

Table S1. PCR primer pairs used to confirm gene fusions detected by RNA-Seq. *ABL1*, *ABL2*, *PDGFRB*, *JAK2* and *CRLF2* gene rearrangements were confirmed by FISH.

Case	Gene fusion	Forward primer 5' – 3'	Reverse primer 5' – 3'
9D20G	<i>PAX5-GREB1L</i>	ACAGGGCAGCTACTCAGCAC	GTGTGGGCTGGAGTGGAG
10K11K	<i>PAX5-NCOA5</i>	GGTACCCTCCACACGTCC	CTGGGTCTTGATGGAGCCG
12L7P	<i>PAX5-ETV6</i>	GTGCCTAGCGTCAGTTCCAT	GTGTTGCTGTCAATTGGCCTTAA
14F25F	<i>PAX5-FOXP1</i>	CAGATGCGGGGAGACTTGTT	GCTGCTGAAGAAGGAGCTGT
17F5J	<i>PAX5-NOL4L</i>	CCTCGGTGAGCACGGATT	CTGGTGCTGGTGCTGGAG
9H3B,14M8D	<i>EP300-ZNF384</i>	TCAGATGCCGACACAACCC	GGGGATAGAAGGCCAGAAGT
10B12K	<i>TCF3-ZNF384</i>	CCCGGATCACTCAAGCAATA	GGGGATAGAAGGCCAGAAGT
12J19S	<i>ETV6-RUNX2</i>	CTGGCTTACATGAACCACATCAT	GGCTGCAGGCTGCTGGA
15L11P	<i>CUX1-NUTM1</i>	TCCAAGAATTAGTAGCCATGTCC	GAAGTGCAGGGGATGGAGA
14B14C	<i>KMT2A-CBL</i>	TGGGAGGCTTAGGAATCTTGA	GGCAGATGAGGAAGGTTTGAT
17A9B	<i>KMT2A-ATP5L</i>	AAGTGGCTCCCCGCCCAA	CTCCGACATAAAACCACATCAAC

Table S2. Identified JAK-STAT and Ras pathway gene point mutations in B-ALL study cases.

Signaling pathway	Mutated gene	Transcript (HGVSp)	Mutation	Case
JAK-STAT pathway	<i>JAK1</i>	NP_002218.2	p.E668D	15A8F
			p.F838V	9D20G
	<i>JAK2</i>	NP_004963.1	p.R564L	15A8F
			p.G571S	11L22A
			p.R683G	17D21G
			p.D873N	12J19R
			p.R1063H	11G26F, 15G1V, 15G3M
	<i>CRLF2</i>	NP_071431.2	p.F232C	17H7B
Ras pathway	<i>KRAS</i>	NP_203524.1	p.G12D	17D21G, 16B3M, 12G27L, 17G18E,
			p.G12V	10K11K, 17K27M, 13H14F
			p.G12S	15G1V
			p.G13D	9J16H, 13K17K, 16C18M, 17D10G, 11J29T, 13M30G
			p.Q61P	16D27F
			p.A146V	10K25B, 17D4K
	<i>NRAS</i>	NP_002515.1	p.G12A	13M13C
			p.G12C	14F25F, 15B20E
			p.G12D	17K27M, 11J19A, 11L30H, 13C21P, 14B12H, 16K14K, 11A19G
			p.G12V	11H24O
			p.G12S	10D16A, 13M13C
			p.G13D	15G3M, 16B3M, 11C25G, 14H12E, 17H21L, 15J23K
			p.G13R	14K20J, 10B12K
			p.Q61H	10B12K, 14K8E, 11D11E
			p.Q61K	16C21B, 17H21A
			p.Q61R	10G26E, 16G11K
			p.A146T	16D26K
	<i>PTPN11</i>	NP_002825.3	p.D61H	11H24O
			p.D61Y	14D30V
			p.A72V	15E18G, 12H10E
			p.E76G	11G26F
			p.E76K	14H12M
			p.E139D	11M8A

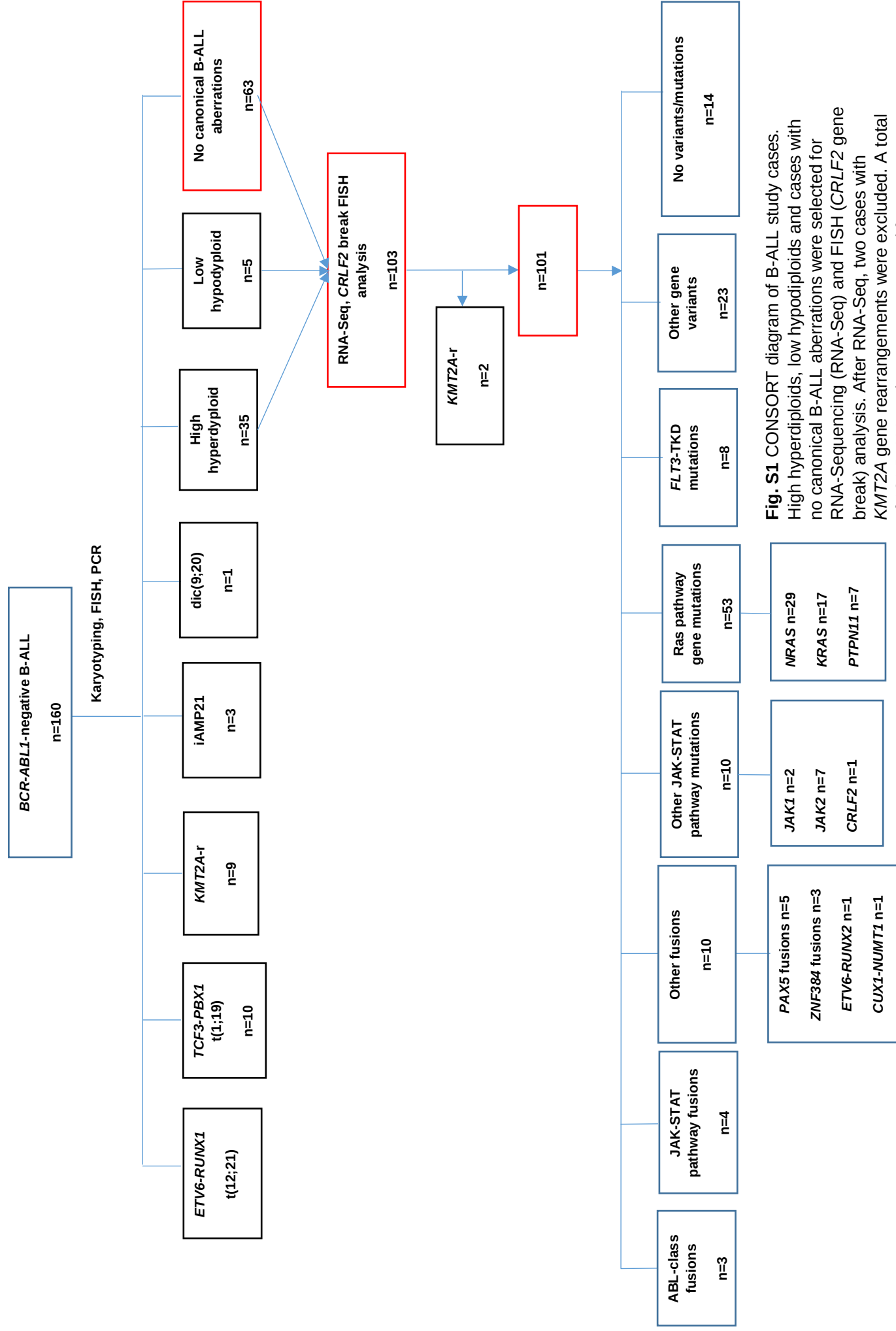


Fig. S1 CONSORT diagram of B-ALL study cases. High hyperdiploids, low hypodiploids and cases with no canonical B-ALL aberrations were selected for RNA-Sequencing (RNA-Seq) and FISH (CRLF2 gene break) analysis. After RNA-Seq, two cases with KMT2A gene rearrangements were excluded. A total of 101 B-ALL patients were screened for non-canonical B-ALL alterations. The number of FLT3-TKD, other JAK-STAT and Ras pathway mutations corresponds to the total number of specific alterations in sequenced cases.