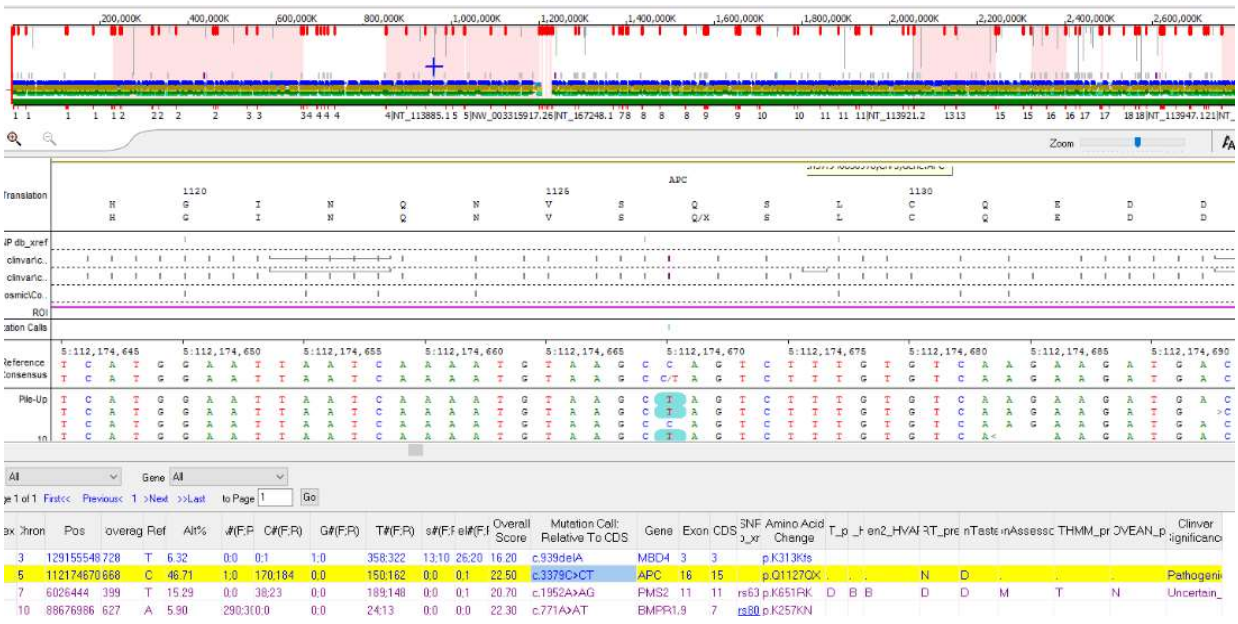
Supplementary Note 1

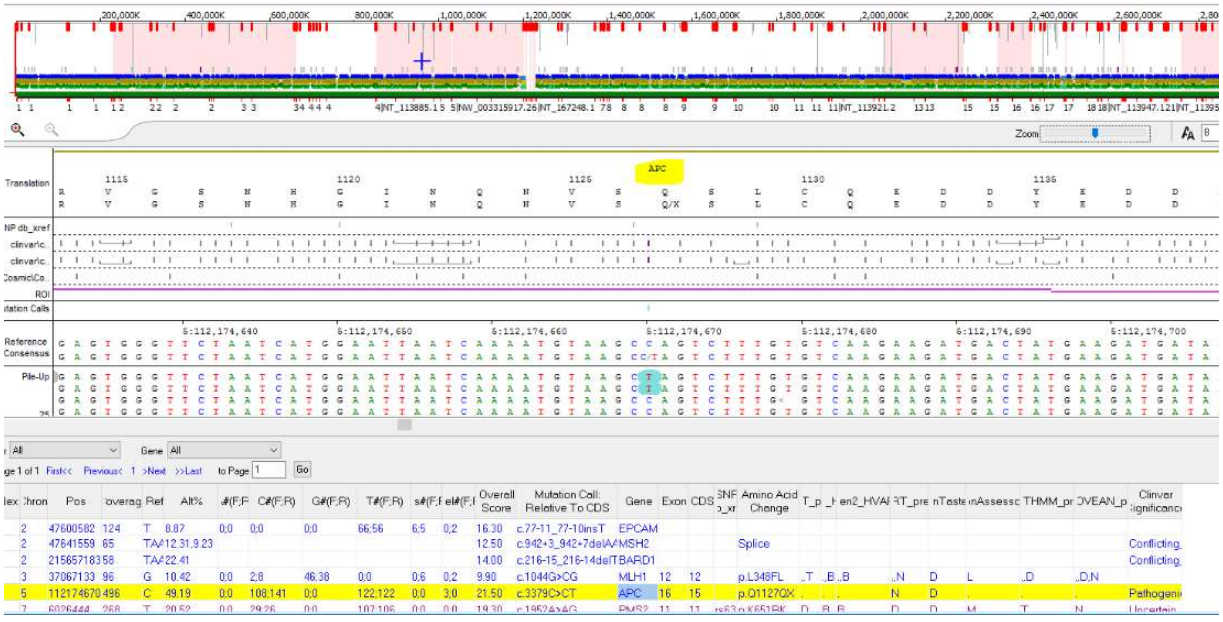
The patient's WDFLAC was initially sequenced using the clinical Solid Tumour Panel (i.e. AmpliSeq Focus Panel), which detects clinically relevant DNA and RNA alterations in 52 genes. 35 genes (*AKT1, ALK, BRAF, CDK4, CTNNB1, DDR2, EGFR, ERBB2, ERBB3, ERBB4, ESR1, FGFR2, FGFR3, GNA11, GNAQ, HRAS, IDH1, IDH2, JAK1, JAK2, KIT, KRAS, MAP2K1, MAP2K2, MET, MTOR, NRAS, PDGFRA, PIK3CA, RAF1, RET, ROS1* and *SMO*) are analyzed for the presence of single-nucleotide variants (SNVs) and small insertions/deletions, 19 genes (*ALK, AR, BRAF, CCND1, CDK4, CDK6, EGFR, ERBB2, FGFR1, FGFR2, FGFR3, FGFR4, KIT, KRAS, MET, MYC, MYCN, PDGFRA* and *PIK3CA*) are analyzed for copy number variants (CNVs) and 23 genes (*ABL1, ALK, AKT3, AXL, BRAF, EGFR, ERBB2, ERG, ETV1, ETV4, ETV5, FGFR1, FGFR2, FGFR3, MET, NTRK1, NTRK2, NTRK3, PDGFRA, PPARG, RAF1, RET,* and *ROS1*) are analyzed for recurrent gene fusions and other aberrant splicing events.

A)

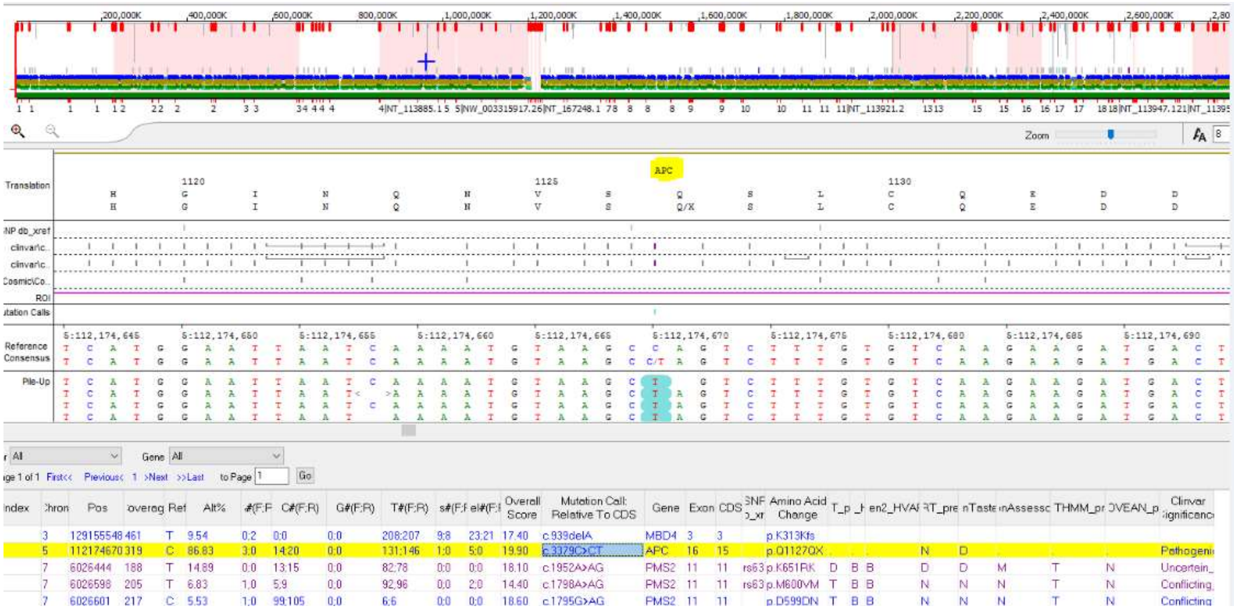


ex	Chron	Pos	overag	Ref	Alt%	#(F,R	C#(F,R)	G#(F,R)	T#(F,R)	s#(F,R	el#(F,R	Overall Score	Mutation Call: Relative To CDS	Gene	Exon	CDS	SNP	Amino Acid Change	T_p	_H	en2_HVAR	T_pre	nTaste	nAssess	THMM_pr	OVEAN_p	Clinvar Significance
	3	129155548	728	T	6.32	0;0	0;1	1;0	358;322	13;10	26;20	16.20	c.939delA	MBD4	3	3		p.K313Kfs									
	5	112174670	668	C	46.71	1;0	170;184	0;0	150;162	0;0	0;1	22.50	c.3379C>CT	APC	16	15		p.Q1127QX	.	.	.		N	D	.	.	Pathogenic
	7	6026444	399	T	15.29	0;0	38;23	0;0	189;148	0;0	0;1	20.70	c.1952A>AG	PMS2	11	11	rs63	p.K651RK	D	B	B		D	D	M	T	N	Uncertain_
	10	88676986	627	A	5.90	290;3	0;0	0;0	24;13	0;0	0;0	22.30	c.771A>AT	BMPR1B	7		rs80	p.K257KN									

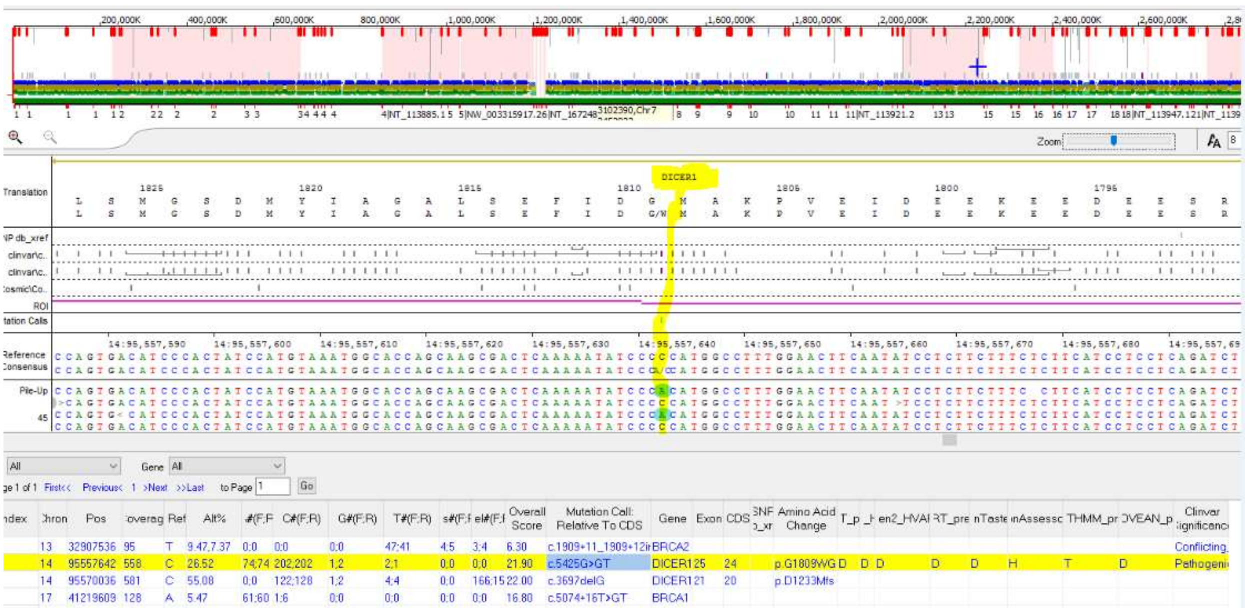
B)



ex	Chron	Pos	overag	Ref	Alt%	#(F,R	C#(F,R)	G#(F,R)	T#(F,R)	s#(F,R	el#(F,R	Overall Score	Mutation Call: Relative To CDS	Gene	Exon	CDS	SNP	Amino Acid Change	T_p	_H	en2_HVAR	T_pre	nTaste	nAssess	THMM_pr	OVEAN_p	Clinvar Significance
	2	47600582	124	T	8.87	0;0	0;0	0;0	66;56	6;5	0;2	16.30	c.77-11_77-10insT	EPCAM													
	2	47641559	65	TA	12.31.9.23							12.50	c.942+3_942+7delAAGMSH2					Splice									Conflicting_
	2	21565718	358	TA	22.41							14.00	c.216-15_216-14delTTBARD1														Conflicting_
	3	37067133	96	G	10.42	0;0	2;8	46;38	0;0	0;6	0;2	9.90	c.1044G>CG	MLH1	12	12		p.L348FL	_T	_B	_B	_N	D	L	_D	_D;N	
	5	112174670	496	C	49.19	0;0	108;141	0;0	122;122	0;0	3;0	21.50	c.3379C>CT	APC	16	15		p.Q1127QX	.	.	.		N	D	.	.	Pathogenic
	7	6026444	268	T	20.52	0;0	29;26	0;0	107;106	0;0	0;0	19.30	c.1952A>AG	PMS2	11	11	rs63	p.K651RK	D	B	B		D	D	M	T	N	Uncertain_


APC
Translation
Reference
Consensus
Pile-Up
Gene All
Index Chrom Pos Coverage Ref Alt% Overall Score Mutation Call: Relative To CDS Gene Exon CDS Amino Acid Change Clinvar Significance
3 129155548 461 T 9.54 17.40 c.939delA MBD4 3 3 p.K313Kfs
5 112174670 319 C 86.83 19.90 c.3379C>CT APC 16 15 p.Q1127QX Pathogenic
7 6026444 188 T 14.89 18.10 c.1952A>AG PMS2 11 11 p.K651RK Uncertain
7 6026598 205 T 6.83 14.40 c.1798A>AG PMS2 11 11 p.M600VM Conflicting
7 6026601 217 C 5.53 18.60 c.1795G>AG PMS2 11 11 p.D599DN Conflicting

C)

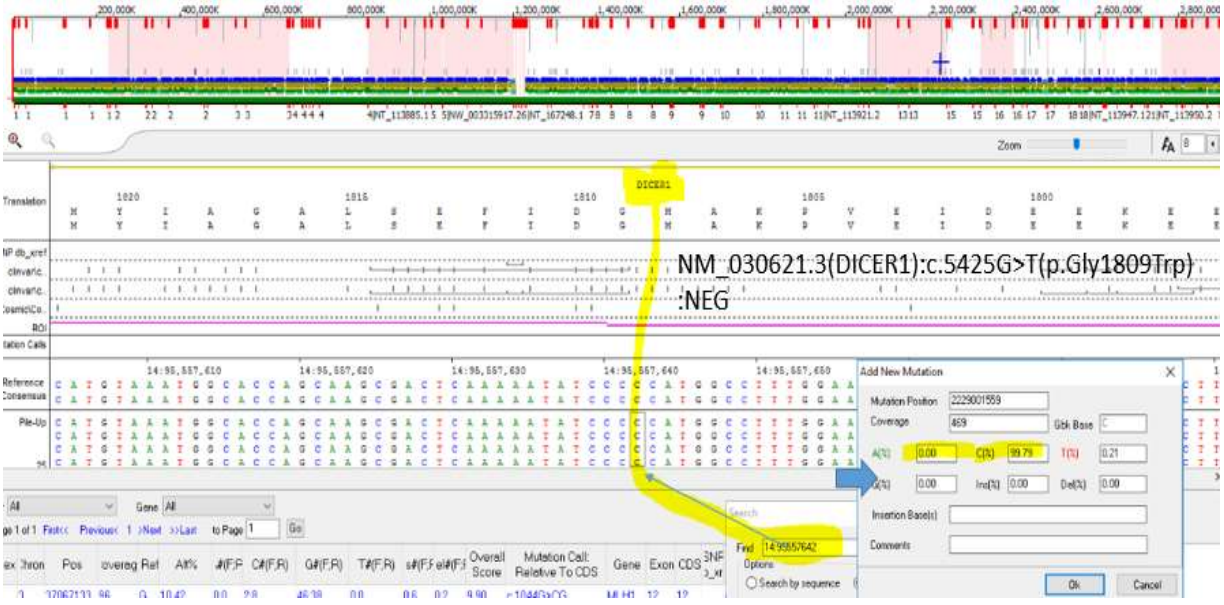

DICER1
Translation
Reference
Consensus
Pile-Up
Gene All
Index Chrom Pos Coverage Ref Alt% Overall Score Mutation Call: Relative To CDS Gene Exon CDS Amino Acid Change Clinvar Significance
13 32907536 95 T 6.30 BRCA2 Conflicting
14 95557642 558 C 26.52 21.90 c.5425G>GT DICER1 25 24 p.G1809WG Pathogenic
14 95570036 581 C 55.08 c.3697delG DICER1 21 20 p.D1233Mfs
17 41219609 128 A 5.47 16.80 c.5074+16T>GT BRCA1
19 50912061 181 G 47.51 18.00 c.1795G>AG POLD1 15 14 p.A599TA Conflicting

D)

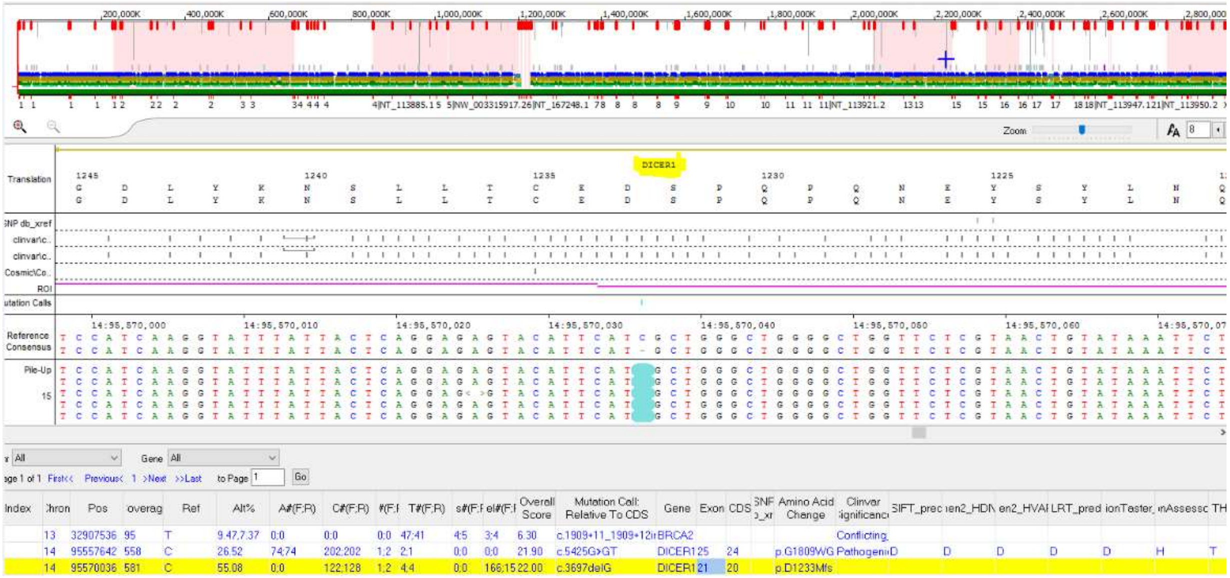
E)


NM_030621.3(DICER1):c.5425G>T(p.Gly1809Trp):NEG_
DICER1
Add New Mutation
Mutation Position
Coverage
Gbk Base
Mutation Call: Relative To CDS
Gene
Exon
CDS

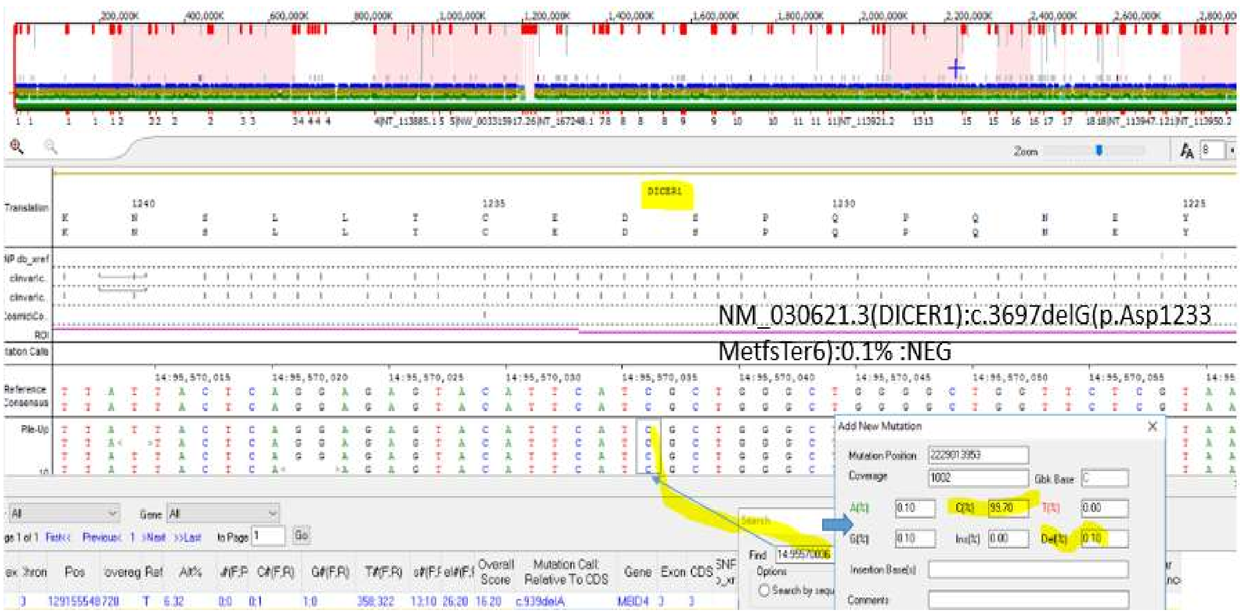
F)


NM_030621.3(DICER1):c.5425G>T(p.Gly1809Trp)
:NEG
DICER1
Add New Mutation
Mutation Position
Coverage
Gbk Base
Insertion Base(s)
Comments
Ok
Cancel
Mutation Call: Relative To CDS
Gene
Exon
CDS

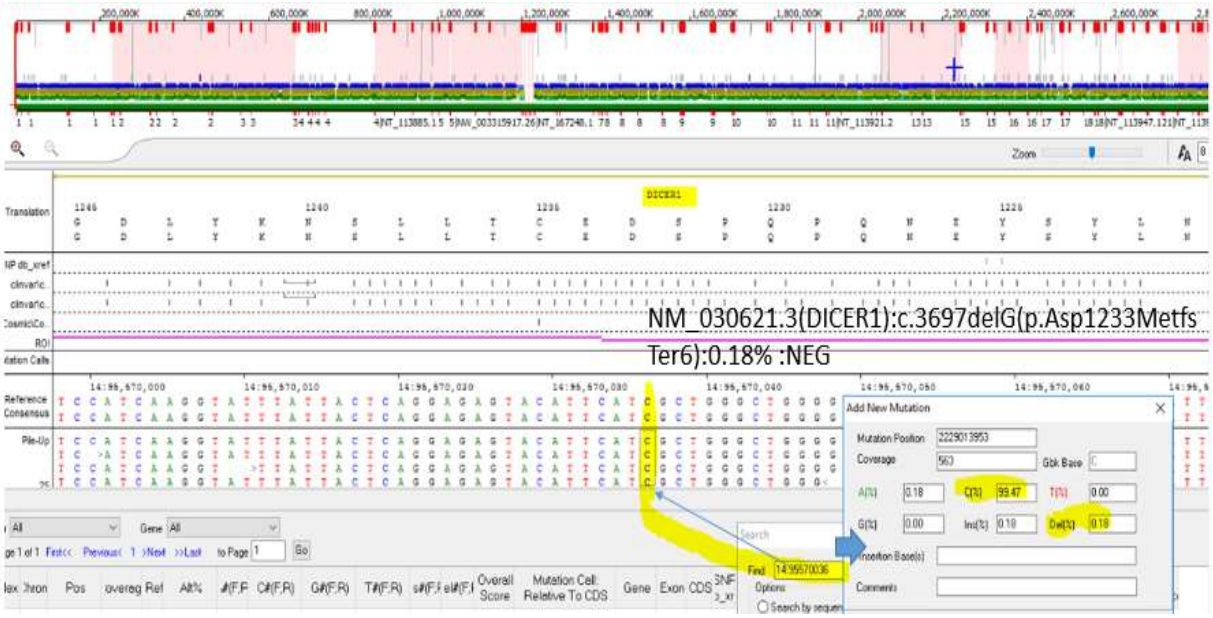
G)


DICER1
Translation
Reference
Consensus
Pile-Up

H)


DICER1
NM_030621.3(DICER1):c.3697delG(p.Asp1233
MetfsTer6):0.1% :NEG
Add New Mutation

I)



Supplementary Figure 1: Results of sequencing the patient's blood lymphocyte DNA, WDFLAC tumour DNA, and normal lung tissue DNA for pathogenic variants in *APC* and *DICER1*. Alterations are indicated in blue. A-B) The blood DNA and normal lung DNA are positive for the *APC* variant c.3379C>T (p.Q1127*) at a VAF of 46.7% and 49.2%, respectively, as expected for a heterozygous carrier. C) The same mutation is present at a VAF of 86.8% in the WDFLAC tumour. D) The tumour also has the *DICER1* hotspot variant c. 5425G>T (p.G1809W) at a VAF of 26.5%, which is not found in the blood (E) and normal lung (F). The truncating *DICER1* variant c.3697delG (p.D1233Mfs*6) is similarly only found in the tumour at a VAF of 55% (G), but not in the blood (H) nor the normal lung (I).