

Table SI. HaloPlex custom panels used in the present study.

Version 1	Version 2
<i>PIK3CD</i>	<i>PIK3CD</i>
<i>MTOR</i>	<i>MTOR</i>
<i>MTHFR</i> ^a	<i>CSF3R</i>
<i>RPL11</i> ^a	<i>MPL</i>
<i>CSF3R</i>	<i>TAL1</i>
<i>MPL</i>	<i>JAK1</i>
<i>TAL1</i>	<i>RPL5</i>
<i>JAK1</i>	<i>NRAS</i>
<i>RPL5</i>	<i>NOTCH2</i> ^a
<i>NRAS</i>	<i>HAX1</i>
<i>HAX1</i>	<i>DNMT3A</i>
<i>H3F3A</i> ^a	<i>ALK</i>
<i>DNMT3A</i>	<i>MSH2</i>
<i>ALK</i>	<i>CXCR4</i>
<i>MSH2</i>	<i>STAT1</i>
<i>CXCR4</i>	<i>SF3B1</i>
<i>STAT1</i>	<i>IDH1</i>
<i>SF3B1</i>	<i>ERBB4</i>
<i>IDH1</i>	<i>IKZF2</i>
<i>ERBB4</i>	<i>VHL</i>
<i>IKZF2</i>	<i>RARB</i>
<i>VHL</i>	<i>MLH1</i>
<i>RARB</i>	<i>CTNNB1</i>
<i>MLH1</i>	<i>SMARCC1</i>
<i>CTNNB1</i>	<i>GATA2</i>
<i>SMARCC1</i>	<i>PIK3CB</i>
<i>GATA2</i>	<i>MECOM</i>
<i>PIK3CB</i>	<i>TERC</i> ^a
<i>MECOM</i>	<i>PIK3CA</i>
<i>PIK3CA</i>	<i>FGFR3</i>
<i>FGFR3</i>	<i>PDGFRA</i>
<i>PDGFRA</i>	<i>KIT</i>
<i>KIT</i>	<i>SRP72</i>
<i>SRP72</i>	<i>NFKB1</i>
<i>rs2231137</i> ^a	<i>TET2</i>
<i>NFKB1</i>	<i>IL15</i>
<i>TET2</i>	<i>FBXW7</i>
<i>IL15</i>	<i>TERT</i>
<i>rs17015014</i> ^a	<i>IL7R</i>
<i>FBXW7</i>	<i>PIK3R1</i>
<i>TERT</i>	<i>CSF1R</i>
<i>IL7R</i>	<i>PDGFRB</i>
<i>PIK3R1</i>	<i>EBF1</i>
<i>CSF1R</i>	<i>NPM1</i>
<i>PDGFRB</i>	<i>NSD1</i>
<i>EBF1</i>	<i>TPMT</i>
<i>NPM1</i>	<i>CDKN1A</i>
<i>NSD1</i>	<i>HOXA11</i>
<i>TPMT</i>	<i>IKZF1</i>
<i>CDKN1A</i>	<i>EGFR</i>
<i>MYB</i> ^a	<i>SBDS</i>
<i>HOXA11</i>	<i>CDK6</i>
<i>IKZF1</i>	<i>PIK3CG</i>
<i>EGFR</i>	<i>MET</i>
<i>SBDS</i>	<i>SMO</i>
<i>ABCBI</i> ^a	<i>BRAF</i>
<i>CDK6</i>	<i>EZH2</i>
<i>PIK3CG</i>	<i>SMARCD3</i>
<i>MET</i>	<i>FGFR1</i>

Table SI. Continued.

Version 1	Version 2
<i>SMO</i>	<i>RAD21</i>
<i>BRAF</i>	<i>SMARCA2</i>
<i>EZH2</i>	<i>JAK2</i>
<i>SMARCD3</i>	<i>CDKN2A</i>
<i>FGFR1</i>	<i>FANCG</i>
<i>RAD21</i>	<i>PAX5</i>
<i>SMARCA2</i>	<i>FANCC</i>
<i>JAK2</i>	<i>ABL1</i>
<i>CDKN2A</i>	<i>NOTCH1</i>
<i>FANCG</i>	<i>GATA3</i>
<i>PAX5</i>	<i>TRDMT1</i> ^a
<i>FANCC</i>	<i>RET</i>
<i>ABL1</i>	<i>TET1</i>
<i>NOTCH1</i>	<i>PTEN</i>
<i>GATA3</i>	<i>NFKB2</i>
<i>TRDMT1</i> ^a	<i>FGFR2</i>
<i>RET</i>	<i>HRAS</i>
<i>TET1</i>	<i>FANCF</i>
<i>PTEN</i>	<i>PAX6</i>
<i>NFKB2</i>	<i>WT1</i>
<i>FGFR2</i>	<i>LMO2</i>
<i>HRAS</i>	<i>SPI1</i>
<i>FANCF</i>	<i>ATM</i>
<i>PAX6</i>	<i>MLL</i>
<i>WT1</i>	<i>CBL</i> ^a
<i>LMO2</i>	<i>CHEK1</i>
<i>SPI1</i>	<i>ETV6</i>
<i>ATM</i>	<i>CDKN1B</i>
<i>MLL</i>	<i>SLCO1B1</i>
<i>CBL</i> ^a	<i>KRAS</i>
<i>CHEK1</i>	<i>SMARCD1</i>
<i>ETV6</i>	<i>SMARCC2</i>
<i>CDKN1B</i>	<i>BTG1</i>
<i>SLCO1B1</i>	<i>SOCS2</i>
<i>KRAS</i>	<i>SH2B3</i>
<i>SMARCD1</i>	<i>PTPN11</i>
<i>SMARCC2</i>	<i>NCOR2</i> ^a
<i>BTG1</i>	<i>FLT3</i>
<i>SOCS2</i>	<i>BRCA2</i>
<i>SH2B3</i>	<i>RB1</i>
<i>PTPN11</i>	<i>TINF2</i>
<i>NCOR2</i> ^a	<i>BCL11B</i>
<i>FLT3</i>	<i>AKT1</i>
<i>BRCA2</i>	<i>DLL4</i>
<i>RB1</i>	<i>MAP2K1</i>
<i>TINF2</i>	<i>IDH2</i>
<i>BCL11B</i>	<i>CREBBP</i>
<i>AKT1</i>	<i>CTCF</i>
<i>DLL4</i>	<i>FANCA</i>
<i>MAP2K1</i>	<i>TP53</i>
<i>IDH2</i>	<i>AURKB</i>
<i>CREBBP</i>	<i>MAP2K4</i>
<i>CTCF</i>	<i>NCOR1</i> ^a
<i>FANCA</i>	<i>NF1</i>
<i>TP53</i>	<i>ERBB2</i>
<i>AURKB</i>	<i>IKZF3</i>
<i>MAP2K4</i>	<i>SMARCE1</i>
<i>NCOR1</i> ^a	<i>STAT5B</i>
<i>NF1</i>	<i>STAT3</i>
<i>ERBB2</i>	
<i>IKZF3</i>	
<i>SMARCE1</i>	
<i>STAT5B</i>	
<i>STAT3</i>	

Table SI. Continued.

Version 1	Version 2
<i>AURKB</i>	<i>BRCA1</i>
<i>MAP2K4</i>	<i>RAD51C</i>
<i>NF1</i>	<i>SMARCD2</i>
<i>ERBB2</i>	<i>STEBP1</i>
<i>IKZF3</i>	<i>SMAD4</i>
<i>SMARCE1</i>	<i>BCL2</i>
<i>STAT5B</i>	<i>ELANE</i>
<i>STAT3</i>	<i>STK11</i>
<i>BRCA1</i>	<i>TCF3</i>
<i>RAD51C</i>	<i>DOT1L</i>
<i>SMARCD2</i>	<i>MAP2K2</i>
<i>STEBP1</i>	<i>DNMT1</i>
<i>SMAD4</i>	<i>DNM2</i>
<i>BCL2</i>	<i>SMARCA4</i>
<i>ELANE</i>	<i>CALR</i>
<i>STK11</i>	<i>JAK3</i>
<i>TCF3</i>	<i>CEBPA</i>
<i>DOT1L</i>	<i>RPS19</i>
<i>MAP2K2</i>	<i>ASXL1</i>
<i>DNMT1</i>	<i>DNMT3B</i>
<i>DNM2</i>	<i>E2F1</i>
<i>SMARCA4</i>	<i>SRC</i>
<i>CALR</i>	<i>AURKA</i>
<i>LYL1^a</i>	<i>RUNX1</i>
<i>JAK3</i>	<i>U2AF1</i>
<i>CEBPA</i>	<i>SLC19A1</i>
<i>RPS19</i>	<i>SMARCB1</i>
<i>ASXL1</i>	<i>CHEK2</i>
<i>DNMT3B</i>	<i>CRLF2</i>
<i>E2F1</i>	<i>BCOR</i>
<i>SRC</i>	<i>WAS</i>
<i>AURKA</i>	<i>GATA1</i>
<i>RUNX1</i>	<i>AR</i>
<i>U2AF1</i>	<i>BTK</i>
<i>SLC19A1</i>	<i>PHF6</i>
<i>SMARCB1</i>	<i>DKC1</i>
<i>CHEK2</i>	<i>CRLF2</i>
<i>CRLF2</i>	
<i>BCOR</i>	
<i>WAS</i>	
<i>GATA1</i>	
<i>AR</i>	
<i>FOXO4^a</i>	
<i>BTK</i>	
<i>PHF6</i>	
<i>DKC1</i>	
<i>CRLF2</i>	

^aGenes included in only one panel.

Table SII. Quality metrics of next-generation sequencing.

UPN	Sample class	Panel used	No. of reads in bam file	Average read length	Average read depth in analyzable target regions	Percentage of analyzable regions covered			
						By at least 10 reads	By at least 20 reads	By at least 50 reads	By at least 100 reads
1	Fresh	1	1,260,644	136	243	97.14	95.4	88.84	76.24
	CR	1	1,176,026	135	232	98.63	94.65	87.1	73.62
	Relapse	1	998,341	135	193	96.55	94.38	85.89	69.61
2	Fresh	1	3,618,486	133	644	97.76	97.01	94.78	90.02
	CR	1	1,304,976	133	240	96.06	93.61	84.69	70.54
	Relapse	1	1,860,566	134	351	97.16	95.94	91.35	82.35
3	Fresh	2	1,392,112	120	251	96.81	94.47	86.43	73.21
	CR	2	3,464,384	118	657	98.21	97.35	94.99	90.22
	Relapse	2	1,164,600	118	227	97.12	94.81	86.47	72.03
4	Fresh	1	1,809,996	134	244	71.5	70.49	66.72	59.23
	CR	1	1,510,980	134	284	96.68	94.62	88.09	75.84
	Relapse	1	2,153,794	133	396	97.35	96.13	91.56	83.33
5	Fresh	1	4,103,426	133	723	97.88	97.17	95.18	90.73
	CR	1	3,877,850	134	688	97.8	97.22	95.24	90.99
	Relapse	1	3,781,600	133	688	97.83	97.11	94.96	90.53
6	Fresh	1	1,308,022	136	258	98.05	97.09	94.29	88.68
	CR	1	1,271,062	136	251	96.83	95.02	88.39	76.34
	Relapse	1	1,251,183	136	247	96.92	95.07	88.52	76.35
7	Fresh	2	1,381,354	116	277	97.35	95.44	88.39	75.91
	CR	2	1,028,212	117	168	95.35	90.83	77.14	58.15
	Relapse	2	1,353,922	119	254	97.18	95.14	87.41	73.98
8	Fresh	2	1,652,912	119	319	97.64	96.15	90.38	79.5
	CR	2	1,217,716	119	234	97.4	95.18	87.16	72.97
	Relapse	2	1,405,880	118	280	97.13	94.9	87.5	75.29
9	Fresh	2	1,363,944	119	277	97.57	95.69	89.29	77.1
	CR	2	1,697,248	119	283	97.14	95.07	87.64	75.01
	Relapse	2	1,307,666	118	265	97.49	95.8	90.25	77.39
10	Fresh	2	1,319,874	118	270	97.42	95.8	90.07	78.01
	CR	2	1,317,284	117	269	97.46	95.91	89.88	77.59
	Relapse	2	1,442,870	119	287	97.08	95.02	88.36	76.48
11	Fresh	2	2,012,364	119	359	97.81	96.7	92.28	83.97
	CR	2	1,407,634	118	282	97.13	95.55	89.1	76.76
	Relapse	2	1,285,454	119	261	97.17	95.04	87.47	74.82
12	Fresh	2	1,209,622	119	243	96.64	94.03	84.62	70.53
	CR	2	1,533,670	120	307	97.45	95.95	90.15	80.11
	Relapse	2	1,512,724	119	301	97.45	95.48	89.6	79.09
13	Fresh	2	1,397,642	117	286	97.48	95.85	89.13	76.79
	CR	2	1,630,892	119	325	97.61	96.2	90.53	80.02
	Relapse	2	1,454,454	119	296	97.39	95.62	88.82	77.76
14	Fresh	2	1,601,992	117	302	97.76	96.49	91	80.44
	CR	2	1,421,290	120	289	97.45	95.61	89.38	78.46
	Relapse	2	1,376,750	117	275	97.36	95.69	89.31	77.07
15	Fresh	1	1,291,118	133	233	95.72	92.91	83.45	68.4
	CR	1	1,107,012	133	202	95.75	92.28	81.36	64.04
	Relapse	1	1,237,990	133	233	95.8	92.91	83.62	68.56
16	Fresh	1	1,816,194	133	348	97.06	95.57	90.51	81.1
	CR	1	1,680,862	134	312	97.11	95.62	90.78	80.68
17	Fresh	1	2,139,132	135	411	97.41	96.43	92.97	85.97
	CR	1	1,800,830	134	349	97.23	96.12	91.73	82.78
18	Fresh	1	1,228,768	136	244	96.21	93.6	85	70.86
	CR	1	1,122,844	135	213	96.66	94.9	87.34	73
19	Fresh	1	1,945,698	134	374	97.48	96.23	91.65	83.33
	CR	1	2,038,572	135	395	97.3	96.24	92.31	84.49
20	Fresh	1	2,156,308	135	418	97.47	96.24	92.34	85.29
	CR	1	1,735,998	134	331	97.05	95.26	89.89	79.67

Table SII. Continued.

UPN	Sample class	Panel used	No. of reads in bam file	Average read length	Average read depth in analyzable target regions	Percentage of analyzable regions covered			
						By at least 10 reads	By at least 20 reads	By at least 50 reads	By at least 100 reads
21	Fresh	2	1,576,912	116	302	97.28	95.54	89.32	77.82
	CR	2	2,467,160	120	452	98.12	97.51	94.63	88.68
22	Fresh	1	3,477,176	133	638	97.75	96.82	93.98	88.61
	CR	1	4,083,488	133	757	97.71	97.09	95.11	91.05
23	Fresh	1	3,796,666	133	708	97.86	97.19	95	90.79
	CR	1	3,492,668	133	651	97.76	96.87	94.74	90.1
24	Fresh	1	3,333,846	133	582	97.76	96.89	94.1	88.13
	CR	1	4,333,332	133	742	97.73	97.09	95.1	90.96
25	Fresh	1	2,746,792	134	449	97.98	96.98	94.07	87.94
	CR	1	3,160,052	133	528	97.82	97.18	94.56	89.24
26	Fresh	1	1,984,042	134	374	97.26	95.88	91.58	82.76
	CR	1	1,671,060	134	322	96.2	94.19	88.32	77.96
27	Fresh	1	1,784,934	134	345	97.21	95.8	90.54	80.85
	CR	1	1,441,268	134	267	98.1	97.44	95.09	89.68
Average			1,917,277	-	-	-	-	-	-
Min			998,341	116	168	71.5	70.49	66.72	58.15
Max			4,333,332	136	757	98.63	97.51	95.24	91.05

CR, complete response; UPN, unique patient number.

Table SIII. Candidate germline variants detected in the present study.

UPN	FAB classification	Gene	Detected variants, amino acid	Detected variants, nucleotide	COSMIC, FATHMM prediction	ClinVar	ExAC
9	M4	<i>MET</i>	T200A	g.116339736A>G	NR	NR	NR
14	M4	<i>TET2</i>	L1385V	g.106190875T>G	NR	NR	NR
18	M3	<i>MTOR</i>	S1777G	g.11193172T>C	NR	NR	NR
19	M5	<i>BCOR</i>	G1056E	g.39930297C>T	NR	NR	NR
20	M4	<i>CHEK2</i>	C420S	g.29091699A>T	NR	NR	NR
24	M2	<i>FBXW7</i>	D90V	g.153332687T>A	NR	NR	NR
25	M2	<i>BRCA2</i>	N2374S	g.32929111A>G	NR	Conflicting result, likely benign and uncertain significance	NR
26	M5	<i>KMT2A</i>	Q3170E	g.118376124C>G	NR	NR	NR

FAB, French-American-British; FATHMM, Functional Analysis through Hidden Markov Models; NR, not reported; UPN, unique patient number.