

Branched clonal evolution: nodal follicular lymphoma and primary diffuse large B-cell lymphoma of the central nervous system

Gilberto I. Barranco,^{1,2} Sara Fernández,³ Raquel Oña,⁴ Julia González-Rincón,⁵ Angel Martínez-Ramírez,⁶ Ana Teijo,¹ Francisca I. Camacho,⁷ Fernando J. Pinedo,⁸ Margarita Sánchez-Beato,⁵ Lucía Pedrosa,⁵ Adolfo de la Fuente,⁴ Mónica Estévez,⁴ Rebeca Iglesias,⁴ Carlos Montalbán⁴ and Juan F. García^{1,3}

¹Hospital General de México, Instituto Nacional de Cancerología, Ciudad de México, Mexico; ²Department of Pathology, MD Anderson Cancer Center Madrid, Centro de Investigación Biomédica en Red de Oncología (CIBERONC-ISCI), Madrid, Spain; ³Translational Research, MD Anderson Cancer Center Madrid, CIBERONC-ISCI, Madrid, Spain; ⁴Hematology, MD Anderson Cancer Center Madrid, Spain; ⁵Lymphoma Research Group, Medical Oncology Department, Instituto de Investigación Sanitaria Puerta de Hierro-Segovia de Arana (IDIPHISA), CIBERONC-ISCI, Madrid, Spain; ⁶Cytogenetics, MD Anderson Cancer Center Madrid, Madrid, Spain; ⁷Department of Pathology, Hospital Universitario de Getafe, Madrid, Spain and ⁸Department of Pathology, Hospital Fundación Alcorcón, Madrid, Spain.

Correspondence: JUAN F. GARCIA.

jfgarcia@mdanderson.es.

doi:10.3324/haematol.2018.214981

Branched clonal evolution: nodal follicular lymphoma and primary diffuse large B-cell lymphoma of the central nervous system

Gilberto I. Barranco^{1,2}; Sara Fernández³; Raquel Oña⁴; Julia González-Rincón⁵; Angel Martínez-Ramírez⁶; Ana Teijo¹; Francisca I. Camacho⁷; Fernando J. Pinedo⁸; Margarita Sánchez-Beato⁵; Lucia Pedrosa⁵; Adolfo de la Fuente⁴; Mónica Estévez⁴; Rebeca Iglesias⁴, Carlos Montalbán⁴; and Juan F. García^{1,3}.

¹ Hospital General de México - Instituto Nacional de Cancerología, Ciudad de México, Mexico. Department of Pathology ², Translational Research ³, Hematology ⁴, and Cytogenetics⁶; MD Anderson Cancer Center Madrid; Centro de Investigación Biomédica en Red de Oncología, CIBERONC-ISCI, Madrid, Spain.

⁵ Lymphoma Research Group, Medical Oncology Department, Instituto de Investigación Sanitaria Puerta de Hierro-Segovia de Arana (IDIPHISA) ; Centro de Investigación Biomédica en Red de Oncología, CIBERONC-ISCI, Madrid, Spain.

⁷ Department of Pathology, Hospital Universitario de Getafe, Madrid, Spain.

⁸ Department of Pathology, Hospital Fundación Alcorcón, Madrid, Spain.

Supplementary Information

Supplementary Table 1

File Type: HaloPlex Design Report

Platform: Ion Torrent PGM/S5

167 Target IDs resolved to 167 targets comprising 2,707 regions.

Region Size: 548.261 kbp

Amplicon Summary

Total Amplicons: 71,850

Total Target Bases Analyzable: 547.27 kbp

Total Sequenceable Design Size: 1.50 Mbp

Target Coverage: 99.82 %

Target Parameters

Databases: RefSeq, Ensembl, CCDS

Region: Coding Exons

Region Extension: 10 bases from 3' end and 10 bases from 5' end.

Allow Synonyms: No

Probe Tiling Parameters

Stringency: Balanced

Optimize for FFPE Samples: Yes

Target and Probe Details

TargetID: The identifier entered in the Targets list.

Interval: The genomic interval of the target.

Regions: The number of regions within this target.

Size: The total size (in base pairs) of the regions.

Database(s): The databases in which this target was found.

TargetID	Interval	Region Size	Databases	HighCoverage
<i>ABCA3</i>	chr16:2326665-2376477	30	5715	100
<i>AFF3</i>	chr2:100167926-100720926	23	4216	100
<i>ALK</i>	chr2:29416080-30143535	29	5443	100
<i>APC</i>	chr5:112043405-112179833	16	9017	99.91
<i>ARID1A</i>	chr1:27022885-27107257	20	7258	99.55
<i>ARID3B</i>	chr15:74836268-74888125	8	1843	100
<i>ATM</i>	chr11:108098342-108236245	62	10411	100
<i>ATRX</i>	chrX:76763819-77041497	35	8179	99.96
<i>B2M</i>	chr15:45003735-45008550	3	420	100
<i>BACH2</i>	chr6:90642117-90718573	4	2606	100
<i>BAX</i>	chr19:49458176-49464903	6	882	100

<i>BCL10</i>	chr1:85733300-85742045	3	762	100
<i>BCL11A</i>	chr2:60679690-60780415	5	2710	100
<i>BCL2</i>	chr18:60795848-60985909	2	793	100
<i>BCL6</i>	chr3:187440236-187451491	8	2281	100
<i>BCL7A</i>	chr12:122459988-122497079	6	816	100
<i>BCOR</i>	chrX:39911352-39937192	14	5548	100
<i>BIRC3</i>	chr11:102195231-102207843	8	1975	100
<i>BRAF</i>	chr7:140434387-140624513	18	2661	100
<i>BRCA2</i>	chr13:32890588-32972917	26	10777	99.97
<i>BTG1</i>	chr12:92537846-92539321	2	556	100
<i>CARD11</i>	chr7:2946262-2998150	24	3945	100
<i>CBL</i>	chr11:119077118-119170501	16	3041	100
<i>CCND1</i>	chr11:69456072-69466060	5	988	100
<i>CCND3</i>	chr6:41903668-41909397	5	979	100
<i>CD58</i>	chr1:117057425-117113604	6	877	100
<i>CD70</i>	chr19:6586021-6591023	3	642	100
<i>CD79B</i>	chr17:62006576-62009631	6	813	100
<i>CDC25A</i>	chr3:48200425-48229447	15	1875	100
<i>CDC42</i>	chr1:22404962-22418020	6	786	100
<i>CDK3</i>	chr17:73997497-74001514	7	1058	100
<i>CDKN2A</i>	chr9:21968218-21994340	5	1012	100
<i>CEACAM8</i>	chr19:43087388-43098990	5	1150	100
<i>CHD2</i>	chr15:93444458-93567945	38	6251	100
<i>CHRM5</i>	chr15:34354909-34356527	1	1619	100
<i>CIITA</i>	chr16:10971178-11017170	19	3773	100
<i>CREBBP</i>	chr16:3777709-3929927	31	7949	99.60
<i>CSMD3</i>	chr8:113236990-114449093	72	12622	100
<i>DDX3X</i>	chrX:41193496-41206982	17	2329	100
<i>DFFB</i>	chr1:3774158-3800315	7	1157	100
<i>DMXL1</i>	chr5:118407255-118582924	43	9944	100
<i>EGFR</i>	chr7:55086961-55273320	30	4489	100
<i>ELN</i>	chr7:73442508-73483040	34	3074	100
<i>EP300</i>	chr22:41488999-41574970	31	7865	100
<i>EPHA1</i>	chr7:143088540-143105908	18	3291	100
<i>EPHA2</i>	chr1:16451700-16482437	17	3271	100
<i>EPHA7</i>	chr6:93953134-94129069	17	3337	100
<i>EPHB2</i>	chr1:23037466-23240073	16	3284	100
<i>ERBB2</i>	chr17:37856482-37884307	27	4308	100
<i>ERBB3</i>	chr12:56474075-56495849	28	4720	100
<i>ERBB4</i>	chr2:212248330-213403264	28	4487	100
<i>ETS1</i>	chr11:128332246-128443035	10	1740	100
<i>EZH2</i>	chr7:148504728-148544400	19	2636	100
<i>FANCD2</i>	chr3:10070332-10142956	43	5351	100
<i>FAS</i>	chr10:90750624-90774217	9	1188	100

<i>FAT2</i>	chr5:150885116-150948502	23	13510	100
<i>FBXW7</i>	chr4:153244023-153332965	13	2822	100
<i>FGFR1</i>	chr8:38271136-38318634	19	3015	100
<i>FOXO1</i>	chr13:41133650-41240359	2	2008	100
<i>GATA2</i>	chr3:128199852-128205884	5	1543	100
<i>GNA13</i>	chr17:63010365-63052721	4	1214	100
<i>GRM5</i>	chr11:88241750-88781050	9	3819	100
<i>HDAC5</i>	chr17:42155734-42194893	26	3892	100
<i>HDAC7</i>	chr12:48177614-48213578	26	3496	100
<i>HIST1H1C</i>	chr6:26056005-26056666	1	662	100
<i>HIST1H1E</i>	chr6:26156609-26157288	1	680	100
<i>HIST1H3B</i>	chr6:26031868-26032298	1	431	100
<i>HOXA11</i>	chr7:27222405-27224773	2	982	100
<i>HRAS</i>	chr11:532626-534332	5	733	100
<i>ID3</i>	chr1:23885441-23885927	2	400	100
<i>IDH1</i>	chr2:209101793-209116285	8	1405	100
<i>IDH2</i>	chr15:90627488-90645632	11	1579	100
<i>IKZF1</i>	chr7:50358648-50468335	7	1700	100
<i>IRF4</i>	chr6:393143-407608	8	1516	100
<i>IRF8</i>	chr16:85936612-85954898	8	1441	100
<i>KDR</i>	chr4:55946098-55991470	30	4671	100
<i>KDSR</i>	chr18:60999005-61034361	10	1199	100
<i>KIT</i>	chr4:55524172-55604733	21	3351	100
<i>KLHL14</i>	chr18:30254610-30350564	8	2047	100
<i>KLHL6</i>	chr3:183209705-183273451	7	2006	100
<i>KMT2C</i>	chr7:151833907-152132881	59	15916	99.77
<i>KMT2D</i>	chr12:49415553-49449117	54	17694	99.03
<i>KRAS</i>	chr12:25362719-25398328	5	787	100
<i>LRP1B</i>	chr2:140990745-142888308	91	15620	99.84
<i>MALT1</i>	chr18:56338866-56415084	17	2815	100
<i>MAPK1</i>	chr22:22123483-22221740	8	1243	100
<i>MAX</i>	chr14:65472912-65569067	8	861	100
<i>MDM2</i>	chr12:69202248-69233639	11	1714	100
<i>MEF2B</i>	chr19:19256596-19261554	8	1267	100
<i>MLH1</i>	chr3:37035029-37092154	19	2651	100
<i>MTOR</i>	chr1:11167532-11319476	57	8790	100
<i>MUC2</i>	chr11:1074892-1104273	49	9434	93.93
<i>MYB</i>	chr6:135502642-135539128	16	2606	99.69
<i>MYC</i>	chr8:128748830-128753214	3	1425	100
<i>MYD88</i>	chr3:38180143-38182787	5	1054	100
<i>NACA</i>	chr12:57106312-57118315	10	2978	98.89
<i>NFKB2</i>	chr10:104155707-104162143	22	3143	100
<i>NFKBIA</i>	chr14:35871209-35873860	6	1074	100
<i>NFKBIE</i>	chr6:44226946-44233510	6	1623	100

<i>NOTCH1</i>	chr9:139390513-139440248	34	8348	100
<i>NOTCH2</i>	chr1:120457919-120612030	34	8149	99.91
<i>NRAS</i>	chr1:115251146-115258791	4	650	100
<i>PARK7</i>	chr1:8022836-8045124	6	690	99.71
<i>PAX2</i>	chr10:102506008-102587450	12	1641	100
<i>PAX5</i>	chr9:36840516-37034038	10	1407	100
<i>PCLO</i>	chr7:82387881-82791918	25	15946	99.99
<i>PCSK2</i>	chr20:17207941-17462725	12	2157	100
<i>PDE1C</i>	chr7:31792988-32338357	22	2892	100
<i>PDGFC</i>	chr4:157684232-157892065	6	1158	100
<i>PDGFRA</i>	chr4:55124926-55161449	22	3710	100
<i>PIK3CA</i>	chr3:178916604-178952162	20	3607	99.64
<i>PIK3CD</i>	chr1:9770504-9787114	22	3575	100
<i>PIK3R1</i>	chr5:67522494-67593439	17	2637	100
<i>PIM1</i>	chr6:37138069-37141877	6	1335	100
<i>PIM2</i>	chrX:48771398-48776121	6	1056	100
<i>PIM3</i>	chr22:50354586-50356785	6	1101	100
<i>PLEKHG5</i>	chr1:6527613-6579581	25	3949	100
<i>POT1</i>	chr7:124464006-124537237	15	2205	100
<i>POU2AF1</i>	chr11:111224976-111249912	5	871	100
<i>POU2F2</i>	chr19:42595694-42636573	14	1724	100
<i>PRDM1</i>	chr6:106534419-106555371	8	2647	100
<i>PRKCQ</i>	chr10:6470159-6557107	17	2461	100
<i>PTEN</i>	chr10:89624217-89725239	9	1392	100
<i>PTGS2</i>	chr1:186643475-186649432	10	2015	98.61
<i>RAF1</i>	chr3:12626003-12660230	16	2267	99.56
<i>RB1</i>	chr13:48878039-49054217	27	3327	100
<i>REL</i>	chr2:61108966-61149680	11	2080	100
<i>RHOA</i>	chr3:49397632-49413032	4	662	100
<i>RUNX1</i>	chr21:36164422-36421206	9	1668	99.94
<i>RUNX3</i>	chr1:25228603-25291072	6	1426	100
<i>SAMHD1</i>	chr20:35521325-35580056	16	2201	100
<i>SERPINB2</i>	chr18:61558669-61570549	7	1388	100
<i>SETD2</i>	chr3:47058573-47205424	21	8115	99.95
<i>SF3B1</i>	chr2:198257017-198299733	26	4455	100
<i>SGK1</i>	chr6:134491396-134638608	17	2275	100
<i>SI</i>	chr3:164697140-164793810	47	6424	100
<i>SIGLEC10</i>	chr19:51914343-51920845	11	2314	100
<i>SLC38A8</i>	chr16:84043379-84075772	10	1508	100
<i>SMARCA2</i>	chr9:2029013-2192749	33	5433	100
<i>SMARCA4</i>	chr19:11094818-11172502	35	5749	100
<i>SOCS1</i>	chr16:11348690-11349345	1	656	100
<i>SOX11</i>	chr2:5832844-5834189	1	1346	100
<i>STAT3</i>	chr17:40467753-40500544	23	2773	100

<i>STAT6</i>	chr12:57490345-57502071	21	2964	100
<i>TGM7</i>	chr15:43568643-43594458	13	2393	100
<i>TLR2</i>	chr4:154624050-154626424	1	2375	100
<i>TLX1</i>	chr10:102891289-102896680	3	1076	100
<i>TMEM30A</i>	chr6:75965808-75994364	7	1226	100
<i>TNFAIP3</i>	chr6:138192355-138202466	8	2533	100
<i>TNFRSF10A</i>	chr8:23049197-23082584	10	1607	100
<i>TNFRSF10B</i>	chr8:22880174-22926417	9	1503	100
<i>TNFRSF11A</i>	chr18:59992576-60052277	10	2051	100
<i>TNFRSF14</i>	chr1:2488094-2494722	8	1012	100
<i>TNFRSF25</i>	chr1:6521484-6526177	10	1485	100
<i>TNFRSF9</i>	chr1:7980885-8000064	7	908	100
<i>TNRC6B</i>	chr22:40521812-40719255	25	6115	100
<i>TP53</i>	chr17:7572917-7579922	12	1503	100
<i>TP63</i>	chr3:189349295-189612301	16	2520	100
<i>TP73</i>	chr1:3598920-3649653	14	2230	100
<i>TRAF3</i>	chr14:103336529-103372131	10	1907	100
<i>TRAF6</i>	chr11:36511378-36523075	6	1689	100
<i>TRPM6</i>	chr9:77339519-77502782	41	6925	100
<i>UNC5D</i>	chr8:35093293-35648091	17	3202	100
<i>WHSC1</i>	chr4:1902372-1980646	22	4610	100
<i>WNT1</i>	chr12:49372424-49375433	4	1193	100
<i>XPO1</i>	chr2:61705945-61761042	24	3696	100
<i>ZMYM3</i>	chrX:70460756-70473115	24	4611	100

Supplementary Table 2

Sample	Position	Genotype	Normal Genotype	Allele Frequency	Gene	Transcript	Amino Acid Change	Variant Effect
FL	chr16:11348972	C/T	C/C	21%	<i>SOCS1</i>	NM_003745.1	p.Gly122Arg	missense
FL	chr16:11349099	G/C	G/G	16%	<i>SOCS1</i>	NM_003745.1	p.Phe79Leu	missense
FL	chr16:11349328	G/C	G/G	7%	<i>SOCS1</i>	NM_003745.1	p.Ala3Gly	missense
FL	chr3:183225946	G/C	G/G	13%	<i>KLHL6</i>	NM_130446	p.Y270X	stopgain
FL	chr6:26157109	C/T	C/C	32%	<i>HIST1H1E</i>	NM_005321.2	p.Ala164Val	missense
FL	chr6:37138554	G/A	G/G	25%	<i>PIM1</i>	NM_002648.3	p.Glu30Lys	missense
FL	chr8:113564889	G/T	G/G	14%	<i>CSMD3</i>	NM_198123.1	p.Pro1432His	missense
FL	chrX:76912081	C/A	C/C	14%	<i>ATRX</i>	NM_000489.4	p.Glu1395Ter	nonsense
PCNSL	chr2:100210093	G/A	G/G	36%	<i>AFF3</i>	NM_001025108.1	p.Ser702Leu	missense
PCNSL	chr3:38182292	G/A	G/G	47%	<i>MYD88</i>	NM_001172567.1	p.Ser251Asn	missense
PCNSL	chr6:41903709	G/A	G/G	20%	<i>CCND3</i>	NM_001760.4	p.Thr283Ile	missense
PCNSL	chr7:2977605	A/G	A/A	33%	<i>CARD11</i>	NM_032415.5	p.Met360Thr	missense
PCNSL	chr7:82785041	T/G	T/T	20%	<i>PCLO</i>	NM_033026.5	p.Ile306Leu	missense
PCNSL	chr8:113564889	G/T	G/G	37%	<i>CSMD3</i>	NM_198123.1	p.Pro1432His	missense
PCNSL	chrX:76939829	T/G	./.	48%	<i>ATRX</i>	NM_000489.4	p.Lys307Gln	missense