN875621	#189 clone 1	50.307.784	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATC	TCGCCGG	AGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.941
Δ2-7	LN875622	#189 clone 2	50.307.787	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGC	AGGCG	GGAAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.931
Δ2-7	LN875623	#198	50.307.788	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCA	CCT	TAGTGTAACTGTTTCTTCTTCAAGGT	50.395.945
Δ2-7	LN875624	#199	50.306.409	TGAACTAAATGGTCATGTTTTCTTCCCCTTTTGTTTCACGGTGA	NNNNNNNNNNN	ACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.935
Δ2-7	LN875625	#204	50.307.784	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATC	CGGGGG	CTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.944
Δ2-7	LN875626	#210	50.307.782	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGA	NNNNNNNNNNNNNNG	CTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.944
Δ2-7	LN875627	#215 clone 1	50.307.784	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATC	GATTCTC	AAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.933
Δ2-7	LN875628	#215 clone 2	50.307.785	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCA	CCATAG	GTGTAACTGTTTCTTCTTCAAGGT	50.395.947
Δ2-7	LN875629	#217	50.307.789	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCAT	CCC	GAAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.932
Δ2-7	LN875630	#221	50.307.361	ATGTTGGTTCTTGTCATATTCTAAGGGAGATTGATGTAAGTGGC	CCTAGGGGG	ACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.935
Δ2-7	LN875631	#226	50.307.766	GATCTAGGTCTTAGAAAC	TCGCGG	CATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.936
Δ2-7	LN875632	#243	50.307.790	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCATT	CTCCCC	AAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.933
Δ2-7	LN875633	#256	50.307.793	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCATTATA	ATCCCCAC	GAAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.932
Δ2-7	LN875634	#266	50.307.790	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCATT	CCACAGGG	CATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.936
Δ2-7	LN875635	#276	50.307.789	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCAT	CCCCATN	TCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.938
Δ2-7	LN875636	#285	50.307.789	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCAT	NNNNNNNNNN	CATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.936
Δ2-7	LN875637	#291	50.305.733	AATTTCCCACTGCGCCGCAGGCAGTATATTTCAGCTTTGAGATA	TCGGCCGGGGACG	AGTGTAACTGTTTCTTCTTCAAGGT	50.395.946
Δ2-7	LN875638	#307	50.307.788	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCA	CCCT	AAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.933
Δ2-7	LN875639	#316	50.307.779	GATCTAGGTCTTAGAAACGTAGAGTTTCAGA	AGCATTCCTCGCGG	ACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.935
Δ2-7	LN875640	#329	50.307.788	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCA	NNNNNNNNNNNN	ACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.935
Δ2-7	LN875641	#335	50.307.791	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCATTA	A	GAAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.932
Δ2-7	LN875642	#337	50.307.787	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGC	CTTTCTTC	TCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.938
Δ2-7	LN875643	#340	50.307.787	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGC	NNNNNNNNNNNNN	CATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.936
Δ2-7	LN875644	#349	50.307.790	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCATT	CGCCTTT	AAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.933

Δ2-7	LN875645	#360	50.307.789	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCAT	CACGGGG	AACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.934
Δ2-7	LN875646	#365	50.307.788	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCA	CCCCAAG	CATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.936
Δ2-7	LN875647	#395	50.307.787	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGC	NNNNNNNN	ATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.937
Δ2-7	LN875648	#410	50.307.793	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCATTATA		GGAAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.931
Δ2-7	LN875649	#414	50.307.792	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCATTAT	NN	GAAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.932
Δ2-7	LN875650	#432	50.307.794	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCATTATAC	CTGAGG	CATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.936
Δ2-7	LN875651	#450	50.307.795	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCATTATACA	GG	ACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.935
Δ2-7	LN875652	#454	50.307.789	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCAT	CTCCCCC	GAAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.932
Δ2-7	LN875653	#461	50.307.789	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCAT	NNNNNNNNNNNNNN	AGTGTAACTGTTTCTTCTTCAAGGT	50.395.946
Δ2-7	LN875654	#470 clone 1	50.307.785	GATCTAGGTCTTAGAAACGTA**T**AGTTTCAAAGGATCA	NCCTCCC	AACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.934
Δ2-7	LN875655	#470 clone 2	50.307.766	GATCTAGGTCTTAGAAAC	CCATGG	GTGTAACTGTTTCTTCTTCAAGGT	50.395.947
Δ2-8	LN875656	#1	50.307.793	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCATTATA	GAA	GGGCTGACATGCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.755
Δ2-8	LN875657	#12	50.307.766	GATCTAGGTCTTAGAAAC	AGGGCGCTGCGACAT	TGCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.764
Δ2-8	LN875658	#99	50.307.778	GATCTAGGTCTTAGAAACGTAGAGTTTCAG	CCTCCCG	GGGTCTACGTGGAATAGTGCTTTTCCACAGAGTAGCTACTAGCCACAC	50.416.223
Δ2-8	LN875659	#104	50.307.790	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCATT	CCCA	TGGGCTGACATGCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.754
Δ2-8	LN875660	#160	50.307.787	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGC	CCCGGGGA	TGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.767
Δ2-8	LN875661	#458	50.307.784	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATC	CCTTCCCGGGGG	GCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.765
Δ2-8	LN875662	#461 clone 1	50.307.787	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGC	CCCTGGGG	TGCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.764
Δ2-8	LN875663	#461 clone 2	50.307.787	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGC	CCTA	TGGGCTGACATGCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.754
Δ2-8	LN875664	#464	50.307.789	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCAT	CATGG	GGGCTGACATGCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.755
Δ2-8	LN875665	#482	50.307.787	GATCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGC	CGGGGA	TGGGCTGACATGCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.754
Δ4-7	LN875666	#7	50.345.193	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACA	CCCT	ACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.935
Δ4-7	LN875667	#17	50.345.192	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTAC	NNNNNNNNNN	ATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.937
Δ4-7	LN875668	#20	50.345.194	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACAT	NNNNCNAGGN	ATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.937
Δ4-7	LN875669	#25	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCC	GGGGG	AACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.934
Δ4-7	LN875670	#29	50.345.193	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACA	CCCCTAG	GTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.942
Δ4-7	LN875671	#40	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCC	AGG	CATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.936
Δ4-7	LN875672	#58	50.345.195	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATC		GAAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.932
Δ4-7	LN875673	#80	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCC	GAT	CATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.936

Δ4-7	LN875674	#87	50.345.192	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTAC	CCCTTCGTCCCGGC CCGTTTTGTGTGGG TTGAATCGTAGCCAC TATATCCACCACAGT CTGACATCGCCTGAC AATAACCACACCTGG AACTGGAGGCGGGG CTGTCAGGAGGAG CTTCCCAGGGAACA GGGAGGGTCCAGAC AGCTGAGCCAGGGG CCCCCAGGACTGGG GACGTGGGGGGCT GCTTAGGTACCAGAC ATGGCCTCCCATCGG	GTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.942
Δ4-7	LN875675	#88	50.345.192	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTAC	TCTTCCC	GAAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.932
Δ4-7	LN875676	#100	50.345.186	GAATTGACGGCATCCAGGGATCTCAGAAATTAT	AGGG	TCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.938
Δ4-7	LN875677	#103	50.345.195	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATC	GGG	ATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.937
Δ4-7	LN875678	#108	50.345.195	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATC	GGG	ACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.935
Δ4-7	LN875679	#110	50.345.193	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACA	GAGGGG	ACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.935
Δ4-7	LN875680	#111	50.345.195	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATC	NNNN	ATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.937
Δ4-7	LN875681	#113	50.345.193	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACA	CCCA	GAAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.932
Δ4-7	LN875682	#116	50.345.167	GAATTGACGGCATC	AGTTGCGGGAGC	CAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.939
Δ4-7	LN875683	#121	50.345.190	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGT	TCTCTTC	GAAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.932
Δ4-7	LN875684	#126	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCC		TCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.938
Δ4-7	LN875685	#127	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCC		AAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.933
Δ4-7	LN875686	#133	50.345.195	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATC	GACCTTCCCTAGT GCCCAGCGGGGGT GGGAAAGGT	ACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.935
Δ4-7	LN875687	#138	50.345.175	GAATTGACGGCATCCAGGGATC	CCTGTCCAA	GCTGTGGAAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.926
Δ4-7	LN875688	#142	50.345.196	GAATTGATGGCATCCAGGGATCTCAGAAATTATTAGTACATCC	TGCGGGTGGGCC GGGA	TCGAAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.930
Δ4-7	LN875689	#146 clone 1	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCC		ACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.935
Δ4-7	LN875690	#146 clone 2	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCC	CC	ACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.935
Δ4-7	LN875691	#148	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCC	GAGTGGG	CATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.936
Δ4-7	LN875692	#170	50.345.192	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTAC	GCC	GGAAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.931
Δ4-7	LN875693	#174	50.345.197	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCCC	G	GGAAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.931
Δ4-7	LN875694	#175	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCC		AAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.933
Δ4-7	LN875695	#179	50.345.197	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCCC	CC	GAAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.932
Δ4-7	LN875696	#186	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCC	GCCGCCCGCTG	AACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.934
Δ4-7	LN875697	#197	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCC	GAC	ACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.935
Δ4-7	LN875698	#198	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCC	AAACAGG	CAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.939

Δ4-7	LN875699	#203	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCC	AAAC	CATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.936
Δ4-7	LN875700	#205	50.345.194	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACAT	AGGG	ACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.935
Δ4-7	LN875701	#207	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCC	GGG	TCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.938
Δ4-7	LN875702	#217	50.345.195	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATC	T	AACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.934
Δ4-7	LN875703	#233	50.345.181	GAATTGACGGCATCCAGGGATCTCAGAA	CCCCGAACG	AGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.941
Δ4-7	LN875704	#236	50.345.192	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTAC		GAAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.932
Δ4-7	LN875705	#257	50.345.192	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTAC	TTT	ACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.935
Δ4-7	LN875706	#267	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCC	GGGAGGG	ATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.937
Δ4-7	LN875707	#276	50.345.197	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCCC	C	CATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.936
Δ4-7	LN875708	#285	50.345.192	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTAC	CCTCCCCCACCAGAG	CATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.936
Δ4-7	LN875709	#295	50.345.192	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTAC	CCAGAGCCGGG	GTGTAACTGTTTCTTCTTCAAGGT	50.395.947
Δ4-7	LN875710	#320	50.345.197	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCCC	TCGG	AACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.934
Δ4-7	LN875711	#335	50.345.189	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAG	NNNNNNN	AAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.933
Δ4-7	LN875712	#338 clone 1	50.345.195	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATC	TGGTTCTC	GAAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.932
Δ4-7	LN875713	#338 clone 2	50.373.284	TCCAATGCTTCCCTGCTGTTCTGCTCCCCACCTGCAAGCGCCCA	T	ACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.935
Δ4-7	LN875714	#342	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCC	GA	GAAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.932
Δ4-7	LN875715	#343	50.345.192	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTAC	CCCC	GAAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.932
Δ4-7	LN875716	#345	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCC	G	GGAAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.931
Δ4-7	LN875717	#355	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCC	NNNN	CATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.936
Δ4-7	LN875718	#356	50.345.192	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTAC	G	GGAAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.931
Δ4-7	LN875719	#361	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCC	GGGG	AACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.934
Δ4-7	LN875720	#362	50.345.195	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATC	GAAAGTCTGGGC	GTAACTGTTTCTTCTTCAAGGT	50.395.949
Δ4-7	LN875721	#365	50.345.193	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACA	CCCCAAGGGGG	ACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.935
Δ4-7	LN875722	#370	50.345.193	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACA	CGGGGCG	ACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.935
Δ4-7	LN875723	#376	50.345.188	GAATTGACGGCATCCAGGGATCTCAGAAATTATTA		AACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.934
Δ4-7	LN875724	#395	50.345.192	GAATTGATGGCATCCAGGGATCTCAGAAATTATTAGTAC	NN	TAGTGTAACTGTTTCTTCTTCAAGGT	50.395.945
Δ4-7	LN875728	#400	50.345.192	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTAC	TT	AAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.933
Δ4-7	LN875729	#403	50.345.195	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATC	GGGGACGA	ATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.937
Δ4-7	LN875727	#405	50.345.192	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTAC	CCGTCAGG	GTGTAACTGTTTCTTCTTCAAGGT	50.395.947
Δ4-7	LN875730	#407	50.345.193	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACA	CCCC	AAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.933
Δ4-7	LN875731	#414	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCC	GGCT	AACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.934
Δ4-7	LN875732	#417	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCC	GG	AACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.934
Δ4-7	LN875733	#425	50.345.197	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCCC	CAG	ACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.935
Δ4-7	LN875734	#434	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCC	T	AAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.933

Δ4-7	LN875725	#437	50.345.197	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCCC		GAAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.932
Δ4-7	LN875735	#441	50.345.195	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATC	TTTTAAGGG	CATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.936
Δ4-7	LN875736	#452	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCC	GA	GAAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.932
Δ4-7	LN875737	#461	50.345.193	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACA	NNNNNNNNNNNNN	AGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.941
Δ4-7	LN875726	#470	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCC	GN	AACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.934
Δ4-7	LN875738	#479	50.345.192	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTAC	CCCGGGG	ATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.937
Δ4-7	LN875739	#483	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCC	TT	CATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.936
Δ4-7	LN875740	#500	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCC	GGAG	CATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.936
Δ4-7	LN875741	#509	50.345.192	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTAC	CCTTG	AACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.934
Δ4-8	LN875742	#46	50.345.122	AGAAGTCTGGAGTCTGTGAAGGTCACACCCTCTGGT	GGGGGATAATCTGG	CCTGTATGCCGAGACATGCTTGGG	50.416.778
Δ4-8	LN875743	#49	50.345.195	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATC	GGA	CTGACATGCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.758
Δ4-8	LN875744	#59	50.345.197	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCCC	CA	TGGGCTGACATGCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.754
Δ4-8	LN875745	#97	50.345.164	GAATTGACGGC	GTCG	GGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.768
Δ4-8	LN875746	#101 clone 1	50.345.157	GAAT	CCGACGGCGG	GTGGGCTGACATGCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.753
Δ4-8	LN875747	#101 clone 2	50.345.192	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTAC	TCCCAA	ATCAAGGGTCTACGTGGAATAGTGCTTTTCCACAGAGTAGCTACTAGC	50.416.218
Δ4-8	LN875748	#108	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCC	ATA	GGCTGACATGCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.756
Δ4-8	LN875749	#111 clone 1	50.345.177	GAATTGACGGCATCCAGGGATCTC	NNNNNNNNNNN	TGACATGCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.759
Δ4-8	LN875750	#111 clone 2	50.345.195	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATC	AGGGTATTA	TGTTTCTTTCTTTCCCCACATCAAGGGTCTACGTGGAATAGTGCTTTT	50.416.199
Δ4-8	LN875751	#123	50.345.184	GAATTGACGGCATCCAGGGATCTCAGAAATT	CTCCTTGCGA	GCTGACATGCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.757
Δ4-8	LN875752	#127	50.345.197	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCCC	C	GGCTGACATGCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.756
Δ4-8	LN875753	#139	50.345.161	GAATTGAC	CCAGGGA	GTTTCTGTGACTTCCAGTCCCCTCCTGCCAGTAGCAACCTACAAAACA	50.416.848
Δ4-8	LN875754	#143	50.345.178	GAATTGACGGCATCCAGGGATCTCA	CTTC	CTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.770
Δ4-8	LN875755	#154	50.345.192	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTAC	CC	GCTGACATGCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.757
Δ4-8	LN875756	#160	50.345.192	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTAC	NNNNNNN	GCTGACATGCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.757
Δ4-8	LN875757	#175	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCC	NNNNNNNNNNNNNNN	TGACATGCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.759
Δ4-8	LN875758	#189	50.345.194	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACAT	NNN	GGGCTGACATGCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.755
Δ4-8	LN875759	#191	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCC	GGAGGG	GGGCTGACATGCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.755
Δ4-8	LN875760	#210	50.345.192	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTAC	TCCCA	TGGGCTGACATGCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.754
Δ4-8	LN875761	#243	50.345.192	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTAC	CCA	TGGGCTGACATGCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.754
Δ4-8	LN875762	#289	50.345.192	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTAC	CCCCAAA	GCTGACATGCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.757
Δ4-8	LN875763	#360 clone 1	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTA**T**TACATCC	GGGGACA	TGGGCTGACATGCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.754

Δ4-8	LN875764	#360 clone 2	50.345.173	GAATTGACGGCATCCAGGGA	AGG	GCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.765
Δ4-8	LN875765	#365	50.345.192	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTAC	CCAG	GGGCTGAC**G**TGCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.755
Δ4-8	LN875766	#395	50.345.196	GAATTGANGGCATCCAGGGATCTCAGAAATTATTAGTACATCC	NN	GGGCTGACATGCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.755
Δ4-8	LN875767	#400	50.345.193	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACA	N	GGGCTGACATGCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.755
Δ4-8	LN875768	#406	50.345.192	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTAC	CCCCA	TGGGCTGACATGCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.754
Δ4-8	LN875769	#469	50.345.195	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATC	TCCTCCCCC CCCGCCG	TGTATGCCGAGACATGCTTGGG	50.416.780
Δ4-8	LN875770	#470 clone 1	50.345.196	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAGTACATCC	TCCAGAG	TCAAGGGTCTACGTGGAATAGTGCTTTTCCACAGAGTAGCTACTAGCC	50.416.219
Δ4-8	LN875771	#470 clone 2	50.345.172	GAATTGACGGCATCCAGGG	NNNNNNN	GCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.765
Δ4-8	LN875772	#470 clone 3	50.345.163	GAATTGACGG	CCCTCGG	GCTGGCTCTCTTCCCTGTATGCCGAGACATGCTTGGG	50.416.765
Δ4-8	LN875773	#495	50.345.189	GAATTGACGGCATCCAGGGATCTCAGAAATTATTAG	CCCCCGG	TCTTTCTTTCCCCACATCAAGGGTCTACGTGGAATAGTGCTTTTCCAC	50.416.203
Δ5-7	LN875774	#225	50.378.449	AAGGTAGGCTACCCTGTGATAGACACTTAACAGGATACTCGGGG		ACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.935
Δ5-7	LN875775	#424	50.378.410	TCCCAGCCTCGCCTTTGTAATGAGGTGGAAATTAACATGAAGGT	TTCCGGGGC	TCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGT	50.395.938

Supplementary Table 11: Putative cryptic recombination signal sequences near breakpoints

1. four major breakpoint clusters

breakpoint cluster	breakpoint region (cluster underlined)	RSS (5'-3')	strand	type
intron 1	TCTAGGTCTTAGAAACGTAGAGTTTCAGAGGATCAGCATTAT ACACACTGTCACACACACACACACTTAAAATTCAGATGAGGA	CACTGTCACACACACACACA CTTAAAAT	+	RSS12
intron 3	TAATCTGAATTGACGGCATCCAGGGATCTCAGAAATTATTAG TACATCCCACAGTGAATTACCACCTTACTAAAATATTC	CACAGTGAATTACCACCTTAC TAAAATA	+	RSS12
intron 7	TTTTAGATTTTGCTGATGGCATTGCTTGTTGAATGTTGCTGT GGAAACATCAAGTCTAGTGTAACTGTTTCTTCTTCAAGGTGA TTTG	CACAGCAACATTCAACAAGC AATGCCATCAGCAAAATCT	-	RSS23
3'UTR	CATGTGCTTTTTCTCAAGCAGGCACACTGGTCCCTTTCAAGG TGTGGGCTGACATGCTGGCTCTCTTCCCTGTATGCCGA	CACACCTTGAAAGGGACCAG TGTGCCTGCTTGAGAAAAA	-	RSS23

2. atypical breakpoints outside clusters

nr	patient	Δel	RSS (5'-3')	strand	location	type
1	#36	Δ2-3	CAGAGTGAGGAGGAGCTGATCTGACATT	+	intron 3	RSS12
2			CACTCTGATCTTTACCATCACCAGACTC	+	intron 3	RSS12
3	#46	Δ2-3	CACCCCCACTCCCCATATTATAAAAACT	-	intron 3	RSS12
4			CACAGTAACTCTTAATTGTTTAATTCAGTTCGTGTGTTA	+	intron 3	RSS23
5	#58	Δ2-3	CACAGCCAGGACAGGAGCTGCAGCAACT	-	intron 1	RSS12
6			CACTGTCACACACACACACACTTAAAAT	+	intron 1	RSS12
7			CATAGAGACACCAGAGAGAGAACAATGTTCACAGCCAGG	-	intron 1	RSS23
8	#85	Δ2-7	CAACATCCTCAAAAACAATACAATGATA	-	intron 7	RSS12
9			CACAGCAACATTCAACAAGCAATGCCATCAGCAAAATCT	-	intron 7	RSS23
10	#113	Δ2-3	CACTGAGCTGTGACTCTTGGGGGAAAGA	+	intron 3	RSS12
11			CATGCTGGGAAACTGTCCTGTGAAAGAGAATAGAAACCT	+	intron 3	RSS23
12			CACATTGGGTGGGGGAAAAATTCCTGTTTTCCCCAACCA	-	intron 3	RSS23
13			CAATGTGCTGCATTTTCTAATTTTCTATGAACACTTCCT	+	intron 3	RSS23
14			CACTGTCACACACACACACACTTAAAAT	+	intron 1	RSS12
15	#118	Δ2-3	CACTGTGAGATGCAAGCTGAAATAAACC	-	intron 3	RSS12
16			CACAGTGTGGTGTTCAGAGGCATAGGCTCTAGGCTCCCT	+	intron 3	RSS23
17			CACACTCAATCATTTGTTCTGGAGTCCAGAGGGAAAATA	-	intron 3	RSS23
18	#119	Δ2	CACTGTGACTTCCGGCCCCAGGGAAGCT	-	intron 2	RSS12
19			CACAGTCATGACTGTTTGTTCATTAAGC	+	intron 2	RSS12
20			CACAGTGCTTGGTATGCTCATGGGGGAGGAATAGGGGCT	+	intron 2	RSS23
21	#143	Δ2-3	CACTGTGAGATGCAAGCTGAAATAAACC	-	intron 3	RSS12
22			CACAGTGTGGTGTTCAGAGGCATAGGCTCTAGGCTCCCT	+	intron 3	RSS23
23			CACACTCAATCATTTGTTCTGGAGTCCAGAGGGAAAATA	-	intron 3	RSS23
24			CACAGTGGGTGGCCTGAGCCCAGAGCAGCTCCCCATATC	+	intron 1	RSS23
25			CACAGGGATATGGGGAGCTGCTCTGGGCTCAGGCCACCC	-	intron 1	RSS23
26	#157	Δ2-3	CACATTTGCATAAATATAGACAGAAAGC	-	intron 3	RSS12
27			CACAGTGGGTGGCCTGAGCCCAGAGCAGCTCCCCATATC	+	intron 1	RSS23
28			CACAGGGATATGGGGAGCTGCTCTGGGCTCAGGCCACCC	-	intron 1	RSS23
29	#174	Δ2-3	CACTCTCTTTAGGCACAGTTGTAAAAAT	-	intron 3	RSS12
30			CACAGTATATGGAATTTGATTCAAAAAT	-	intron 1	RSS12
31			CACAGTATATGGAATTTGATTCAAAAATCAGGTTCCTTA	-	intron 1	RSS23
32	#199	Δ2-3	CACAGTGAATTACCACCTTACTAAAATA	+	intron 3	RSS12
33			CATATTACTCAGAATCATATTGTCTCCAAAGCACAAACT	+	intron 3	RSS23
34			CACCGTGAAACAAAAGGGGAAGAAAACA	-	intron 1	RSS12
35			CACAGTCAATCAGAGCTGGTGACCAGAACATTTTATTGA	+	intron 1	RSS23
36	#199	Δ2-7	CAACATCCTCAAAAACAATACAATGATA	-	intron 7	RSS12

37			CACAGCAACATTCAACAAGCAATGCCATCAGCAAAATCT	-	intron 7	RSS23
38			CACCGTGAAACAAAAGGGGAAGAAAACA	-	intron 1	RSS12
39			CACAGTCAATCAGAGCTGGTGACCAGAACATTTTATTGA	+	intron 1	RSS23
40	#204	Δ2-3	CACAGTGAATTACCACCTTACTAAAATA	+	intron 3	RSS12
41			CATATTACTCAGAATCATATTGTCTCCAAAGCACAAACT	+	intron 3	RSS23
42			CACCGTGAAACAAAAGGGGAAGAAAACA	-	intron 1	RSS12
43			CACAGTCAATCAGAGCTGGTGACCAGAACATTTTATTGA	+	intron 1	RSS23
44	#215	Δ2-3	CACAGCCAGGACAGGAGCTGCAGCAACT	-	intron 1	RSS12
45			CACTGTCACACACACACACACTTAAAAT	+	intron 1	RSS12
46			CATAGAGACACCAGAGAGAGAACAATGTTCACAGCCAGG	-	intron 1	RSS23
47	#221	Δ2-7	CAACATCCTCAAAAACAATACAATGATA	-	intron 7	RSS12
48			CACAGCAACATTCAACAAGCAATGCCATCAGCAAAATCT	-	intron 7	RSS23
49			CAATCTCCCTTAGAATATGACAAGAACC	-	intron 1	RSS12
50			CACAGCCAGGACAGGAGCTGCAGCAACT	-	intron 1	RSS12
51			CATAGAGACACCAGAGAGAGAACAATGTTCACAGCCAGG	-	intron 1	RSS23
52	#225	Δ5-7	CAACATCCTCAAAAACAATACAATGATA	-	intron 7	RSS12
53			CACAGCAACATTCAACAAGCAATGCCATCAGCAAAATCT	-	intron 7	RSS23
54			CACTGTACAGTCAGGCTTTAAATGAATT	-	intron 4	RSS12
55			CACACTCAGCCCTAAGTGAAGCAAGCGTGCATGAGAGTA	+	intron 4	RSS23
56	#256	Δ2-3	CACTGAGCTGTGACTCTTGGGGGAAAGA	+	intron 3	RSS12
57			CATGCTGGGAAACTGTCCTGTGAAAGAGAATAGAAACCT	+	intron 3	RSS23
58			CACATTGGGTGGGGGAAAAATTCCTGTTTTCCCCAACCA	-	intron 3	RSS23
59			CAATGTGCTGCATTTTCTAATTTTCTATGAACACTTCCT	+	intron 3	RSS23
60			CACTGTCACACACACACACACTTAAAAT	+	intron 1	RSS12
61	#257	Δ2-3	CACTGAGCTGTGACTCTTGGGGGAAAGA	+	intron 3	RSS12
62			CATGCTGGGAAACTGTCCTGTGAAAGAGAATAGAAACCT	+	intron 3	RSS23
63			CACATTGGGTGGGGGAAAAATTCCTGTTTTCCCCAACCA	-	intron 3	RSS23
64			CAATGTGCTGCATTTTCTAATTTTCTATGAACACTTCCT	+	intron 3	RSS23
65			CACTGTCACACACACACACACTTAAAAT	+	intron 1	RSS12
66	#266	Δ2-3	CACAACACATGTACCACATGCACATATA	-	intron 3	RSS12
67			CACCACATATACCCCCCACATATATACA	-	intron 3	RSS12
68			CACATACATGCACACACAAACATATGAC	-	intron 3	RSS12
69			CACACACATACATGCACACACAAACATA	-	intron 3	RSS12
70			CACAGAACTTCATGACAGTTTTGATTTTAGATTAAAGTA	+	intron 3	RSS23
71			CACATACATATACATACATCACACACCACATATACCCCC	-	intron 3	RSS23
72			CACATACATGCACACACAAACATATGACACACACAACAT	-	intron 3	RSS23
73			CACACACATACATGCACACACAAACATATGACACACACA	-	intron 3	RSS23
74			CACATACACACACACACCACACACATACATGCACACACA	-	intron 3	RSS23
75	#291	Δ2-7	CAACATCCTCAAAAACAATACAATGATA	-	intron 7	RSS12
76			CACAGCAACATTCAACAAGCAATGCCATCAGCAAAATCT	-	intron 7	RSS23
77	#304	Δ2-3	CATCCAGGGTAGGGACTGAACAAAGTCA	-	intron 3	RSS12
78	#327	Δ2-3	CACAGTGAATTACCACCTTACTAAAATA	+	intron 3	RSS12
79			CATATTACTCAGAATCATATTGTCTCCAAAGCACAAACT	+	intron 3	RSS23
80			CACCGTGAAACAAAAGGGGAAGAAAACA	-	intron 1	RSS12
81			CACAGTCAATCAGAGCTGGTGACCAGAACATTTTATTGA	+	intron 1	RSS23
82	#351	Δ2-3	CACTGAGCTGTGACTCTTGGGGGAAAGA	+	intron 3	RSS12
83			CATGCTGGGAAACTGTCCTGTGAAAGAGAATAGAAACCT	+	intron 3	RSS23
84			CACATTGGGTGGGGGAAAAATTCCTGTTTTCCCCAACCA	-	intron 3	RSS23
85			CAATGTGCTGCATTTTCTAATTTTCTATGAACACTTCCT	+	intron 3	RSS23
86			CACTGTCACACACACACACACTTAAAAT	+	intron 1	RSS12

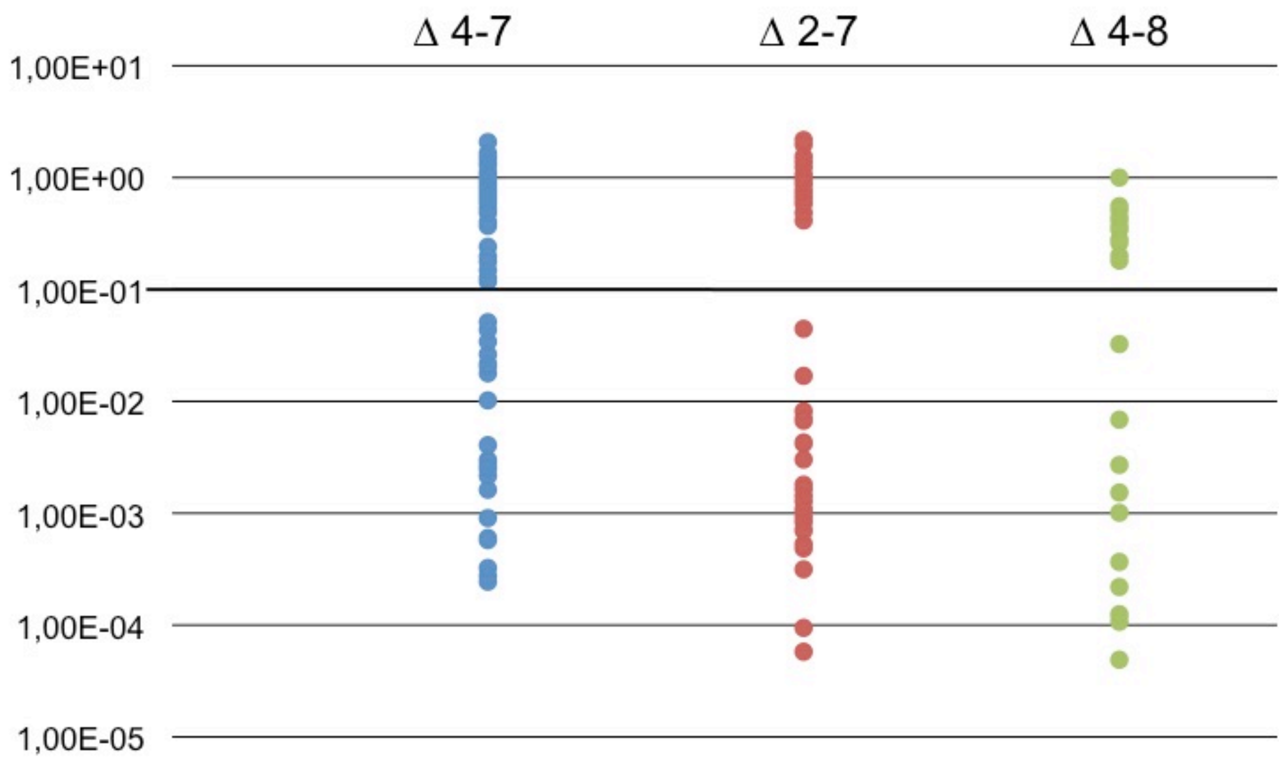
87	#424	Δ5-7	CAACATCCTCAAAAACAATACAATGATA	-	intron 7	RSS12
88			CACAGCAACATTCAACAAGCAATGCCATCAGCAAAATCT	-	intron 7	RSS23
89			CACTGTACAGTCAGGCTTTAAATGAATT	-	intron 4	RSS12
90			CACACTCAGCCCTAAGTGAAGCAAGCGTGCATGAGAGTA	+	intron 4	RSS23
91	#443	Δ2-3	CACTGAGAGCTGTAACAGAACCAAAAGA	-	intron 3	RSS12
92			CACTGTCACTGAGAGCTGTAACAGAACC	-	intron 3	RSS12
93			CACAATGGATGCTGCCTTAGATATCACA	-	intron 3	RSS12
94			CACATTGACCTCAGGACAGTATGTGATAGGCTCTTGTGC	+	intron 3	RSS23
95			CACTCTGGCTCAGGCCCACCCTGGGCTCTTTCACTGACT	-	intron 3	RSS23
96			CACTGTCACTGAGAGCTGTAACAGAACCAAAAGAGAACT	-	intron 3	RSS23
97			CACAGTGGGTGGCCTGAGCCCAGAGCAGCTCCCCATATC	+	intron 1	RSS23
98			CACAGGGATATGGGGAGCTGCTCTGGGCTCAGGCCACCC	-	intron 1	RSS23
99	#101 #111 #495	Δ4-8	CACAGTGAATTACCACCTTACTAAAATA	+	intron 3	RSS12
100			CATATTACTCAGAATCATATTGTCTCCAAAGCACAAACT	+	intron 3	RSS23
101			CACTGTGCTGCAGGTTCTGGCGTCATGATGTTCCTTCCA	-	3'UTR	RSS23
102			CACAGTGTGTTTCTTTCTTTCCCCACATCAAGGGTCTAC	+	3'UTR	RSS23
103	#139	Δ4-8	CACAGTGAATTACCACCTTACTAAAATA	+	intron 3	RSS12
104			CATATTACTCAGAATCATATTGTCTCCAAAGCACAAACT	+	intron 3	RSS23
105			CACACCTTGAAAGGGACCAGTGTGCCTGCTTGAGAAAAA	-	3'UTR	RSS23
106	#470	Δ4-8	CACAGTGAATTACCACCTTACTAAAATA	+	intron 3	RSS12
107			CATATTACTCAGAATCATATTGTCTCCAAAGCACAAACT	+	intron 3	RSS23
108			CACTGTGCTGCAGGTTCTGGCGTCATGATGTTCCTTCCA	-	3'UTR	RSS23
109			CACAGTGTGTTTCTTTCTTTCCCCACATCAAGGGTCTAC	+	3'UTR	RSS23
110			CACTGTGCTAGACCTTGGGGAGCTCCAGGGAGCAAGGCA	-	3'UTR	RSS23
111			CACAGTGCCTGGCACAAGGTGAGGGGGGTGCCCAGAAAA	+	3'UTR	RSS23
112			CACAAGGTGAGGGGGGTGCCCAGAAAAGATTCAATTCCC	+	3'UTR	RSS23
113	#99	Δ2-8	CACTGTCACACACACACACACTTAAAAT	+	intron 1	RSS12
114			CACTGTGCTGCAGGTTCTGGCGTCATGATGTTCCTTCCA	-	3'UTR	RSS23
115			CACAGTGTGTTTCTTTCTTTCCCCACATCAAGGGTCTAC	+	3'UTR	RSS23
116			CACTGTGCTAGACCTTGGGGAGCTCCAGGGAGCAAGGCA	-	3'UTR	RSS23
117			CACAGTGCCTGGCACAAGGTGAGGGGGGTGCCCAGAAAA	+	3'UTR	RSS23
118			CACAAGGTGAGGGGGGTGCCCAGAAAAGATTCAATTCCC	+	3'UTR	RSS23

Supplementary Table 12: Comparison between diagnosis and relapse of 20 mutations in 16 patients with *IKZF1* mutations at the time of diagnosis.

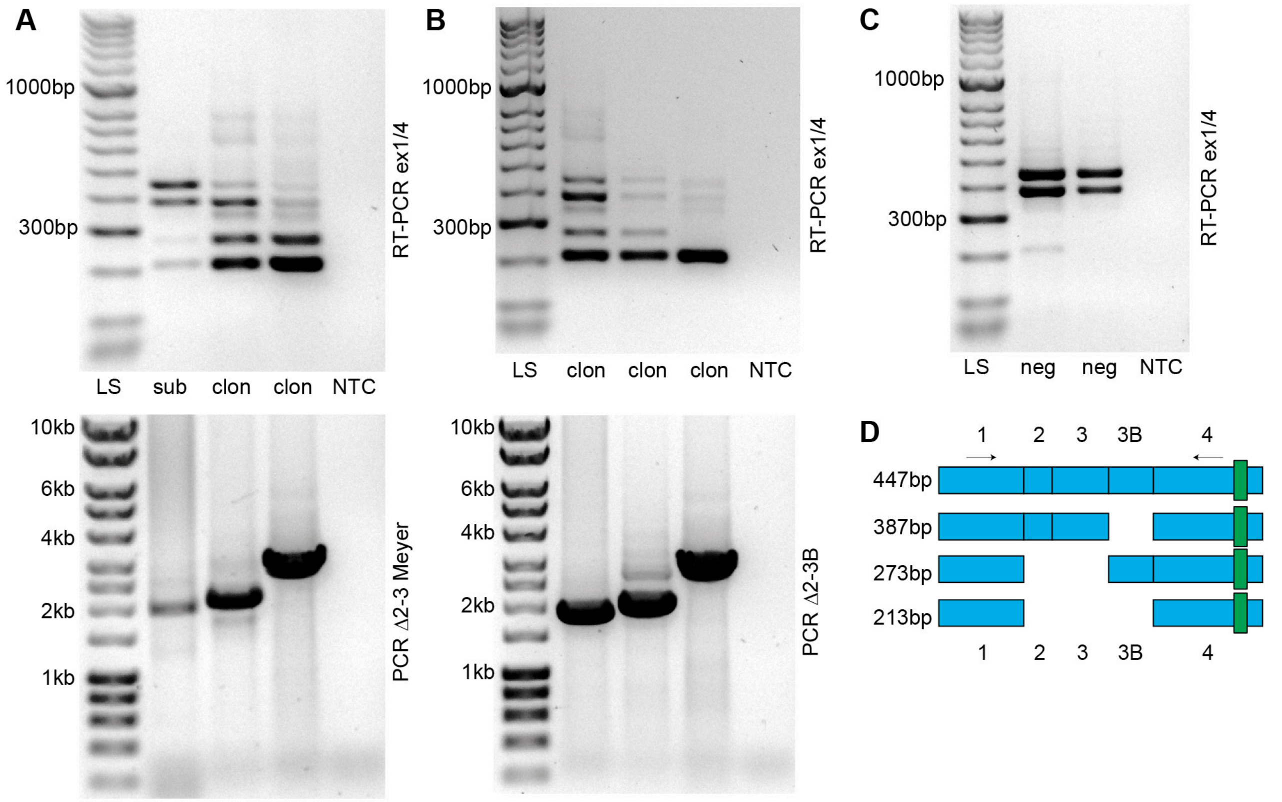
patient	deletion	deletion load	relapse
#110	Δ4-7	high deletion load	conserved
#112	Δ2-7	high deletion load	conserved
#119	Δ2	high deletion load	lost
#121	Δ4-7	high deletion load	conserved
#130	Δ2-7	high deletion load	conserved
#179	Δ4-7	low deletion load	lost
#198	Δ2-7	low deletion load	lost
	Δ4-7	high deletion load	lost
#199	Δ2-3	N/A	conserved
	Δ2-7	low deletion load	conserved
#204	Δ2-3	high deletion load	lost
	Δ2-7	high deletion load	conserved
#243	Δ2-7	high deletion load	conserved
	Δ4-8	high deletion load	conserved
#289	Δ4-8	high deletion load	lost
#479	Δ4-7	high deletion load	conserved
#482	Δ2-8	high deletion load	conserved
#483	Δ4-7	high deletion load	conserved
#495	Δ4-8	high deletion load	conserved
#500	Δ4-7	low deletion load	lost

Supplementary Figures

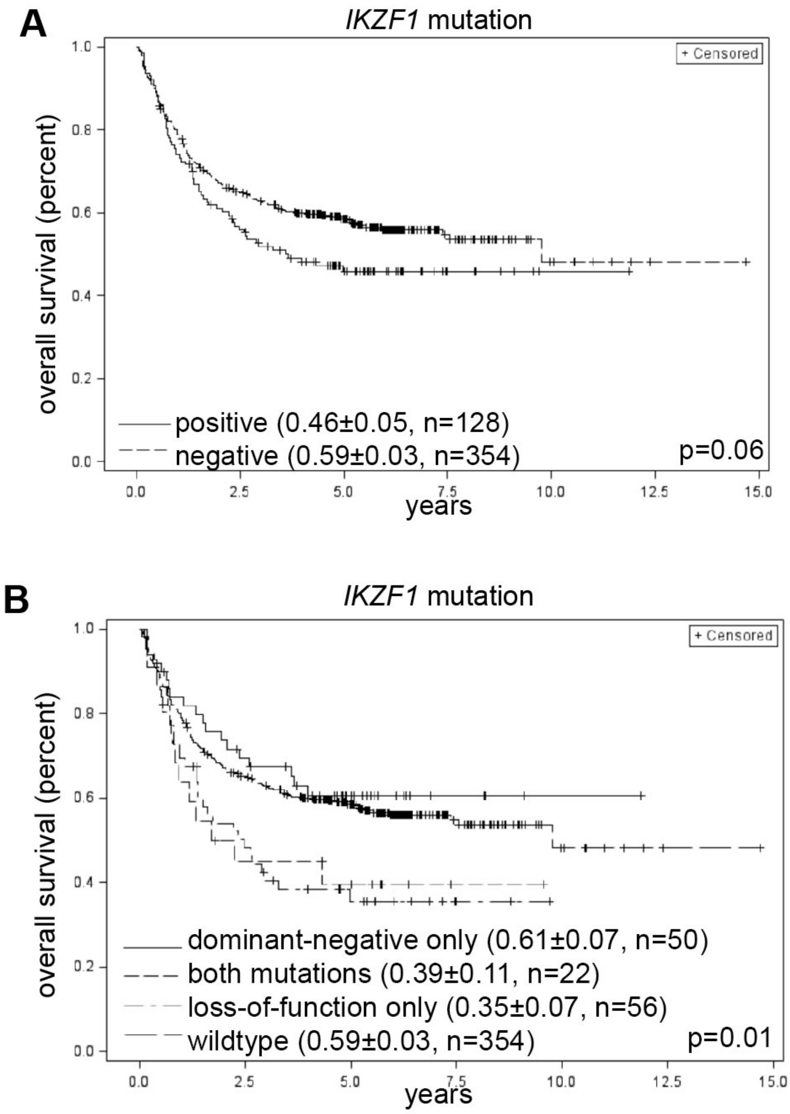
Supplementary Figure 1: Quantification of deletions Δ4-7, Δ2-7 and Δ4-8 by quantitative PCR. Relative concentration of deleted cells was calculated in relation to a standard curve by cell line BV-173 (Δ4-7) or patient DNA (#100 for Δ2-7, #101 for Δ4-8). Deletions with a relative concentration >1,00E-01 are considered „high deletion load“, all other deletions are considered „low deletion load“.



Supplementary Figure 2: Detection of Δ2-3 by RT-PCR. (A) Patients positive for Δ2-3 on RT-PCR (above) show a corresponding lesion detectable by the PCR described by Meyer (below). (B) In this subgroup of patients positive for Δ2-3 in RT-PCR ex1/4, a genomic breakpoint could only by identified by a novel PCR Δ2-3 B. (C) Patients negative for Δ2-3 on RT-PCR. (D) Structure of the 4 PCR products detectable by RT-PCR ex1/4.



Supplementary Figure 3: Additional evaluation of the prognostic effect of IKZF1 mutations. (A) Overall survival of patients with and without any *IKZF1* mutation. (B) Overall survival of patients with *IKZF1* loss-of-function mutations only, *IKZF1* dominant-negative mutations only or both forms of *IKZF1* mutations.



Supplementary Figure 4: Detection of rare breakpoints by RT-PCR. (A) Patients #85 and #291 show Ik10 expression on RT-PCR (above), no breakpoint by PCR Δ2-7 (middle) and a breakpoint by PCR Δ2-7 variant (below). (B) Patient #338 exhibits Ik6 and Ik6Δ on RT-PCR (above), a breakpoint by PCR Δ4-7 (middle) and a second breakpoint distal to exon 3b by PCR Δ4-7 variant (below). (C) Patient #424 shows Ik6 and Ik6Δ expression by RT-PCR (above), no PCR Δ4-7 (middle) and a band by a PCR Δ5-7 (below). (D) Structure of isoforms Ik6 and Ik6Δ.