

## Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1: Genomic Coverage of Next-Generation Sequencing Platform

eTable 1: Genomic Coverage of Next-Generation Sequencing Platforms	
OMNISEQ ADVANCE	FOUNDATIONONE HEME
Single Nucleotide Variants (SNVs), Insertions, Deletions, and Indels	Full Coding Sequence
Hotspot	<i>ABL1, ACTB, AKT1, AKT2, AKT3, ALK, AMER1, (FAM123B, or, WTX),</i>
<i>ABL1, AKT1, ALK, AR, ARAF, BRAF, BTK, CBL, CDK4, CHEK2, CSF1R, CTNNB1, DDR2, DNMT3A, EGFR, ERBB2, ERBB3, ERBB4, ESR1, EZH2, FGFR1, FGFR2, FGFR3, FLT3, FOXL2, GATA2, GNA11, GNAQ, GNAS, HNF1A, HRAS, IDH1, IDH2, IFITM1, IFITM3, JAK1, JAK2, JAK3, KDR, KIT, KNSTRN, KRAS, MAGOH, MAP2K1, MAP2K2, MAPK1, MAX, MED12, MET, MLH1, MPL, MTOR, MYD88, NFE2L2,</i>	<i>APC, APH1A, AR, ARAF, ARFRP1, ARHGAP26, (GRAF), ARID1A, ARID2, ASMTL, ASXL1, ATM, ATR, ATRX, AURKA, AURKB, AXIN1, AXL, B2M, BAP1, BARD1, BCL10, BCL11B, BCL2, BCL2L2, BCL6, BCL7A, BCOR, BCORL1, BIRC3, BLM, BRAF, BRCA1, BRCA2, BRD4, BRIP1, (BACH1), BRSK1, BTG2, BTK, BTLA, C11, orf30, (EMSY), CAD, CALR, CARD11, CBFEB, CBL, CCND1, CCND2, CCND3, CCNE1, CCT6B, CD22, CD274, (PDL1), CD36, CD58, CD70, CD79A, CD79B, CDC73, CDH1, CDK12, CDK4, CDK6, CDK8, CDKN1B, CDKN2A, CDKN2B, CDKN2C, CEBPA, CHD2, CHEK1, CHEK2, CIC, CIITA, CKS1B, CPS1, CREBBP, CRKL, CRLF2, CSF1R,</i>

<p><i>NPM1, NRAS, PAX5, PDGFRA, PIK3CA, PPP2R1A, PTPN11, RAC1, RAF1, RET, RHEB, RHOA, SF3B1, SMO, SPOP, SRC, STAT3, U2AF1, XPO1</i></p>	<p><i>CSF3R, CTCF, CTNNA1, CTNNB1, CUX1, CXCR4, DAXX, DDR2, DDX3X, DNMT2, DNMT3A, DOT1L, DTX1, DUSP2, DUSP9, EBF1, ECT2L, EED, EGFR, ELP2, EP300, EPHA3, EPHA5, EPHA7, EPHB1, ERBB2, ERBB3, ERBB4, ERG, ESR1, ETS1, ETV6, EXOSC6, EZH2,</i></p>
<p>Full Coding Sequence</p>	<p><i>FAF1, FAM46C, FANCA, FANCC, FANCD2, FANCE, FANCF, FANCG,</i></p>
<p><i>APC, ATM, BAP1, BRCA1, BRCA2, CDH1, CDKN2A, FBXW7, GATA3, MSH2, NF1, NF2, NOTCH1, PIK3R1, PTCH1, PTEN, RB1, SMAD4, SMARCB1, STK11, TET2, TP53, TSC1, TSC2, VHL, WT1</i></p>	<p><i>FANCL, FAS, (TFRSF6), FBXO11, FBXO31, FBXW7, FGF10, FGF14, FGF19, FGF23, FGF3, FGF4, FGF6, FGFR1, FGFR2, FGFR3, FGFR4, FHIT, FLCN, FLT1, FLT3, FLT4, FLYWCH1, FOXL2, FOXO1, FOXO3, FOXP1, FRS2, GADD45B, GATA1, GATA2, GATA3, GID4, (C17orf39), GNA11, GNA12, GNA13, GNAQ, GNAS, GPR124, GRIN2A, GSK3B, GTSE1, HDAC1, HDAC4, HDAC7, HGF, HIST1H1C, HIST1H1D, HIST1H1E, HIST1H2AC, HIST1H2AG, HIST1H2AL, HIST1H2AM, HIST1H2BC, HIST1H2BJ, HIST1H2BK, HIST1H2BO, HIST1H3B, HNF1A, HRAS, HSP90AA1, ICK, ID3, IDH1, IDH2, IGF1R, KBKE, IKZF1, IKZF2, IKZF3, IL7R, INHBA, INPP4B, INPP5D, (SHIP), IRF1, IRF4, IRF8, IRS2, JAK1, JAK2, JAK3, JARID2, JUN, KAT6A,</i></p>

*(MYST3), KDM2B, KDM4C, KDM5A, KDM5C, KDM6A, KDR, KEAP1, KIT, KLHL6, KMT2A, (MLL), KMT2C, (MLL3), KMT2D, (MLL2), KRAS, LEF1, LRP1B, LRRK2, MAF, MAFB, MAGED1, MALT1, MAP2K1, MAP2K2, MAP2K4, MAP3K1, MAP3K14, MAP3K6, MAP3K7, MAPK1, MCL1, MDM2, MDM4, MED12, MEF2B, MEF2C, MEN1, MET, MIB1, MITF, MKI67, MLH1, MPL, MRE11A, MSH2, MSH3, MSH6, MTOR, MUTYH, MYC, MYCL, (MYCL1), MYCN, MYD88, MYO18A, NCOR2, NCSTN, NF1, NF2, NFE2L2, NFKBIA, NKX2-1, NOD1, NOTCH1, NOTCH2, NPM1, NRAS, NT5C2, NTRK1, NTRK2, NTRK3, NUP93, NUP98, P2RY8, PAG1, PAK3, PALB2, PASK, PAX5, PBRM1, PC, PCBP1, PCLO, PDCD1, PDCD11, PDCD1LG2, (PDL2), PDGFRA, PDGFRB, PDK1, PHF6, PIK3CA, PIK3CG, PIK3R1, PIK3R2, PIM1, PLCG2, POT1, PPP2R1A, PRDM1, PRKAR1A, PRKDC, PRSS8, PTCH1, PTEN, PTPN11, PTPN2, PTPN6, (SHP-1), PTPRO, RAD21, RAD50, RAD51, RAF1, RARA, RASGEF1A, RB1, RELN, RET, RHOA, RICTOR, RNF43, ROS1, RPTOR, RUNX1, S1PR2, SDHA,SDHB,*

	<p><i>SDHC, SDHD, SERP2, SETBP1, SETD2, SF3B1, SGK1, SMAD2, SMAD4, SMARCA1, SMARCA4, SMARCB1, SMC1A, SMC3, SMO, SOCS1, SOCS2, SOCS3, SOX10, SOX2, SPEN, SPOP, SRC, SRSF2, STAG2, STAT3, STAT4, STAT5A, STAT5B, STAT6, STK11, SUFU, SUZ12, TAF1, TBL1XR1, TCF3, (E2A), TCL1A, (TCL1), TET2, TGFBR2, TLL2, TMEM30A, TMSB4XP8, (TMSL3), TNFAIP3, TNFRSF11A, TNFRSF14, TNFRSF17, TOP1, TP53, TP63, TRAF2, TRAF3, TRAF5, TSC1, TSC2, TSHR, TUSC3, TYK2, U2AF1, U2AF2, VHL, WDR90, WHSC1, (MMSET, or, NSD2), WISP3, WT1, XBP1, XPO1, YY1AP1, ZMYM3, ZNF217, ZNF24, (ZSCAN3), ZNF703, ZRSR</i></p>
Copy Number Gain	DNA Rearrangements
<p><i>ACVRL1, AKT1, APEX1, AR, ATP11B, BCL2L1, BCL9, BIRC2, BIRC3, CCND1, CCNE1, CD274, CD44, CDK4, CDK6, CSNK2A1, DCUN1D1, EGFR, ERBB2,</i></p>	<p><i>ALK, BCL2, BCL6, BCR, BRAF, CCND1, CRLF2, EGFR, EPOR, ETV1, ETV4, ETV5, ETV6, EWSR1, FGFR2, IGH, IGK, IGL, JAK1, JAK2, KMT2A, (MLL), MYC, NTRK1, PDGFRA, PDGFRB, RAF1, RARA, RET, ROS1, TMPRSS2, TRG</i></p>



*HOXA9, HOXC11, HOXC13, HOXD11, HOXD13, HSP90AA1, HSP90AB1, IGH, IGK, IGL, IKZF1, IL21R, IL3, IRF4, ITK, JAK1, JAK2, JAK3, JAZF1, KAT6A, (MYST3), KDSR, KIF5B, KMT2A, (MLL), LASP1, LCP1, LMO1, LMO2, LPP, LYL1, MAF, MAFB, MALT1, MDS2, MECOM, MKL1, MLF1, MLLT1, (ENL), MLLT10, (AF10), MLLT3, MLLT4, (AF6), MLLT6, MN1, MNX1, MSI2, MSN, MUC1, MYB, MYC, MYH11, MYH9, NACA, NBEAP1, (BCL8), NCOA2, NDRG1, NF1, NF2, NFKB2, NIN, NOTCH1, NPM1, NR4A3, NSD1, NTRK1, NTRK2, NTRK3, NUMA1, NUP214, NUP98, NUTM2A, OMD, P2RY8, PAFAH1B2, PAX3, PAX5, PAX7, PBX1, PCM1, PCSK7, PDCD1LG2, (PDL2), PDE4DIP, PDGFB, PDGFRA, PDGFRB, PER1, PHF1, PICALM, PIM1, PLAG1, PML, POU2AF1, PPP1CB, PRDM1, PRDM16, PRRX1, PSIP1, PTCH1, PTK7, RABEP1, RAF1, RALGDS, RAP1GDS1, RARA, RBM15, RET, RHOH, RNF213, ROS1, RPL22, RPN1, RUNX1, RUNX1T1, (ETO), RUNX2, SEC31A, SEPT5, SEPT6, SEPT9, SET, SH3GL1, SLC1A2, SNX29, (RUNDC2A), SRSF3, SS18,*

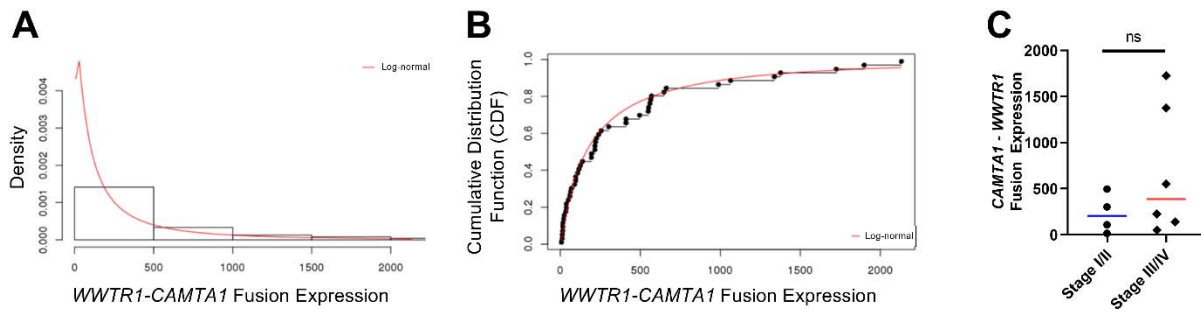
	<p><i>SSX1, SSX2, SSX4, STAT6, STL, SYK, TAF15, TAL1, TAL2, TBL1XR1, TCF3, (E2A), TCL1A, (TCL1), TEC, TET1, TFE3, TFG, TFPT, TFRC, TLX1, TLX3, TMPRSS2, TNFRSF11A, TOP1, TP63, TPM3, TPM4, TRIM24, TRIP11, TTL, TYK2, USP6, WHSC1, (MMSET, or, NSD2), WHSC1L1, YPEL5, ZBTB16, ZMYM2, ZNF384, ZNF521</i></p>
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eTable 2: Description of Pathways

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Cell Cycle Regulation	DNA Damage Repair	Epigenetics		Growth Signaling		Other
<i>CCND3</i>	<i>ABL1</i>	<i>APC</i>	<i>MED12</i>	<i>ADGRA2</i>	<i>INPP5D</i>	<i>BCOR</i>
<i>CDKN2A</i>	<i>BAP1</i>	<i>ATRX</i>	<i>PCBP1</i>	<i>ALK</i>	<i>LRRK2</i>	<i>CASP8</i>
<i>CDKN2B</i>	<i>BARD1</i>	<i>AXIN1</i>	<i>RARA</i>	<i>AR</i>	<i>MAP2K2</i>	<i>CIITA</i>
<i>DKC1</i>	<i>BRCA1</i>	<i>BCORL1</i>	<i>RPS19</i>	<i>ASXL1</i>	<i>MAP3K1</i>	<i>CRBN</i>
<i>MEF2B</i>	<i>BRCA2</i>	<i>EED</i>	<i>RUNX1</i>	<i>CCT6B</i>	<i>MAP3K13</i>	<i>ECT2L</i>
<i>MKI67</i>	<i>CHEK2</i>	<i>HIST1H1E</i>	<i>SETBP1</i>	<i>CD36</i>	<i>MYO18A</i>	<i>FAS</i>
<i>NUP98</i>	<i>FANCA</i>	<i>JARID2</i>	<i>SMARCA4</i>	<i>CPS1</i>	<i>NCOR1</i>	<i>FAT3</i>
<i>POT1</i>	<i>FANCL</i>	<i>KDM4C</i>	<i>TAF1</i>	<i>CSF1R</i>	<i>NCOR2</i>	<i>FBXO31</i>
<i>RB1</i>	<i>MLH1</i>	<i>KDM5C</i>	<i>TCF3</i>	<i>DDX3X</i>	<i>NOTCH1</i>	<i>FBXW7</i>
<i>RELN</i>	<i>MSH2</i>	<i>KMT2A</i>	<i>TERT</i>	<i>DTX1</i>	<i>NOTCH2</i>	<i>GATA3</i>
<i>SGK1</i>	<i>MSH3</i>	<i>KMT2C</i>	<i>TET2</i>	<i>EPHA3</i>	<i>NOTCH3</i>	<i>IKZF3</i>
<i>SMC1A</i>	<i>MUTYH</i>	<i>KMT2D</i>	<i>TOP1</i>	<i>EPHB1</i>	<i>NTRK1</i>	<i>KEAP1</i>
	<i>PMS2</i>	<i>LRP1B</i>	<i>YY1AP1</i>	<i>ERBB2</i>	<i>PASK</i>	<i>NFKBIA</i>
	<i>RAD50</i>	<i>TET2</i>	<i>ZNF217</i>	<i>FGF4</i>	<i>PC</i>	<i>NOD1</i>
	<i>RAD51C</i>		<i>ZNF703</i>	<i>GNAS</i>	<i>PIK3CA</i>	<i>PDCD1LG2</i>
				<i>HGF</i>	<i>PTCH1</i>	<i>TP63</i>
				<i>HSP90</i>	<i>RICTOR</i>	<i>TRAF3</i>
				<i>ICK</i>	<i>ROS1</i>	

				<i>IDH1</i> <i>IGF1R</i>	<i>TSC1</i> <i>TSC2</i> <i>TYK2</i>	
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eFigure 1: Distribution of Genomic *WWTR1-CAMTA1* Fusion Expression

**A,B)** Fusion expression data from 45 subjects with *WWTR1-CAMTA1* fusion data available. *WWTR1-CAMTA1* fusion expression demonstrated a right-skewed, log-normal distribution (**A**) corroborated by the plot between empirical and theoretical cumulative distribution function (CDF; **B**). **C**) In a clinical cohort of 10 subjects with *WWTR1-CAMTA1* fusion data available, subjects with stage III/IV disease demonstrated a non-significant trend towards increased expression of the *WWTR1-CAMTA1* fusion ( $677 \pm 706$  vs  $231 \pm 213$  copies;  $p=0.2$ ).

eTable 3: Gene Variants in EHE

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Gene	Description	Variant Call
<i>ABL1</i>	A1102V	Unknown Pathogenicity
<i>ADGRA2</i>	P1115_S1116insTGEGPP	Unknown Pathogenicity
<i>ALK - ALK</i>	deletion	Unknown Pathogenicity
<i>APC</i>	Q1045*	Known Pathogenicity
<i>APC</i>	I1307K	Known Pathogenicity
<i>APC</i>	3920T>A	Known Pathogenicity
<i>APC</i>	Q1549K	Unknown Pathogenicity
<i>AR</i>	G457_G460del	Unknown Pathogenicity
<i>ASXL1</i>	S214N	Unknown Pathogenicity

<i>ASXL1</i>	M1492V	Unknown Pathogenicity
<i>ATM</i>	Amplification	Known Pathogenicity
<i>ATRX</i>	S1913*	Known Pathogenicity
<i>ATRX</i>	E225*	Known Pathogenicity
<i>ATRX</i>	H475D	Unknown Pathogenicity
<i>AXIN1</i>	R723*	Unknown Pathogenicity
<i>BAP1</i>	P147L	Unknown Pathogenicity
<i>BARD1</i>	F387L	Unknown Pathogenicity
<i>BCOR</i>	L722F	Unknown Pathogenicity
<i>BCOR</i>	T1696M	Unknown Pathogenicity
<i>BCORL1</i>	S1543L	Unknown Pathogenicity

<i>BRCA1</i>	H839fs*7	Known Pathogenicity
<i>BRCA2</i>	S2887T	Unknown Pathogenicity
<i>CAMTA1 - WWTR1</i>	fusion	Known Pathogenicity
<i>CASP8</i>	K384Q	Unknown Pathogenicity
<i>CASP8</i>	M1?	Unknown Pathogenicity
<i>CCND3</i>	R93*	Unknown Pathogenicity
<i>CCT6B</i>	splice site 615-2A>G	Known Pathogenicity
<i>CD36</i>	M156I	Unknown Pathogenicity
<i>CD36</i>	D244N	Unknown Pathogenicity
<i>CDKN2A</i>	R80*	Known Pathogenicity
<i>CDKN2A</i>	P81L	Known Pathogenicity

<i>CDKN2A</i>	deletion	Known Pathogenicity
<i>CDKN2A</i>	Amplification	Known Pathogenicity
<i>CDKN2A</i>	G101R	Unknown Pathogenicity
<i>CDKN2B</i>	deletion	Known Pathogenicity
<i>CHEK2</i>	T367fs*15	Known Pathogenicity
<i>CIITA</i>	V418A	Unknown Pathogenicity
<i>CIITA</i>	A1032V	Unknown Pathogenicity
<i>CPS1</i>	A347S	Known Pathogenicity
<i>CRBN</i>	I154R	Unknown Pathogenicity
<i>CSF1R</i>	V117A	Unknown Pathogenicity
<i>DDX3X</i>	A502T	Known Pathogenicity

<i>DDX3X</i>	I166F	Unknown Pathogenicity
<i>DKC1</i>	K505_A506insK	Unknown Pathogenicity
<i>DTX1</i>	Q291K	Unknown Pathogenicity
<i>ECT2L</i>	R852Q	Known Pathogenicity
<i>EED</i>	M15V	Unknown Pathogenicity
<i>EPHA3</i>	C259*	Unknown Pathogenicity
<i>EPHB1</i>	D602E	Unknown Pathogenicity
<i>ERBB2</i>	R896H	Known Pathogenicity
<i>FANCA</i>	M160I	Known Pathogenicity
<i>FANCA</i>	splice site 3828+1G>C	Known Pathogenicity
<i>FANCL</i>	C132R	Unknown Pathogenicity



<i>FAS</i>	E167K	Unknown Pathogenicity
<i>FAT3</i>	V2757I	Unknown Pathogenicity
<i>FAT3</i>	R258H	Unknown Pathogenicity
<i>FAT3</i>	Y221C	Unknown Pathogenicity
<i>FBXO31</i>	P524L	Unknown Pathogenicity
<i>FBXW7</i>	Amplification	Known Pathogenicity
<i>FGF4</i>	Y166C	Unknown Pathogenicity
<i>GATA3</i>	359 C>T	Unknown Pathogenicity
<i>GNAS</i>	Q332E	Unknown Pathogenicity
<i>GNAS</i>	T415_G423del	Unknown Pathogenicity
<i>HGF</i>	I306N	Unknown Pathogenicity

<i>HIST1H1E</i>	K177_A184del	Unknown Pathogenicity
<i>HSP90AA1</i>	E365_E366insEK	Unknown Pathogenicity
<i>HSP90AA1</i>	G7W	Unknown Pathogenicity
<i>ICK</i>	Q240H	Unknown Pathogenicity
<i>IDH1</i>	R119Q	Known Pathogenicity
<i>IGF1R</i>	D675N	Unknown Pathogenicity
<i>IKZF3</i>	R458C	Unknown Pathogenicity
<i>INPP5D</i>	F846S	Unknown Pathogenicity
<i>JARID2</i>	P139T	Unknown Pathogenicity
<i>KDM4C</i>	A305S	Unknown Pathogenicity
<i>KDM5C</i>	P1429L	Known Pathogenicity

<i>KEAP1</i>	F478fs*2	Known Pathogenicity
<i>KMT2A</i>	P1767fs*53	Unknown Pathogenicity
<i>KMT2C</i>	D2201H	Known Pathogenicity
<i>KMT2C</i>	A374V	Unknown Pathogenicity
<i>KMT2C</i>	P840H	Unknown Pathogenicity
<i>KMT2D</i>	R4238H	Unknown Pathogenicity
<i>LRP1B</i>	R4363G	Unknown Pathogenicity
<i>LRRK2</i>	V2495I	Known Pathogenicity
<i>LRRK2</i>	M2155L	Unknown Pathogenicity
<i>LRRK2</i>	C2154F	Unknown Pathogenicity
<i>MAP2K2</i>	I14S	Unknown Pathogenicity

<i>MAP3K1</i>	V569I	Known Pathogenicity
<i>MAP3K13</i>	D601A	Unknown Pathogenicity
<i>MED12</i>	Q2076_Y2077insQ	Unknown Pathogenicity
<i>MEF2B</i>	L251F	Unknown Pathogenicity
<i>MKI67</i>	E1487V	Unknown Pathogenicity
<i>MKI67</i>	I2958T	Unknown Pathogenicity
<i>MKI67</i>	D751E	Unknown Pathogenicity
<i>MLH1</i>	E605*	Known Pathogenicity
<i>MLH1</i>	R9G	Unknown Pathogenicity
<i>MSH2</i>	E358D	Unknown Pathogenicity
<i>MSH3</i>	K255*	Known Pathogenicity

<i>MSH3</i>	A57_A62del	Unknown Pathogenicity
<i>MUTYH</i>	G382D	Known Pathogenicity
<i>MYO18A</i>	A1314T	Unknown Pathogenicity
<i>NCOR1</i>	V2293M	Unknown Pathogenicity
<i>NCOR2</i>	E859A	Unknown Pathogenicity
<i>NCOR2</i>	A775T	Unknown Pathogenicity
<i>NFKBIA</i>	amplification	Known Pathogenicity
<i>NOD1</i>	F515fs*228	Known Pathogenicity
<i>NOD1</i>	A829G	Unknown Pathogenicity
<i>NOTCH1</i>	3835C>T	Known Pathogenicity
<i>NOTCH1</i>	R1132C	Unknown Pathogenicity

<i>NOTCH2</i>	G2291W	Unknown Pathogenicity
<i>NOTCH3</i>	R75W	Unknown Pathogenicity
<i>NTRK1</i>	splice	Unknown Pathogenicity
<i>NUP98</i>	E948D	Unknown Pathogenicity
<i>PASK</i>	G327S	Unknown Pathogenicity
<i>PC</i>	M1145I	Unknown Pathogenicity
<i>PCBP1</i>	T91I	Unknown Pathogenicity
<i>PDCD1LG2</i>	T217S	Unknown Pathogenicity
<i>PIK3CA</i>	N515S	Known Pathogenicity
<i>PIK3CA</i>	R949Q	Unknown Pathogenicity
<i>PMS2</i>	S46N	Known Pathogenicity

<i>POT1</i>	D617fs*9	Known Pathogenicity
<i>PTCH1</i>	G51del	Unknown Pathogenicity
<i>RAD50</i>	E1232A	Unknown Pathogenicity
<i>RAD51C</i>	R24Q	Unknown Pathogenicity
<i>RARA</i>	T179M	Unknown Pathogenicity
<i>RB1</i>	R320*	Known Pathogenicity
<i>RB1</i>	deletion	Known Pathogenicity
<i>RB1</i>	G203W	Unknown Pathogenicity
<i>RELN</i>	T1916A	Unknown Pathogenicity
<i>RELN</i>	L1732F	Unknown Pathogenicity
<i>RELN</i>	G937A	Unknown Pathogenicity

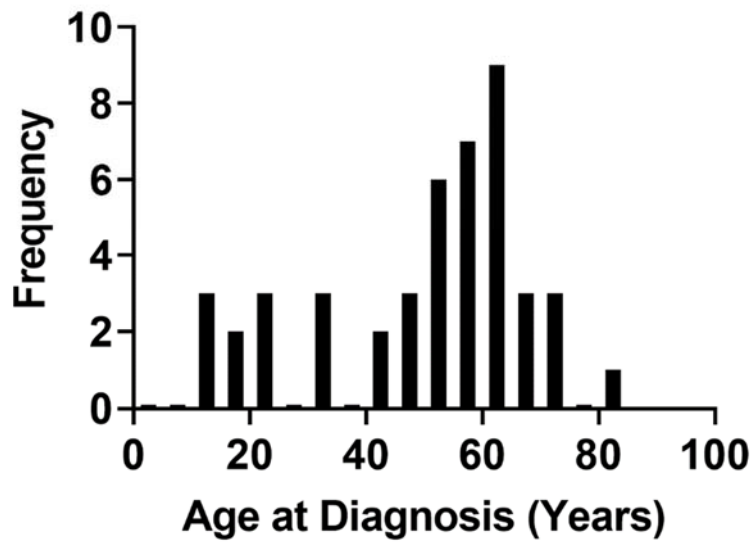
<i>RELN</i>	K3100del	Unknown Pathogenicity
<i>RICTOR</i>	P1397H	Unknown Pathogenicity
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<i>ROS1</i>	R2269*	Unknown Pathogenicity
<i>ROS1</i>	E2244Q	Unknown Pathogenicity
<i>RPS19</i>	R102Q	Unknown Pathogenicity
<i>RUNX1</i>	A187T	Unknown Pathogenicity
<i>SETBP1</i>	R11Q	Unknown Pathogenicity
<i>SGK1</i>	R12Q	Unknown Pathogenicity
<i>SMARCA4</i>	splice site 4911+1G>A	Known Pathogenicity
<i>SMARCA4</i>	K892R	Unknown Pathogenicity



<i>SMC1A</i>	S1188C	Unknown Pathogenicity
<i>TAF1</i>	K424R	Unknown Pathogenicity
<i>TCF3</i>	M415V	Unknown Pathogenicity
<i>TERT</i>	Amplification	Known Pathogenicity
<i>TET2</i>	100C>T	Known Pathogenicity
<i>TOP1</i>	I133V	Unknown Pathogenicity
<i>TP63</i>	N467S	Unknown Pathogenicity
<i>TRAF3</i>	V47M	Unknown Pathogenicity
<i>TSC1</i>	3185G>A	Known Pathogenicity
<i>TSC2</i>	R1159Q	Unknown Pathogenicity
<i>TSC2</i>	K351R	Unknown Pathogenicity

<i>TYK2</i>	R281S	Unknown Pathogenicity
<i>TYK2</i>	M8L	Unknown Pathogenicity
<i>YY1AP1</i>	C42_R45>C	Unknown Pathogenicity
<i>ZNF217</i>	N55fs*31	Unknown Pathogenicity
<i>ZNF703</i>	amplification	Known Pathogenicity
<i>ZNF703</i>	H402_D403>PTHLGGSSCSTCSAHD	Unknown Pathogenicity

eFigure 2: Age At Diagnosis



In 45 EHE subjects with data available, mean age at diagnosis was 50.2 years of age with an apparent bimodal distribution around the 45 year mark.

### eMethods: Models

Utilizing the `mclust` package in R v.3.4.3, a Gaussian finite mixture model was fit to the data. A second forced a one-compartment model was then fit to the same data. These two models were then tested by calculating the difference in model fit by a log-likelihood ratio test (Log-likelihood one-component model -207.2 vs two-component model -197.6, difference 9.6, 95%CI 0.0-23.8,  $p=0.02$ ). The 95% confidence interval (95%CI) was generated by bootstrapping the model comparison for 1,000 iterations. Statistical significance here suggests the distribution of the tested data is significantly different than a one-compartment model distribution.

eTable 4: Clinicogenomic Features of *CDKN2A/B* Variant Subjects

eTable 4: Clinicogenomic Features of <i>CDKN2A/B</i> Variant Subjects							
Case	#1	#2	#3	#4	#5	#6	#7
Age at Diagnosis (year)	51	56	11	50	53	70	65
Gender	Female	Male	Female	Female	Male	Male	Female
TMB	2.4	0.8	0.8	0.8	0	0.8	2.4
Microsatellite Instability (MSI)	Stable	Stable	Stable	N/A	N/A	Stable	Stable
<i>WWTR1-CAMTA1</i> Expression	566	63	69	97	194	550	1376
<i>CDKN2A</i>	R80*	P81L	G101R	Deletion	Deletion	Deletion	Deletion
<i>CDKN2B</i>	-	-	-	Deletion	Deletion	Deletion	Deletion
<i>APC</i>							Q1549K
<i>ATRX</i>			H475D				

<i>AXIN1</i>						R723*	
<i>BARD1</i>	F387L						
<i>BCOR</i>	L722F						
<i>BRCA1</i>	H839fs*7						
<i>BRCA2</i>	S2887T						
<i>DDX3X</i>							I166F
<i>FANCA</i>							M160I
<i>FAS</i>	E167K						
<i>FAT3</i>							Y221C
<i>HIST1H1E</i>							K177_A1 84del
<i>IDH1</i>							R119Q
<i>MKI67</i>				E1487V			
<i>MSH3</i>	K255*; A57_A62 del						
<i>NCOR2</i>				E859A			
<i>NFKBIA</i>							Amplification
<i>SMARCA4</i>		K892 R					
<i>TP63</i>						N467S	
<i>TSC2</i>				R1159Q			

YY1AP1				C42_R45 >C			
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eTable 5: Targetable Genomic Variants

etable 5: Targetable Genomic Variants			
Gene	Subjects With Alteration (%)		OncoKB Level of Evidence
	Know Variant	VUS	
<i>ROS1</i>	1 (2%)	2 (4.1%)	Level 1
<i>TSC1</i>	1 (2%)	0 (0%)	Level 1
<i>TSC2</i>	0 (0%)	2 (4.1%)	Level 1
<i>NTRK1</i>	0 (0%)	1 (2%)	Level 1
<i>BRCA1</i>	1 (2%)	0 (0%)	Level 1
<i>BRCA2</i>	0 (0%)	1 (2%)	Level 1
<i>ERBB2</i>	1 (2%)	0 (0%)	Level 1
<i>IDH1</i>	1 (2%)	0 (0%)	Level 1
<i>PTCH1</i>	0 (0%)	1 (2%)	Level 3
<i>CDKN2A</i>	6 (12.2%)	1 (2%)	Level 4
Total	9 (18.4%)	6 (12.2%)	