

Common Oncogene Mutations and Novel *SND1-BRAF* Transcript Fusion in Lung Adenocarcinoma from Never Smokers

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Supplementary Table S1. Number of detectable mutations for genes examined by OncoCarta™ and Custom Mass Array Panel.

Gene	^a OncoCarta™	Custom Mass Array
<i>EGFR</i>	53	63
<i>BRAF</i>	24	47
<i>MET^b</i>	5	21
<i>PIK3CA</i>	14	17
<i>K-RAS</i>	17	15
<i>ERBB2</i>	8	11
<i>AKT1</i>	7	7
<i>AKT2</i>	2	2
<i>KIT</i>	33	3
<i>JAK</i>	1	1
Total	164	187

^a Only genes shared with Custom Mass Array are shown.

^b Included germ line changes.

Supplementary Table S2. Mutation profiling of NS lung cancer.

Sample	EGFR_Exon	EGFR_1	EGFR_2	BRAF	ERBB2	KRAS	MET ³	PIK3CA	Fusion Gene
Lu-0005					M774_A775insAYVM				SND1-BRAF
Lu-0106	20	V769_D770insASV							
Lu-0124	19	E746_S752A							
Lu-0132	19	L747_S752del							
Lu-0161						G12V			
Lu-0243	21, 20	L858R	S768I						
Lu-0246	20	H773_V774insNPH	S768I						SND1-BRAF
Lu-0253	18	G719A ¹							
Lu-0346	19	E746_S752A							
Lu-0389	19	E746_S752A							
Lu-0426	21	L858R							
Lu-0443	21	L858R							
Lu-0465							N375S		
Lu-0516	19	E746_A750del							
Lu-0587	19	L747_S752del							
Lu-0593				V600E					
Lu-0597									ALK+
Lu-0733	21	L858R							
Lu-0757					G776VC				
Lu-0760	21	L858R							
Lu-0789									ALK+
Lu-0824	19	E746_A750del					T1010I		
Lu-0891	21	L747_S752del							ALK+
Lu-0905	21	L858R							
Lu-0920	19	E746_A750del							
Lu-1014	19	E746_S752A							
Lu-1015				G469V					
Lu-1031					G776VC				
Lu-1033	19	E746_T751del, V ins							
Lu-1068	21	L858R					R988C		
Lu-1096	21	L858R						H1047R	

Lu-1155	19	E746_A750del				
Lu-1222	21	L858R				
Lu-1271	19	E746_A751del			E168D	
Lu-1286	19	E746_A750del				
Lu-1321	19	E746_S752A				
Lu-1333	19	E746_A750del				
Lu-1377	19	H773_V774insPH				
Lu-1437	19	E746_A750del				
Lu-1450				Q61H		
Lu-1479	19	E746_T751del, V ins			T1010I	
Lu-1518	19	E746_A750del				
Lu-1547	21	L858R				
Lu-1566						EZR-ROS
Lu-1606	21	L858R				
Lu-1632	21	L858R				
Lu-1659	19	E746_A750del				
Lu-1660			V600E		T1010I	
Lu-1682				G12D		
Lu-1683	19	E746_A750del			E168D	
Lu-1686				G12A		
Lu-1789					R988C	ALK+
Lu-1790			K601E			
Lu-1806	21	L858R				
Lu-1848				G12D		
Lu-1875	20	S768I ²			E542K	SND1-BRAF
Lu-1908	19	E746_A750del				
Lu-1939	19	E746_A750del			E545K	
Lu-1942	21	L858R				
Lu-1943	19	E746_S752A				
Lu-1995						KIF5B-RET
Lu-2029	19	E746_A750del				
Lu-2040			M774_A775insAYVM			
Lu-2070	20	T790M				

Lu-2172	19	E746_S752A							
Lu-2196	21	L858R				N375S			
Lu-2456	21	L858R							
Lu-2502	19	E746_A750del							
Total	68	49	4	4	5	9	3	9	

¹ OncoCarta™ detected. ² LuCaMSP detected. ³ Germ line changes. ALK* were described based on as previous result (12).

Supplementary Table S3. Fusion gene profiling of NS lung cancer by RNA-Seq.

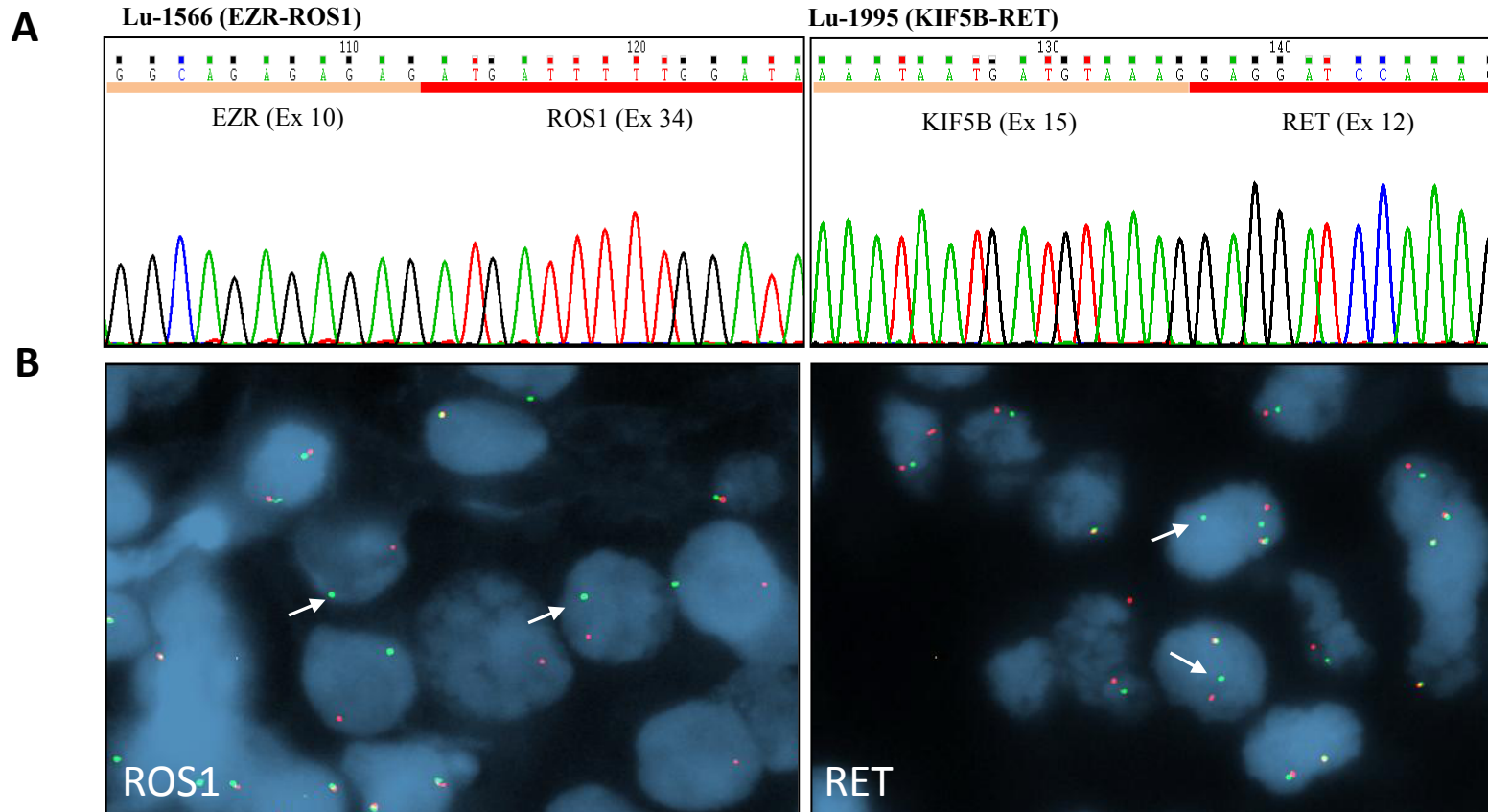
Sample Name	Fusion Gene Direction	Type	Fusion Strand	Encompassing Read Pairs	Total Split Reads	Exon Boundary Fusion	5' Gene Information	3' Gene Information
Lu-0005	HIPK2->TSPAN12	intra-chr	-	51	17	YES	E1:chr7:HIPK2:NM_022740:139477403:139477693:-	E8:chr7:TSPAN12:NM_012338:120427373:120428951:-
	SND1->BRAF	intra-chr	+	29	4	YES	E9:chr7:SND1:NM_014390:127347610:127347701:+	E2:chr7:BRAF:NM_004333:140549910:140550012:-
Lu-0124	CDKL2->TBC1D1	intra-chr	-	22	13	YES	E10:chr4:CDKL2:NM_003948:76521430:76521524:-	E20:chr4:TBC1D1:NM_001253912:38134704:38134878:+
	DNAJC24->ELP4	intra-chr	+	18	9	YES	E2:chr11:DNAJC24:NM_181706:31392262:31392406:+	E4:chr11:ELP4:NM_019040:31616316:31616448:+
	FAM190A->WDFY3	intra-chr	+	6	6	YES	E1:chr4:FAM190A:NM_001145065:91048683:91048982:+	E5:chr4:WDFY3:NM_014991:85771054:85771178:-
	FLJ43663->WDR91	intra-chr	-	41	20	YES	E1:chr7:FLJ43663:NR_015431:130792478:130793562:-	E7:chr7:WDR91:NM_014149:134882744:134882903:-
	LOC100131691->OTC	inter-chr	+	20	20	YES	E1:chr19:LOC100131691:NR_027334:59070552:59070776: +	E5:chrX:OTC:NM_000531:38260527:38260681:+
	LOC730102->SEC16B	intra-chr	-	5	1	YES	E7:chr1:LOC730102:NR_037167:177995289:177995390:-	E2:chr1:SEC16B:NM_033127:177936817:177937174:-
	LRRC28->TPST1	inter-chr	+	9	3	YES	E3:chr15:LRRC28:NM_144598:99816780:99816821:+	E3:chr7:TPST1:NM_003596:65751497:65751696:+
	SMARCC2->CALCOCO2	inter-chr	-	8	4	YES	E7:chr12:SMARCC2:NM_139067:56577644:56577714:-	E11:chr17:CALCOCO2:NM_005831:46937675:46937811:+
	TESC->FBXO21	intra-chr	-	8	5	YES	E1:chr12:TESC:NM_017899:117537029:117537251:-	E5:chr12:FBXO21:NM_033624:117612455:117612602:-
	ZNF516->SYTL5	inter-chr	-	6	3	YES	E2:chr18:ZNF516:NM_014643:74174983:74175097:-	E2:chrX:SYTL5:NM_138780:37892786:37893261:+
Lu-0155	NDE1->C16orf45	intra-chr	+	57	30	YES	E5:chr16:NDE1:NM_001143979:15771657:15771806:+	E2:chr16:C16orf45:NM_033201:15609161:15609285:+
	TFG->GPR128	intra-chr	+	83	25	YES	E3:chr3:TFG:NM_001007565:100438818:100438902:+	E2:chr3:GPR128:NM_032787:100348441:100348555:+
Lu-0158	LOC730102->SEC16B	intra-chr	-	6	2	YES	E7:chr1:LOC730102:NR_037167:177995289:177995390:-	E2:chr1:SEC16B:NM_033127:177936817:177937174:-
Lu-0465	CNOT2->TSPAN8	intra-chr	+	17	7	YES	E2:chr12:CNOT2:NM_014515:70671911:70672054:+	E2:chr12:TSPAN8:NM_004616:71551398:71551567:-
	FRS2->MDM1	intra-chr	+	25	5	YES	E1:chr12:FRS2:NM_006654:69864128:69864310:+	E2:chr12:MDM1:NM_017440:68724886:68725001:-
	SSPN->TSPAN8	intra-chr	+	54	16	YES	E1:chr12:SSPN:NM_001135823:26348268:26348464:+	E2:chr12:TSPAN8:NM_004616:71551398:71551567:-
Lu-0597	LOC285629->ATP10B	intra-chr	-	12	2	YES	E2:chr5:LOC285629:NR_027111:160362996:160363116:-	E2:chr5:ATP10B:NM_025153:160212565:160212810:-
Lu-0847	TSPAN9->NCAPD2	intra-chr	+	23	8	YES	E2:chr12:TSPAN9:NM_001168320:3310342:3310422:+	E18:chr12:NCAPD2:NM_014865:6634748:6634882:+
Lu-0891	ATF7IP2->NUBP1	intra-chr	+	12	8	YES	E1:chr16:ATF7IP2:NM_001256160:10479911:10479979:+	E10:chr16:NUBP1:NM_002484:10861805:10861889:+
	CDH3->TEPP	intra-chr	+	7	5	YES	E2:chr16:CDH3:NM_001793:68679538:68679653:+	E3:chr16:TEPP:NM_199046:58018206:58018268:+
	CYP4B1->CYP4X1	intra-chr	+	12	9	YES	E8:chr1:CYP4B1:NM_001099772:47280745:47280936:+	E2:chr1:CYP4X1:NM_178033:47495661:47495803:+
	EML4->BIRC6	intra-chr	+	37	9	YES	E5:chr2:EML4:NM_001145076:42491845:42491871:+	E69:chr2:BIRC6:NM_016252:32822817:32823035:+
	FBXO11->ATAD2B	intra-chr	-	14	2	YES	E4:chr2:FBXO11:NM_001190274:48065997:48066142:-	E20:chr2:ATAD2B:NM_001242338:24011381:24011517:-
Lu-0918	KRBOX1->FAM198A	intra-chr	+	6	1	YES	E4:chr3:KRBOX1:NM_001205272:42983449:42983563:+	E3:chr3:FAM198A:NM_001129908:43095012:43095135:+
	LINC00189->BACH1	intra-chr	+	52	7	YES	E2:chr21:LINC00189:NR_027072:30566436:30566581:+	E2:chr21:BACH1:NM_001186:30693541:30693835:+
	TAX1BP1->UTP6	inter-chr	+	80	47	YES	E5:chr7:TAX1BP1:NM_001206901:27809294:27809453:+	E3:chr17:UTP6:NM_018428:30221988:30222030:-
Lu-0920	NPC2->SYNDIG1L	intra-chr	-	13	1	YES	E4:chr14:NPC2:NM_006432:74947404:74947482:-	E2:chr14:SYNDIG1L:NM_001105579:74876030:74876504:-
	SHFM1->LOC100506136	intra-chr	-	6	6	YES	E2:chr7:SHFM1:NM_006304:96324109:96324203:-	E5:chr7:LOC100506136:NR_038948:96250968:96251955

Lu-1208	CHD9->RLTPR	intra-chr	+	18	11	YES	E19:chr16:CHD9:NM_025134:53289511:53289691:+	E33:chr16:RLTPR:NM_001013838:67689933:67689970:+
	FAM189A2->PARD6G	inter-chr	+	8	7	YES	E2:chr9:FAM189A2:NM_001127608:71951128:71951185: +	E2:chr18:PARD6G:NM_032510:77960592:77960815:-
	RASEF->HSD17B3	intra-chr	-	19	12	YES	E5:chr9:RASEF:NM_152573:85627348:85627426:-	E3:chr9:HSD17B3:NM_000197:99017149:99017225:-
	TBC1D14->STX18	intra-chr	+	20	19	YES	E2:chr4:TBC1D14:NM_001113361:6925099:6925838:+	E2:chr4:STX18:NM_016930:4473365:4473433:-
Lu-1431	CCT2->BRD9	inter-chr	+	41	27	YES	E10:chr12:CCT2:NM_006431:69987289:69987393:+	E10:chr5:BRD9:NR_027633:879908:880004:-
	MPP6->TOMM7	intra-chr	+	7	2	YES	E6:chr7:MPP6:NM_016447:24690103:24690331:+	E2:chr7:TOMM7:NM_019059:22857618:22857667:-
	NCOA2->ADAMTS2	inter-chr	-	11	2	YES	E1:chr8:NCOA2:NM_006540:71315934:71316020:-:-	E4:chr5:ADAMTS2:NM_014244:178634513:178634716
Lu-1566	TPPP->TRIP13	intra-chr	-	6	4	YES	E1:chr5:TPPP:NM_007030:693392:693510:-	E2:chr5:TRIP13:NM_001166260:894901:895067:+
	C12orf23->SLC35F1	inter-chr	+	16	2	YES	E3:chr12:C12orf23:NM_152261:107360888:107360958:+	E2:chr6:SLC35F1:NM_001029858:118475607:118475783:+
	EZR->ROS1	intra-chr	-	108	153	YES	E10:chr6:EZR:NM_001111077:159191795:159191926:-	E34:chr6:ROS1:NM_002944:117645494:117645578:-
Lu-1825	ROS1->HIPK2	inter-chr	-	51	4	YES	E28:chr6:ROS1:NM_002944:117663562:117663707:-	E5:chr7:HIPK2:NM_022740:139313698:139313785:-
	CLPTM1L->NSMCE2	inter-chr	-	17	18	YES	E2:chr5:CLPTM1L:NM_030782:1344465:1344566:-	E6:chr8:NSMCE2:NM_173685:126369460:126369561:+
Lu-1875	RAP1B->LYZ	intra-chr	+	6	3	YES	E2:chr12:RAP1B:NM_015646:69042478:69042561:+	E2:chr12:LYZ:NM_000239:69743887:69744052:+
	C14orf43->ACER3	inter-chr	-	6	8	YES	E3:chr14:C14orf43:NM_001043318:74203700:74204000:-	E2:chr11:ACER3:NM_018367:76637600:76637711:+
	CRTC3->ZNF592	intra-chr	+	9	2	YES	E1:chr15:CRTC3:NM_001042574:91073197:91073435:+	E2:chr15:ZNF592:NM_014630:85307937:85308046:+
Lu-1908	CYP4B1->CYP4X1	intra-chr	+	7	1	YES	E8:chr1:CYP4B1:NM_001099772:47280745:47280936:+	E2:chr1:CYP4X1:NM_178033:47495661:47495803:+
	KDM2A->PPP6R3	intra-chr	+	32	24	YES	E2:chr11:KDM2A:NM_012308:66888704:66888829:+	E5:chr11:PPP6R3:NM_018312:68312305:68312492:+
	LOC100506393->SARNP	intra-chr	+	31	18	YES	E2:chr12:LOC100506393:NR_040098:20172565:20172630 :+	E10:chr12:SARNP:NR_026723:56154334:56154424:-
	PPP6R3->SYVN1	intra-chr	+	22	13	YES	E3:chr11:PPP6R3:NM_018312:68286968:68287119:+	E10:chr11:SYVN1:NM_172230:64898390:64898507:-
	TTC3->FAM69A	inter-chr	+	11	3	YES	E31:chr21:TTC3:NM_001001894:38534291:38534365:+	E2:chr1:FAM69A:NM_001252273:93341852:93341987:-
Lu-1908	LOC730102->SEC16B	intra-chr	-	5	2	YES	E7:chr1:LOC730102:NR_037167:177995289:177995390:-	E2:chr1:SEC16B:NM_033127:177936817:177937174:-
	NPC2->SYNDIG1L	intra-chr	-	11	3	YES	E4:chr14:NPC2:NM_006432:74947404:74947482:-	E2:chr14:SYNDIG1L:NM_001105579:74876030:74876504:-
	SGK196->HGSNAT	intra-chr	+	22	4	YES	E4:chr8:SGK196:NM_032237:42958670:42958973:+	E6:chr8:HGSNAT:NM_152419:43024315:43024385:+
Lu-1939	MYO9B->FZR1	intra-chr	+	5	6	YES	E35:chr19:MYO9B:NM_001130065:17317921:17318053:+	E2:chr19:FZR1:NM_016263:3522953:3523056:+
	PARP6->MYOM1	inter-chr	-	429	171	YES	E1:chr15:PARP6:NM_020214:72563363:72563628:-	E34:chr18:MYOM1:NM_003803:3079176:3079340:-
	SH2D3A->ZNF562	intra-chr	-	5	5	YES	E1:chr19:SH2D3A:NM_005490:6767397:6767523:-	E2:chr19:ZNF562:NM_017656:9771395:9771550:-
	TRIP12->AP1S3	intra-chr	-	22	17	YES	E33:chr2:TRIP12:NM_004238:230650472:230650571	E2:chr2:AP1S3:NM_001039569:224642407:224642586:-:-
Lu-1942	KPNB1->AP2B1	intra-chr	+	7	16	YES	E12:chr17:KPNB1:NM_002265:45748067:45748198:+	E17:chr17:AP2B1:NM_001282:34009713:34009843:+
	LRIG3->MSRB3	intra-chr	-	15	2	YES	E15:chr12:LRIG3:NM_153377:59271181:59271634:-	E5:chr12:MSRB3:NM_198080:65847507:65847605:+
	LRIG3->TMEM97	inter-chr	-	51	23	YES	E3:chr12:LRIG3:NM_153377:59307762:59307837:-	E2:chr17:TMEM97:NM_014573:26652528:26652673:+
	MAML2->SESN3	intra-chr	-	7	4	YES	E1:chr11:MAML2:NM_032427:96074546:96076344:-	E2:chr11:SESN3:NM_144665:94926620:94926686:-
	MGLL->SLC41A3	intra-chr	-	45	3	YES	E3:chr3:MGLL:NM_007283:127500631:127500738:-	E2:chr3:SLC41A3:NM_017836:125786789:125787089:-
MIB1->ZNF714	inter-chr	+	8	7	YES	E4:chr18:MIB1:NM_020774:19353584:19353689:+	E3:chr19:ZNF714:NM_182515:21280990:21281117:+	

	MPRIP->RPH3AL	intra-chr	+	14	4	YES	E1:chr17:MPRIP:NM_201274:16946073:16946285:+	E7:chr17:RPH3AL:NM_006987:96901:97076:-
	NUP107->PRIM2	inter-chr	+	8	7	YES	E27:chr12:NUP107:NM_020401:69135592:69135760:+	E8:chr6:PRIM2:NM_000947:57372287:57372355:+
	SHFM1->LOC100506136	intra-chr	-	10	3	YES	E2:chr7:SHFM1:NM_006304:96324109:96324203:-	E4:chr7:LOC100506136:NR_038948:96275035:96275248
	TPX2->BCL2L1	intra-chr	+	13	5	YES	E1:chr20:TPX2:NM_012112:30326903:30327424:+	E3:chr20:BCL2L1:NM_138578:30252260:30253889:-
	USP15->MLIP	inter-chr	+	14	5	YES	E4:chr12:USP15:NM_006313:62708570:62708697:+	E2:chr6:MLIP:NM_138569:53986244:53986400:+
	ZMIZ1->KIAA1274	intra-chr	+	5	9	YES	E4:chr10:ZMIZ1:NM_020338:80921809:80921890:+	E2:chr10:KIAA1274:NM_014431:72285678:72285892:+
Lu-1995	EFCAB2->SMYD3	intra-chr	+	35	17	YES	E1:chr1:EFCAB2:NR_026586:245133283:245133745:+	E9:chr1:SMYD3:NM_022743:246027100:246027188:-
	EPSTI1->ENOX1	intra-chr	-	52	13	YES	E8:chr13:EPSTI1:NM_033255:43491676:43491760:-	E15:chr13:ENOX1:NM_017993:43810771:43810874:-
	KIF5B->RET	intra-chr	-	144	82	YES	E15:chr10:KIF5B:NM_004521:32317355:32317499:-	E12:chr10:RET:NM_020975:43612031:43612179:+
	KRBOX1->FAM198A	intra-chr	+	9	1	YES	E4:chr3:KRBOX1:NM_001205272:42983449:42983563:+	E2:chr3:FAM198A:NM_001129908:43073758:43075045:+
	LOC285629->ATP10B	intra-chr	-	9	3	YES	E2:chr5:LOC285629:NR_027111:160362996:160363116:-	E2:chr5:ATP10B:NM_025153:160212565:160212810:-
	MPRIP->SPNS3	intra-chr	+	201	55	YES	E3:chr17:MPRIP:NM_201274:16981324:16981390:+	E9:chr17:SPNS3:NM_182538:4381866:4381932:+
	NCOR1->DRG2	intra-chr	-	21	4	YES	E1:chr17:NCOR1:NM_006311:16118675:16118874:-	E3:chr17:DRG2:NM_001388:18001583:18001673:+
Lu-2045	ACSS3->MGAT4C	intra-chr	+	16	5	YES	E8:chr12:ACSS3:NM_024560:81568566:81568718:+	E3:chr12:MGAT4C:NM_013244:86727842:86727905:-
	CTF1->CPPED1	intra-chr	+	6	3	YES	E2:chr16:CTF1:NM_001330:30910735:30910854	E2:chr16:CPPED1:NM_001099455:12875041:12875260:-
	GMEB2->TERT	inter-chr	-	10	3	YES	E2:chr20:GMEB2:NM_012384:62250619:62250807:-	E4:chr5:TERT:NM_198253:1280272:1280453:-
	KRBOX1->FAM198A	intra-chr	+	5	1	YES	E4:chr3:KRBOX1:NM_001205272:42983449:42983563:+	E3:chr3:FAM198A:NM_001129908:43095012:43095135:+
	MEF2D->GOLPH3L	intra-chr	-	21	7	YES	E1:chr1:MEF2D:NM_005920:156470277:156470529	E3:chr1:GOLPH3L:NM_018178:150636107:150636239:-
	TPPP->BRD9	intra-chr	-	8	12	YES	E1:chr5:TPPP:NM_007030:693392:693310:-	E10:chr5:BRD9:NR_027633:879908:880004:-

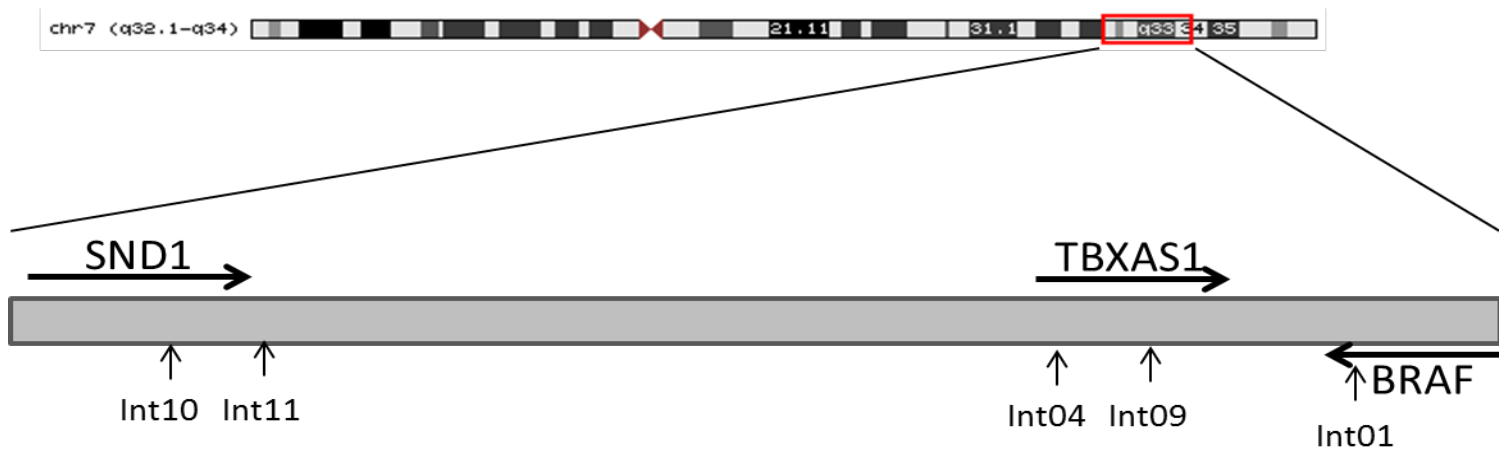
Supplementary Table S4. Sequences of PCR primers and probes for fusion transcripts detection.

Fusion gene	Forward	Reverse	TaqMan Probe
<i>EZR-ROS1</i>	AGCTCAGCCAACTCTTTGTCT	AGAAAAGGAGAGAAACCGTGGA	
<i>EML4-BIRC6</i>	CATCACCAGCTGAAAAGTCACA	GAGGATGAAGACAGAGGCAGT	
<i>KIF5B-RET</i>	GCGAGTATAGATGCTGAGCTTC	TGCTCTGCCTTTCAGATGGAA	
<i>SND1-BRAF</i>	GTGTGGACTGGTCGATTGCA	GGTGTATTCTTCATAGGCCTCCA	
<i>SND1-BRAF</i>	GCAGGCTGAGAATATGGAGAG	GGCCTCTATATGTTCTGTGTC	ACAAGCAGTTTGTTGCCAAGGTGTGG

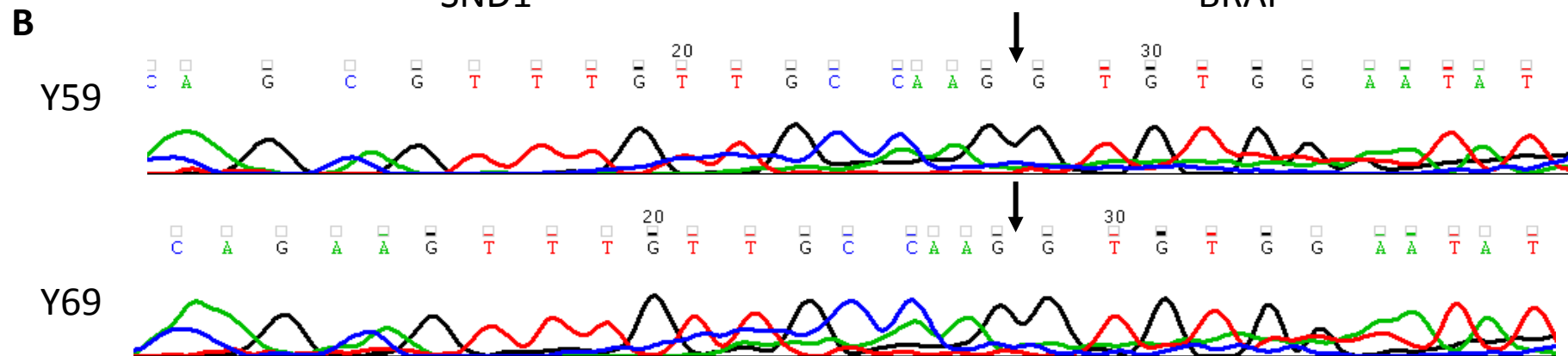
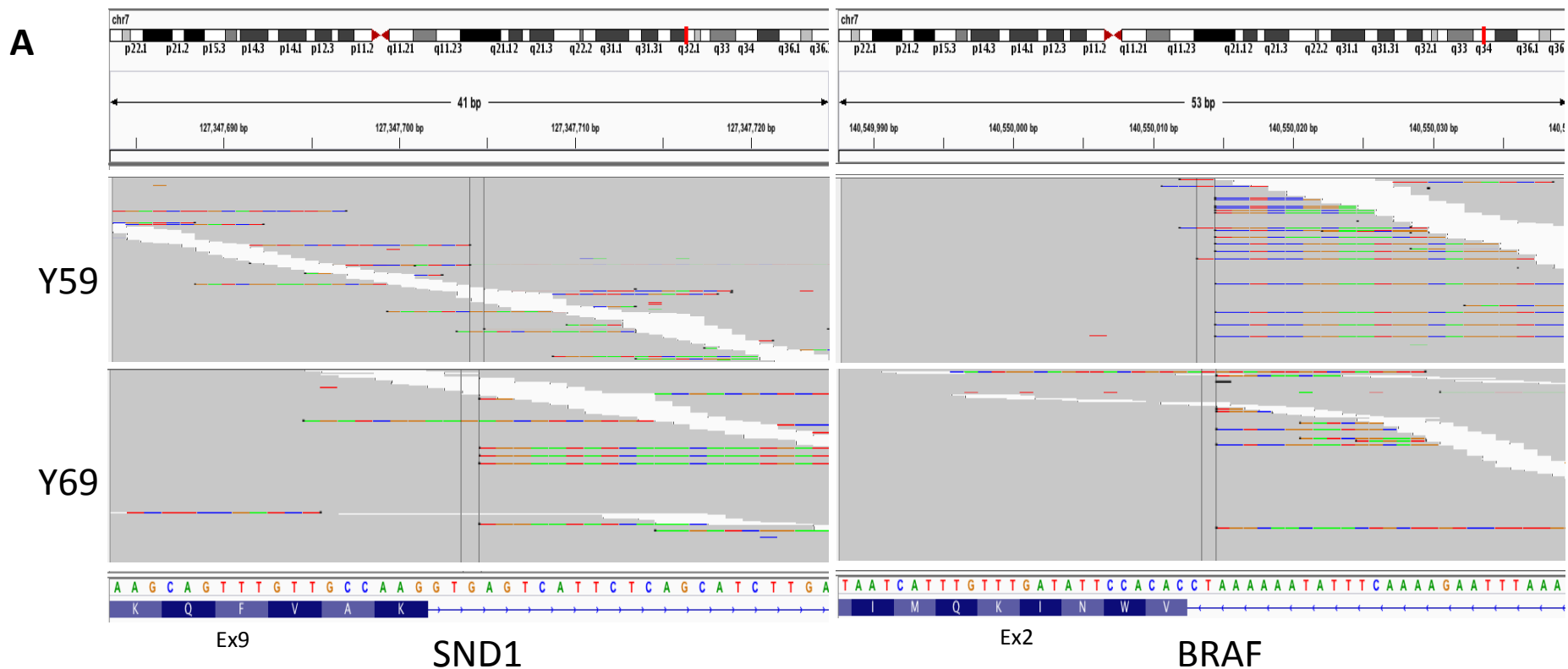


Supplementary Figure S1. Confirmation of fusion transcripts. A. Sanger sequencing traces of fusions involving *EZR* (orange)-*ROS1*(red) and *KIF5B*(orange)-*RET*(red) genes in the samples indicated. B. FISH validation of fusions using break-apart probes. Arrows indicate the break-apart probe adjacent to the *ROS1* or *RET* genes, respectively. Magnification x1000.

Chromosome	5' Gene	Position	Location	Strand	3' Gene	Position	Location	Strand	Type	Genomic Fusion Gene
chr7	SND1	127361983	Intron10	-	BRAF	140572145	Intron 01	-	fusion	SND1-BRAF
chr7	SND1	127453469	Intron11	-	TBXAS1	139517148	Intron 04	-	fusion	SND1-TBXAS1
chr7	SND1	127457072	Intron11	-	TBXAS1	139511559	Intron 04	-	fusion	SND1-TBXAS1
chr7	SND1	127457102	Intron11	-	BRAF	140572118	Intron 01	-	fusion	SND1-BRAF
chr7	TBXAS1	139705930	Intron09	+	BRAF	140582144	Intron 01	+	fusion	TBXAS1-BRAF



Supplementary Figure S2. Genomic rearrangements of the fusion region in Lu-5 based on whole genome sequencing. Int = intron.



Supplementary Figure S3. A, The IGV screen shot of genomic rearrangements for the fusion region in Y59 and Y69 based on whole genome capture sequencing. The vertical lines indicated the break points. Perfectly matched reads are shown in gray. Colors represent mismatched bases soft-clipped around the break points. Both samples were broken and fused at intron 9 of *SND1* and intron 1 of *BRAF*. **B**, Sanger sequencing using cDNA from Y59 and Y69. *SND1*-*BRAF* fusion transcript was confirmed by qRT-PCR and sequenced at the fusion junction spanning exon 9 of *SND1* and exon 2 of *BRAF*. Arrow heads, fusion point.